ELSEVIER

Coordination Chemistry Reviews 237 (2003) 205–212

COORDINATION CHEMISTRY REVIEWS

www.elsevier.com/locate/ccr

Supramolecular interactions of vanadate species: vanadium(V) complexes with *N*-salicylidenehydrazides as versatile models

Winfried Plass *

Anorganische Chemie, Universität Siegen, Adolf-Reichwein-Straße, D-57068 Siegen, Germany

Received 12 June 2002; accepted 23 August 2002

Contents

Abstract . . . 205
1. Introduction . . . 205
   1.1 Vanadium in biological systems . . . 205
   1.2 Hydrogen bonding in biological systems . . . 206
2. Vanadate and supramolecular interactions . . . 206
   2.1 Vanadium haloperoxidases and phosphatases . . . 206
   2.2 Molecular model systems for hydrogen bonding . . . 208
3. Vanadium complexes with *N*-salicylidenehydrazides as model systems . . . 208
   3.1 *N*-salicylidenehydrazides as versatile ligand system . . . 208
   3.2 *N*-salicylidenehydrazides with functionalized side chains and supramolecular interactions . . . 209
4. Conclusions . . . 212
Acknowledgements . . . 212
References . . . 212

Abstract

In vanadium haloperoxidases, vanadate as the prosthetic group is fixed in the active site cavity by solely one covalent bond to a histidine residue and embedded in an environment of hydrogen bonds. Structural similarities between the active sites of vanadium haloperoxidases and some acid phosphatases are evident. Along this line, an important question is concerned with the role of the protein environment via supramolecular interactions for both structure and function of the related enzymatic systems. In this context, the relevance of *cis*-dioxovanadium(V) complexes with the versatile tridentate *N*-salicylidenehydrazide ligand system as models is discussed.

Keywords: Hydrogen bonding; Phosphatase; Schiff base complex; Vanadium complexes; Vanadium haloperoxidase

1. Introduction

The interest in vanadium chemistry from a biological and pharmacological perspective has exploded over the past 20 years. This is mainly based on the discoveries of the insulin-like effect of vanadium compounds, and the presence of vanadium in certain haloperoxidases and nitrogenases [1,2]. A key point for the understanding of how vanadium actually works in biological systems is given by the chemical analogy between vanadate and phosphate. One of the still open questions in this context is whether vanadate generally acts as a stable transition state analog for phosphate blocking specific receptor sites or whether there are cases for which the vanadate substitution actually leads to new active sites that can feature completely different reactivity with consequences for the pharmacological application and the toxicity of vanadium.

1.1. Vanadium in biological systems

Of particular importance is the ability of vanadium to influence phosphate-metabolizing systems and the fact

* Fax: +49-271-740-2555
E-mail address: plass@chemie.uni-siegen.de (W. Plass).

0010-8545/02/$ - see front matter
PII: S0010-8545(02)00228-X

that vanadium is an inherent part of enzymatic active sites. For both types of vanadoenzymes known today, the vanadium-containing haloperoxidases and the vanadium nitrogenases from the nitrogen fixing bacteria *Azotobacter*, functional analogs are found in nature which are either more widely spread or more efficient, e.g. the heme-containing haloperoxidases and the conventional nitrogenases with molybdenum cofactor, respectively. This immediately leads to the question of how this enzyme systems did evolve and in particular whether the vanadium-containing enzymes known today are retained functional analogs, which simply could sustain evolutionary forces. New insight concerning these questions may be gained on the basis of newly found similarities for vanadate and phosphate in biological systems [3].

The wide spread physiological effects of vanadium are mainly attributed to the similarity between its anionic form, vanadate(V), and phosphate. But there are also important differences between these two anions. Due to different pK_a values, the ratios of mono and doubly protonated form of these anions differ at physiological pH values. This is relevant for possible mechanisms of transport systems for these two anions [4–6]. In addition, vanadium is easily reduced under physiological conditions to yield cationic species. The third difference is given by the pronounced ability of vanadium as a transition metal element to adopt higher coordination numbers and hence form stable coordination compounds. This higher coordinative flexibility of vanadium can deliberately be used for the structural characterization of phosphate metabolizing enzymes.

1.2. Hydrogen bonding in biological systems

Besides the well-established structural relevance of hydrogen bonding in biological systems, supramolecular interactions are also important in the regulation of metal ion reactivity as well as in the recognition and transport of various small molecules and ions [7–9]. For the modulation of reactivity at metal ions in biological systems, charge relay mechanisms play an important role. Such mechanisms involving hydrogen bonding have been suggested for systems like cytochrome *c* peroxidase, sulfite reductase, and CooA (CO oxidation activator) transcription factor from *Rhodospirillum rubrum* [10–13].

In the context of supramolecular interactions of vanadate in biological systems, two aspects are of particular importance. One is concerned with the potential activation of substrates metabolized in the vicinity of the vanadate. In light of the biological function of vanadate in vanadium haloperoxidases, an example is found in the effect of a hydrogen bonding network on the activation of coordinated peroxide. A well-known system that exhibits this basic phenomenon is found in the heterolytic cleavage of O–O bonds in heme based peroxidase enzymes [14]. The second aspect is related to recognition and transport of relevant ions. Based on the chemical analogy between phosphate and vanadate, the phosphate transport system is a case of interest for which the effect of hydrogen bonding on mechanism and structure is well-established [4–6]. Also for chloride, another interesting ion in biological systems, hydrogen bonding networks are important for its binding and transport through biological membranes, which has been shown for halorhodopsin, a light driven chloride pump [15]. This is of particular interest here, since chloride is also a substrate metabolized at the active site of vanadium haloperoxidases.

2. Vanadate and supramolecular interactions

2.1. Vanadium haloperoxidases and phosphatases

For several stable enzyme aggregates of phosphatases with vanadate as transition state analog crystal structures have been reported. An interesting example is the protein tyrosine phosphatase [16,17], which is involved in signal transduction mechanisms for controlling and regulating intracellular processes (e.g. the insulin receptor system). Here it is worth noting that vanadate complexes show insulin-like effects [18]. In these aggregates, the vanadium atom is coordinated in a trigonal bipyramidal fashion and linked to the protein with a single axial bound cysteine residue, whereas the oxygen atoms of the vanadate moiety are involved in a hydrogen bonding network. A similar structure is found for the active site of a bacterial acid phosphatase from *Escherichia blattae* with the complexed transition state analog molybdate (Fig. 1) [19]. In this case, the protein linkage of the oxometalate moiety is established through an axial bound histidine residue.

Striking similarities are observed for the structurally characterized vanadium haloperoxidases, e.g. the chloroperoxidase of the fungus *Curvularia inaequalis* (Fig. 2) [20–22]. As in the case of the acid phosphatase from *E. blattae* the oxometalate moiety, here a vanadate, is directly linked to the protein only through an axial bound amino acid residue, here a histidine, and is embedded in the protein via an extensive hydrogen bonding network. A proposed catalytic cycle for vanadium haloperoxidase activity based on chemical, biochemical and crystallographic data is depicted in Fig. 3. After all several interesting aspects still remain unsolved: (1) What is the electronic structure and the protonation of the active site vanadate moiety in the resting state and under turnover conditions? (2) How is the peroxo group and the chloride ion bound to the active site? (3) What is the influence of the protein environment of vanadium

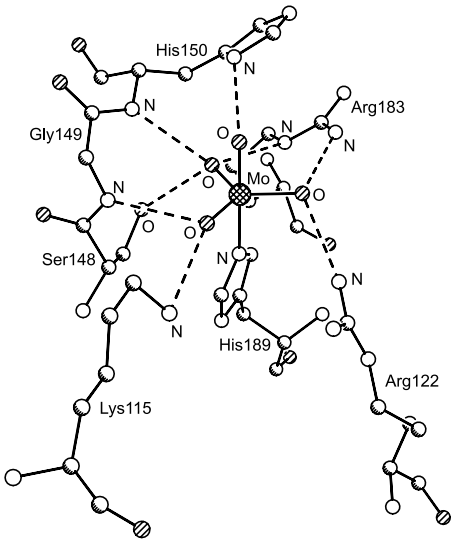


Fig. 1. Structure of the active site of the acid phosphatase from *E. blattae* with the complexed transition state analog molybdate [19]. Hydrogen bonds are shown as broken lines.

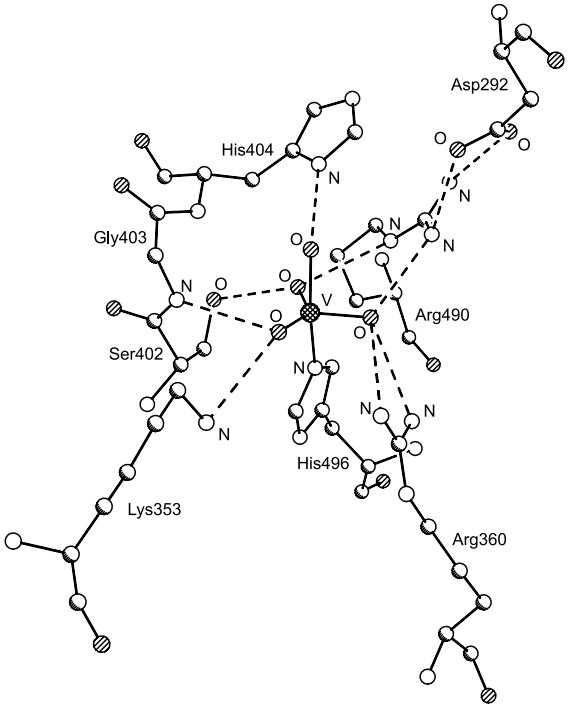


Fig. 2. Structure of the active site of vanadium haloperoxidase form the fungus *C. inaequalis* [20–22]. Hydrogen bonds are shown as broken lines.

haloperoxidases and phosphatases on the structure of the active site and the mechanism?

A key feature to the solution of these questions is the supramolecular environment established by the two enzymatic systems, which exhibit a high structural similarity for the active sites (see Figs. 1 and 2). In addition, it has been shown that the apo-protein of the chloroperoxidase isolated from the fungus *C. inaequalis* exhibits phosphatase activity [23]. Although it is obvious from the kinetic data that the active site of this vanadium chloroperoxidase is not optimized for phosphatase activity, it is nevertheless clear that within the same supramolecular environment it is possible to catalyse two very different reactions such as those of haloperoxidases and phosphatases. Moreover, the opposite conversion of catalytic function can also be achieved, i.e. the use of a phosphatase environment with incorporated vanadate that exhibits haloperoxidase activity [24]. A proposed mechanism for the phosphatase activity of the vanadium haloperoxidase protein environment is depicted in Fig. 4. According to a detailed study on the peroxidase and phosphatase activity of active-site mutants of the vanadium chloroperoxidase from the fungus *C. inaequalis*, an essential role is assigned to the residues His496, Arg490, Arg360, Lys353 and His404 for both catalytic activities [25]. At this point, a difference in the functionality of the supramolecular environment towards the two reactivities becomes obvious for the serin residue. In the native vanadium haloperoxidase structure, this serin residue is most likely utilized as a hydrogen bonding acceptor [26], whereas in the apo-protein this residue could be involved in phosphatase activity. Unfortunately, the potential role of the serin residue Ser402 was not

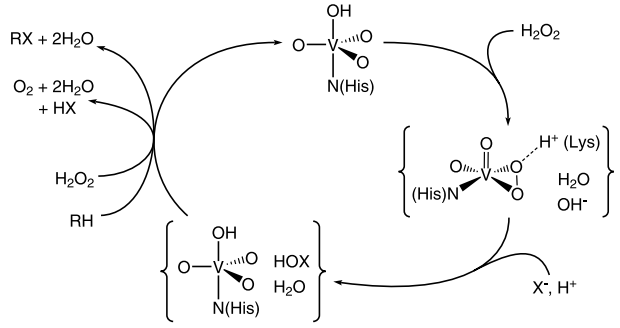


Fig. 3. Schematic representation of the current description of the catalytic cycle for the activity of vanadium haloperoxidases for the two possible reactions ($RH+H_2O_2+HX \rightarrow RX+2H_2O$ and $2H_2O_2+HX \rightarrow 2H_2O+O_2+HX$); the connectivity pattern at the vanadium atom does not represent a Lewis structure.

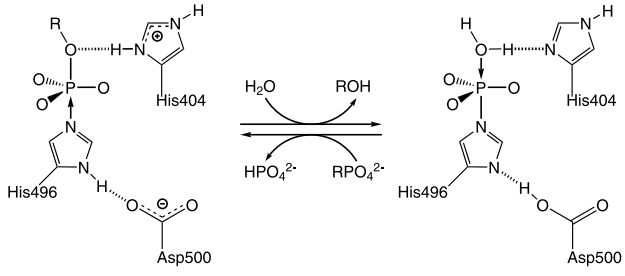


Fig. 4. Schematic representation of the suggested mechanism for the catalytic activity of membrane bound phosphatases (numbering scheme of the amino acids is related to the structure of the vanadium chloroperoxidase from the fungus *C. inaequalis* (see Fig. 2); the connectivity pattern at the phosphorus atom does not represent a Lewis structure.

addressed yet by the investigation of an appropriate active-site mutant of the vanadium chloroperoxidase from the fungus *C. inaequalis*.

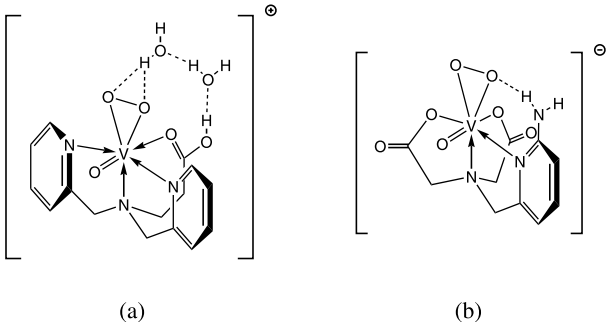
2.2. Molecular model systems for hydrogen bonding

Hydrogen bonding is a common feature for vanadium(IV) and vanadium(V) compounds in the solid state, if appropriate hydrogen bonding donors are present [27,28]. In general, these examples lead to the formation of hydrogen bonded molecular assemblies that range from simple dimers up to three dimensional networks. Nevertheless, in the context of modelling supramolecular interactions of vanadate species relevant for biological systems, the number of known examples is much more limited. Two interesting model compounds that feature some similarities with the hydrogen bonding scheme found for vanadium haloperoxidases are depicted in Fig. 5. Both vanadium(V) peroxo complexes are designed to model the corresponding intermediate of vanadium haloperoxidases. In one case, a water molecule is the hydrogen bonding donor interacting with the peroxo group (Fig. 5a) [29], whereas in the second case this hydrogen bonding interaction is of intramolecular nature (Fig. 5b) [30]. An important difference between the two examples is given by the observation that in the latter case the hydrogen bonding interaction even persists in solution.

3. Vanadium complexes with *N*-salicylidenehydrazides as model systems

3.1. *N*-Salicylidenehydrazides as versatile ligand systems

N-Salicylidenehydrazides are ligands derived from salicylaldehyde and carbonic acid hydrazides that can coordinate as tridentate chelate ligands in either their mono- or dianionic form. The ligand synthesis as well as



(a) (b)

Fig. 5. Peroxovanadium(V) complexes modeling the hydrogen bonding interactions for the peroxo form of chloroperoxidase from the fungus *C. inaequalis* [21]: (a) hydrogen bonding network including water molecules [29]; (b) intramolecular hydrogen bonding interaction of the peroxo group [30].

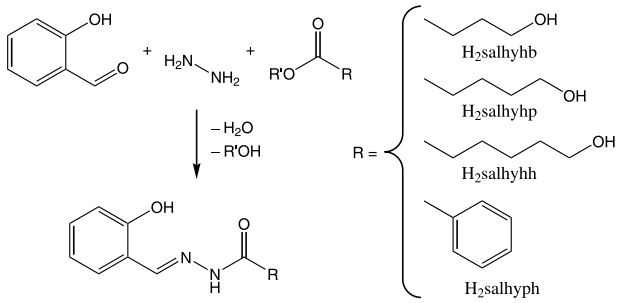


Fig. 6. Synthesis and substitution pattern of *N*-salicylidenehydrazide ligands.

the substitution pattern utilized thus far in our ongoing studies are depicted in Fig. 6. With these ligand systems, we have synthesized a series of model complexes which exhibit hydrogen bonding at the vanadate moiety that is related to the observed supramolecular environment of the native vanadium haloperoxidases (see Fig. 2) [31,32].

As a test case to show the versatility of the *N*-salicylidenehydrazide ligand system, we choose the phenyl substituted derivative H_2salhyph (see Fig. 6). The reaction with potassium metavanadate in methanol solution yields the potassium salt of the corresponding anionic *cis*-dioxovanadium(V) complex K[VO_2(salhyph)]. The molecular structure of K[VO_2(salhyph)] (Fig. 7) contains a *cis*-dioxovanadium(V) moiety with a square pyramidal coordination geometry. The potassium cation is coordinated by seven oxygen donors with three of these in a μ_2-bridging position with a neighboring potassium cation (O1, O2 and O5, see Fig. 7) leading to a one-dimensional coordination polymer.

K[VO_2(salhyph)] can be converted to the corresponding neutral complex [VO_2(Hsalhyph)] by protonation in aqueous solution (Fig. 8). [VO_2(Hsalhyph)] possesses a very poor solubility in organic solvents and is insoluble in water. On the other hand, the protonation in absence of water yields the formal anhydride [V_2O_3(salhyph)$_2$] as dark brown crystals. This anhydride has also been prepared using different synthetic approaches starting from vanadium(IV) precursors [33,34]. The molecular structure of [VO_2(Hsalhyph)] is depicted in Fig. 9.

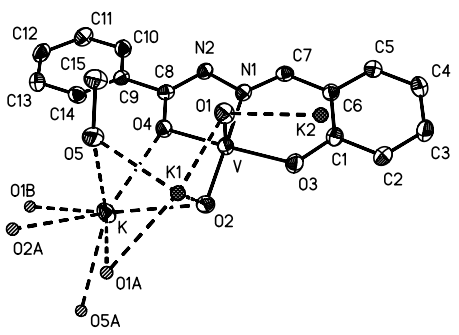


Fig. 7. Molecular structure of K[VO_2(salhyph)] in crystals containing an additional molecule of methanol (C15 and O5); potassium contacts are drawn as broken lines.

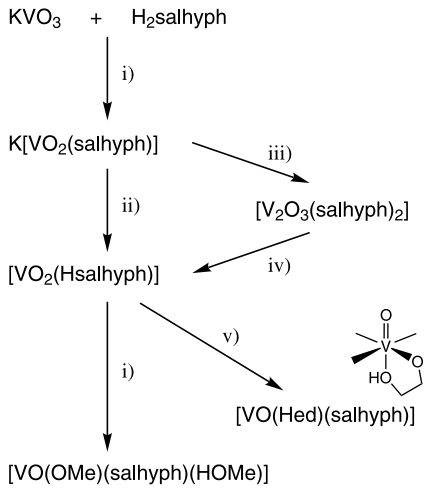


Fig. 8. Synthesis and reactions of K[VO_2(salhyph)]: (i) MeOH, ΔT; (ii) $HClO_4$, H_2O; (iii) (t-BuO)$_2$PO(OH), THF; (iv) H_2O; (v) H_2ed, dioxane, ΔT; ligand abbreviation: H_2ed, ethane-1,2-diol; H_2salhyph, see Fig. 6.

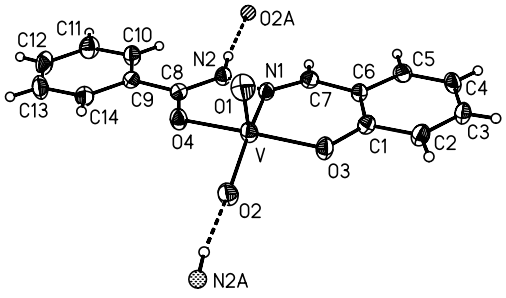


Fig. 9. Molecular structure of [VO_2(Hsalhyph)]; hydrogen bonds are drawn as broken lines.

Although the structure is also characterized by the presence of a square pyramidal *cis*-dioxovanadium(V) moiety, the protonation results in significant changes within the molecular structure of the *cis*-dioxovanadium fragment as compared with the structure of K[VO_2(salhyph)], i.e. the elongation of the V–O4 and N2–C8 bonds whereas the O4–C8 bond length is shortened. The site of protonation within the complex was also verified by the synthesis of the corresponding deuterium derivative that shows the expected frequency shift for the relevant band in the infrared spectrum. Moreover, the crystal structure of [VO_2(Hsalhyph)] reveals that the N2–H group is involved in hydrogen bonding leading to a chain-like association.

A series of different oxovanadium(V) complexes containing the salhyph^{2-} ligand can be synthesized starting from the neutral *cis*-dioxovanadium(V) complex [VO_2(Hsalhyph)]. The complexes [VO(OMe)(salhyph)(HOMe)] and [VO(Hed)(salhyph)] are obtained by reaction with the appropriate alcohol in nearly quantitative yields (see Fig. 8). The resultant dark red–brown complexes are soluble in polar organic solvents like DMSO or alcohols. Both can be reconverted to the neutral *cis*-dioxovanadium(V) complex [VO_2(Hsalhyph)] by reaction with an excess of water.

Starting from ammonium metavanadate as vanadium source, the ammonium salt of the anionic *cis*-dioxovanadium(V) complex NH_4[VO_2(salhyph)] can be isolated, if the synthesis is performed in aprotic solvents like DMF or DMSO [35]. In alcohols as reaction media, the corresponding oxovanadium(V) complexes are directly accessible. Treatment of the ammonium salt NH_4[VO_2(salhyph)] with an excess of water leads to the formation of the neutral complex [VO_2(Hsalhyph)] under release of ammonia. The reconversion can be achieved by deprotonation of the neutral complex in liquid ammonia. The molecular structure of NH_4[VO_2(salhyph)] depicted in Fig. 10 contains as in the case of the potassium salt a *cis*-dioxovanadium(V) moiety with a square pyramidal coordination geometry. An extended hydrogen bonding network is established by the ammonium cation that solely interacts with the four oxygen atoms coordinated at the central vanadium atom.

These results clearly show that *N*-salicylidenehydrazides are tridentate ligands for vanadium(V) complexes that can form both oxo and dioxo species and, moreover, also allow for the variation of the protonation state of the resulting complexes. Since this ligand system can easily be modified, it can be used to introduce additional functional groups in the vicinity of the central vanadium atom.

3.2. *N*-Salicylidenehydrazides with functionalized side chains and supramolecular interactions

The synthesis of vanadium(V) complexes with *N*-salicylidenehydrazides that contain hydroxyl substituted aliphatic side chains (see Fig. 6) in general follows the procedures outlined in the last chapter. However, there

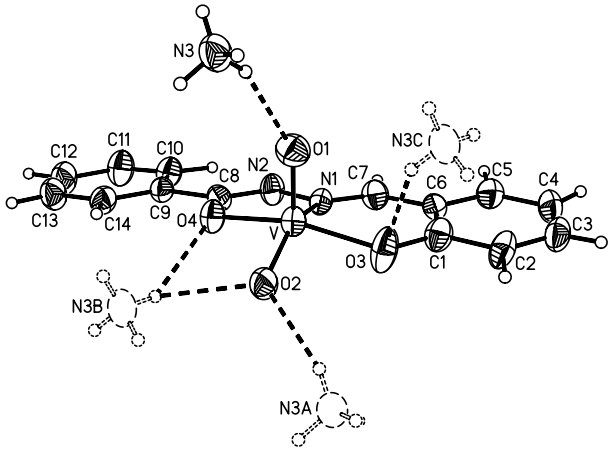


Fig. 10. Molecular structure of NH_4[VO_2(salhyph)]; hydrogen bonds are drawn as broken lines.

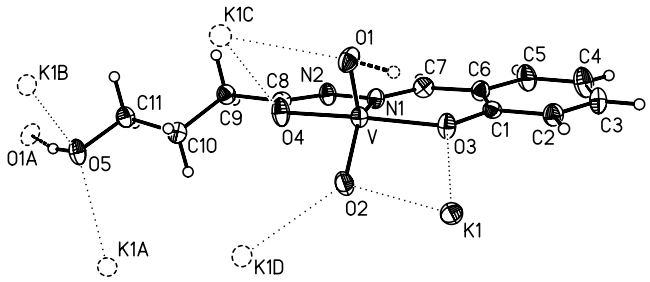


Fig. 11. Molecular structure of K[VO_2(salhyhb)]; hydrogen bonds are drawn as broken lines and potassium contacts as doted lines.

is also a significant difference, since the alcoholic side chain makes it impossible to strictly exclude protolytic conditions during the synthesis. Nevertheless, a series of vanadium(V) complexes can be isolated and characterized that show interesting structural features [36,37].

Reaction of H_2salhyhb (see Fig. 6) with potassium metavanadate yields the potassium salt of the anionic *cis*-dioxovanadium(V) complex K[VO_2(salhyhb)]. The molecular structure of K[VO_2(salhyhb)] depicted in Fig. 11 contains a *cis*-dioxovanadium(V) moiety with a square pyramidal coordination geometry. As in the case of K[VO_2(salhyph)] (cf. Fig. 7) the coordination sphere of the potassium ion includes an alcoholic oxygen donor atom which now belongs to a neighboring molecule. Moreover, the hydroxyl substituted side chain allows for a hydrogen bonding interaction with one of the oxo groups of the *cis*-dioxovanadium(V) moiety of an additional neighboring molecule. The structure of the neutral vanadium(V) complex [VO_2(Hsalhyhb)] given in Fig. 12 also shows similarities with the corresponding phenyl substituted analog [VO_2(Hsalhyph)] (cf. Fig. 9). This is particularly obvious as the hydrogen bonding interactions are concerned, since in both cases the same functional groups of the vanadium coordination environment are constituting parts, i.e. the oxo group O2 and the protonated hydrazide group N2–H. However, the additional hydroxy group present in [VO_2(Hsalhyhb)] also participates in the hydrogen bonding network, as it bridges the aforementioned functional groups of two neighboring molecules.

At first glance, the molecular structure of the ammonium salt NH_4[VO_2(salhyhb)]·H_2O depicted in Fig. 13

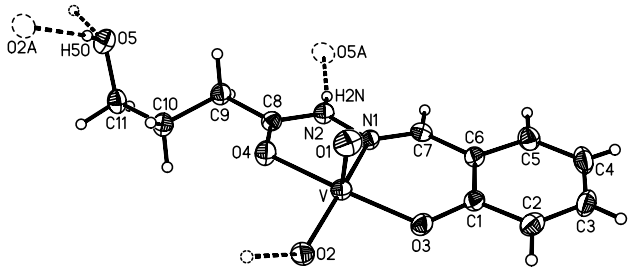


Fig. 12. Molecular structure of [VO_2(Hsalhyhb)]; hydrogen bonds are drawn as broken lines.

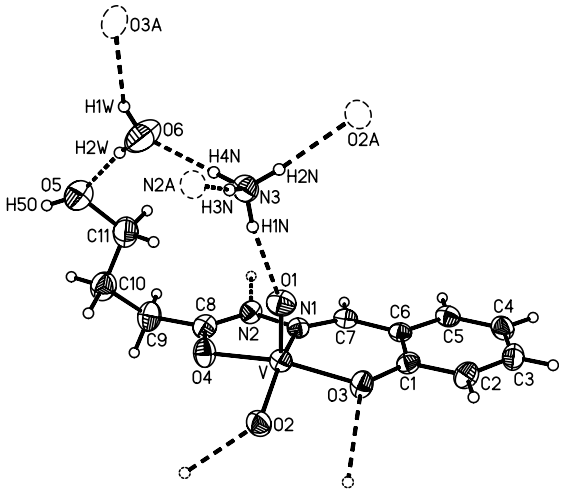


Fig. 13. Molecular structure of NH_4[VO_2(salhyhb)]·H_2O; hydrogen bonds are drawn as broken lines.

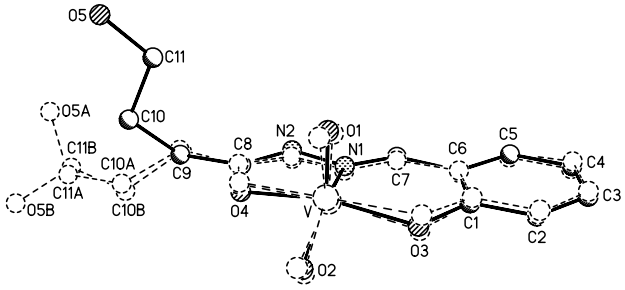


Fig. 14. Overlay of the covalent backbone of the molecular structures of NH_4[VO_2(salhyhb)] (thick lines), [VO_2(Hsalhyhb)] (atom numbering extension A, broken lines) and K[VO_2(salhyhb)] (atom numbering extension B, broken lines).

shows high similarity with those observed for the corresponding potassium salt K[VO_2(salhyhb)] and the neural complex [VO_2(Hsalhyhb)]. The overlay of the covalent parts of the three structures shown in Fig. 14 confirms this. However, from Fig. 14 it is also obvious, that there are significant differences regarding the orientation of the alkyl side chain of the ligand system. This clearly indicates the importance of the influence of hydrogen bonding interactions on the actual molecular structure. In this respect, it is remarkable to note that an additional water molecule is involved in the buildup of the hydrogen bonding network found in the case of NH_4[VO_2(salhyhb)]·H_2O. Moreover, as observed for the ammonium salt of the phenyl derivative NH_4[VO_2(salhyph)] (cf. Fig. 10) both oxo groups of the *cis*-dioxovanadium(V) moiety are participating in the hydrogen bonding network. Nevertheless, there is also an important difference between the phenyl and the hydroxy propyl derivative, in that the network observed for NH_4[VO_2(salhyhb)]·H_2O additionally contains a hydrogen bonding interaction to the hydrazide nitrogen atom N2 (cf. Figs. 10 and 13).

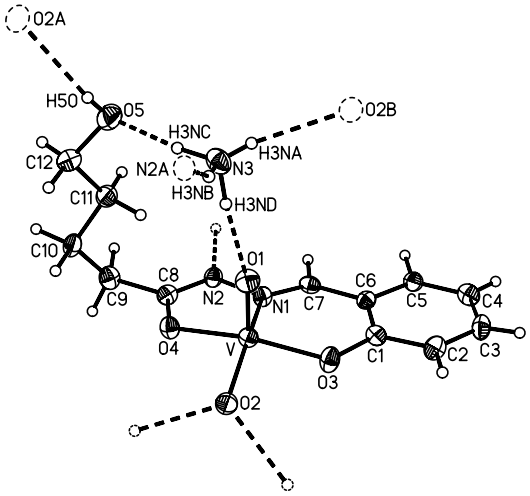


Fig. 15. Molecular structure of $NH_4[VO_2(salhyhp)]$; hydrogen bonds are drawn as broken lines.

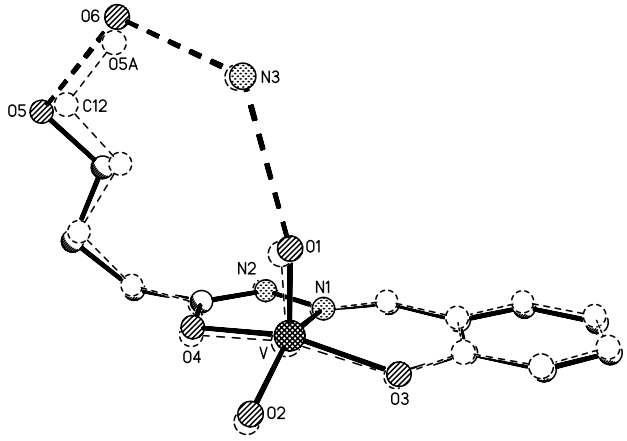


Fig. 16. Overlay of the molecular structures of $NH_4[VO_2(salhyhb)]\cdot H_2O$ (thick lines with the hydrogen bonds as broken lines) and $NH_4[VO_2(salhyhp)]$ (thin broken lines).

Also for the ligand system H_2salhyhp (see Fig. 6) with the side chain extended by one methylene group the ammonium salt of the corresponding anionic *cis*-dioxovanadium(V) complex $NH_4[VO_2(salhyhp)]$ can be isolated. The molecular structure of $NH_4[VO_2(salhyhp)]$ is depicted in Fig. 15. Although the ligand contains an extended side chain, the same basic pattern for the hydrogen bonding network is observed as in the case of the hydroxy propyl derivative (cf. Fig. 13). This can be easily seen from Fig. 16 that shows the direct comparison of both structures. For the structure of $NH_4[VO_2(salhyhp)]$, this simply means that the hydrogen bonding interaction O6–H···O5 found in $NH_4[VO_2(salhyhb)]$ is replaced by the covalent linkage C12–O5.

Although the molecular arrangement found for the $NH_4[VO_2(salhyhp)]$ complex seems to be perfectly suitable for the formation of the hydrogen bonding network, even the further extension of the side chain length to a hydroxy pentyl group leads to a molecular

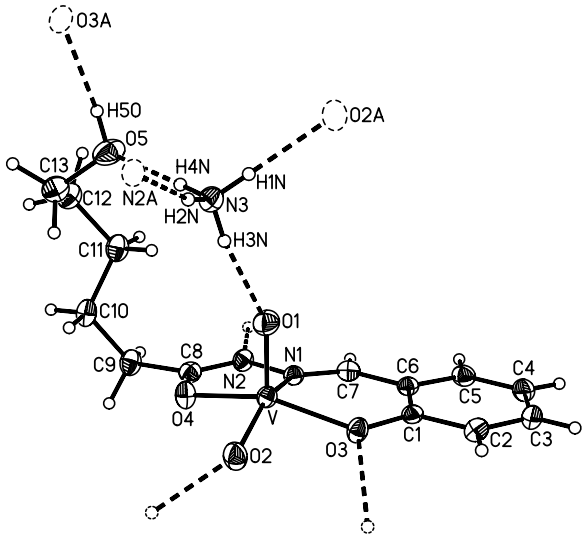


Fig. 17. Molecular structure of $NH_4[VO_2(salhyhh)]$; hydrogen bonds are drawn as broken lines.

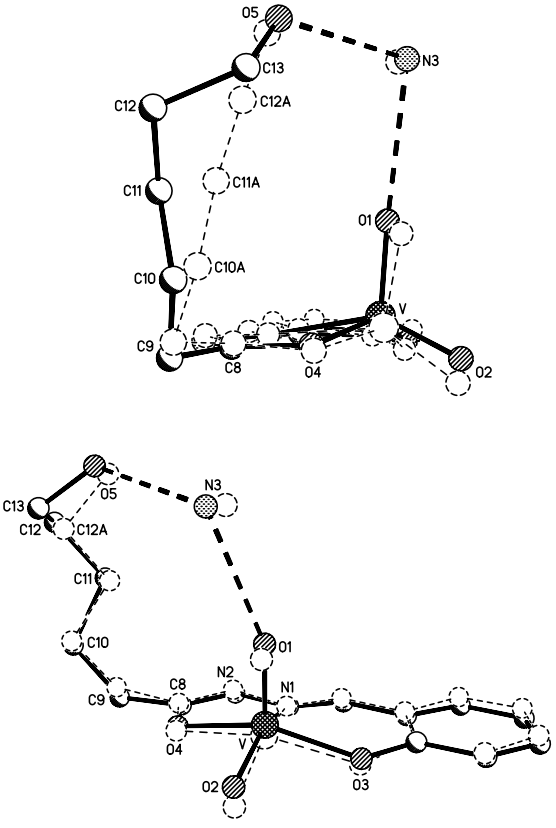


Fig. 18. Overlay of the molecular structures of $NH_4[VO_2(salhyhh)]$ drawn as thick lines with hydrogen bonds as broken lines and $NH_4[VO_2(salhyhp)]$ drawn as thin broken lines (bottom); side view (top).

structure that still shows a high similarity for the hydrogen bonding network, as can be seen from the structure of $NH_4[VO_2(salhyhh)]$ depicted in Fig. 17. This similarity is clearly evident from the overlay of the

structures of $NH_4[VO_2(salhyhp)]$ and $NH_4[VO_2(salhyhh)]$ shown in Fig. 18. As can be seen form Fig. 18, it is the flexibility in the conformation of the organic side chain that enables the overall similarity of the hydrogen bonding pattern for both complexes. Finally, the fact that for all three complexes with varying side chain length the same hydrogen bonding pattern is observed is a clear indication that the presence of supramolecular interactions is important for the molecular structures observed for the series of *cis*-dioxovanadium(V) complexes discussed here.

4. Conclusions

Hydrogen bonding is a key feature to the understanding of the structure and function of vanadium haloperoxidases. The results summarized in this review clearly show that *N*-salicylidenehydrazides can be utilized to generate vanadium(V) complexes capable of modelling the supramolecular interactions found for vanadate in biological systems. The *N*-salicylidenehydrazides are versatile tridentate ligand systems that can form both oxo and dioxo species and, moreover, also allows for the variation of the protonation state of the resulting complexes. Since this ligand system can easily be modified, it can be used to introduce additional functional groups in the vicinity of the vanadate moiety. Further modification of the side chain functional group of the *N*-salicylidenehydrazide ligand system currently in progress are expected to give additional clues related to the structural and functional importance of the supramolecular environment of vanadate in biological systems.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

References

[1] C. Slebodnick, B.J. Hamstra, V.L. Pecoraro, Struct. Bonding 89 (1997) 51.
[2] H. Sigel, A. Sigel (Eds.), Vanadium and its Role in Life Metal Ions in Biological Systems, vol. 31, Marcel Dekker, New York, 1995.
[3] W. Plass, Angew. Chem. Int. Ed. Engl. 38 (1999) 909.
[4] F.A. Quiocho, P.S. Ledvina, Mol. Microbiol. 20 (1996) 17.
[5] H. Luecke, F.A. Quiocho, Nature 347 (1990) 402.
[6] O. Herzberg, P. Reddy, S. Sutrina, J.M.H. Saier, J. Reizer, G. Kapadia, Proc. Natl. Acad. Sci. USA 89 (1992) 2499.
[7] G.A. Jeffrey, W. Saenger, Hydrogen Bonding in Biological Structures, Springer, Berlin, 1991.
[8] R.H. Holm, P. Kennepohl, E.I. Solomon, Chem. Rev. 96 (1996) 2239.
[9] C. Perrin, J.B. Nielson, Ann. Rev. Phys. Chem. 48 (1997) 511.
[10] C.D. Putnam, A.S. Arvai, Y. Bourne, J.A. Tainer, J. Mol. Biol. 296 (2000) 295.
[11] K.M. Vogel, T. Spiro, D. Shelver, M.V. Thorsteinsson, G.P. Roberts, Biochemistry 38 (1999) 2679.
[12] B.R. Crane, L.M. Siegel, E.D. Getzoff, Biochemistry 36 (1997) 12101.
[13] D.B. Goodin, D.E. McRee, D. Shelver, Biochemistry 32 (1993) 3313.
[14] S. Franzen, J. Am. Chem. Soc. 123 (2001) 12578.
[15] M. Kolbe, H. Besir, L.-O. Essen, D. Oesterheld, Science 288 (2000) 1390.
[16] J.M. Denu, D.L. Lohse, J. Vijayalakshmi, M.A. Saper, J.E. Dixon, Proc. Natl. Acad. Sci. USA 93 (1996) 2493.
[17] M. Zhang, M. Zhou, R.L. van Etten, C.V. Stauffacher, Biochemistry 36 (1997) 15.
[18] C. Orvig, K.H. Thompson, M. Battell, J.H. McNeill, Vanadium compounds as insulin mimics, in: H. Sigel, A. Sigel (Eds.), Vanadium and its Role in Life, Metal Ions in Biological Systems, vol. 31, Marcel Dekker, New York, 1995, p. 575.
[19] K. Ishikawa, Y. Mihara, K. Gondoh, E. Suzuki, Y. Asano, EMBO J. 19 (2000) 2412.
[20] A. Messerschmidt, R. Wever, Proc. Natl. Acad. Sci. USA 93 (1996) 392.
[21] A. Messerschmidt, L. Prade, R. Wever, Biol. Chem. 378 (1997) 309.
[22] A. Messerschmidt, R. Wever, Inorg. Chim. Acta 273 (1998) 160.
[23] W. Hemrika, R. Renirie, H.L. Dekker, P. Barnett, R. Wever, Proc. Natl. Acad. Sci. USA 94 (1997) 2145.
[24] N. Tanaka, V. Dumay, Q. Liao, A.J. Lange, R. Wever, Eur. J. Biochem. 269 (2002) 2162.
[25] R. Renirie, W. Hemrika, R. Wever, J. Biol. Chem. 275 (2000) 11650.
[26] M. Bangesh, W. Plass, to be published.
[27] W. Plass, Z. Anorg. Allg. Chem. 623 (1997) 461.
[28] W. Plass, Eur. J. Inorg. Chem. (1998) 799.
[29] M. Časný, D. Rehder, Chem. Commun. (2001) 921.
[30] C. Kimblin, X. Bu, A. Butler, Inorg. Chem. 41 (2002) 161.
[31] W. Plass, A. Pohlmann, H.-P. Yozgatli, J. Inorg. Biochem. 80 (2000) 181.
[32] W. Plass, A. Pohlmann, J. Inorg. Biochem. 86 (2001) 381.
[33] A. Sundheim, R. Mattes, Z. Naturforsch. Sect B 48 (1993) 1848.
[34] E. Ludwig, U. Schilde, E. Uhlemann, F. Weller, K. Dehnicke, Z. Anorg. Allg. Chem. 619 (1993) 669.
[35] W. Plass, H.-P. Yozgatli, Z. Anorg. Allg. Chem., in press.
[36] A. Pohlmann, PhD Thesis, University of Siegen, 2002.
[37] S. Nica, W. Plass, to be published.