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# Interaction of 2-amino-*N*-hydroxypropanamide with vanadium(v) in aqueous solution

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The equilibria between vanadium(v) and 2-amino-*N*-hydroxypropanamide (HL or β-alaninehydroxamic acid, $NH_2CH_2CH_2CONHOH$) in aqueous solution have been studied at 25 °C in 0.10 mol $dm^{-3}$ $NaClO_4$ medium by combined potentiometric, spectrophotometric and $^{51}V$ NMR methods. Complexes are formed between $VO_2^+$ and the β-alaninehydroxamate anion ($L^-$) in the pH range 2.5–10.5, and many of their formation constants have been determined. Complexes with a 1 : 1 and 2 : 1 ligand : metal ratio, depending on pH, can be either protonated or deprotonated, forming positively charged, neutral or negatively charged species: $[VO_2HL]^+$ and $[VO_2H_3L_2]^{2+}$ coexist below pH 3.5, with $[VO_2HL]^+$ predominating over $[VO_2H_3L_2{}^{2+}]$. From pH 3.5 to 7.0 the main species are $[VO_2H_2L_2]^+$ and, to a lesser extent, $[VO_2L]$. Above pH 7, $[VO_2H_2L_2]^+$ deprotonates to form $[VO_2HL_2]$ and $[VO_2L_2]^-$. Above pH 9.5, the prevailing complex species are $[VO_2H_{-1}L]^-$ and $[VO_2H_{-2}L]^{2-}$, being finally replaced by $HVO_4^{2-}$ above pH 10.5.

## 1 Introduction

The interest in the chemistry of vanadium(v) is mainly related to its physiological relevance. Several biological functions of vanadium have been described, including hormonal, cardiovascular, and antitumor activities.[1] Inhibition and stimulation by vanadium(v) of many phosphate metabolising enzymes and the insulin mimetic properties of vanadium compounds have been important subjects of investigation. Complexation of aqueous vanadium(v) with organic ligands consequently has been studied intensively.[2–4]

The $VO_2^+$ cation, is the prevailing vanadium(v) species at low pH. There is however a strong tendency of vanadium(v) to hydrolyse, starting under weakly acidic conditions, forming both mono- and poly-nuclear species, some of which, like the decavanadates, are very slow to react. The possibility of forming these inert species therefore must be avoided in order to perform reliable equilibrium experiments.

Hydroxamic acids by themselves are also of great biological interest and their interactions with several metals ions have been the subject of recent reports.[5–7]

Recently, we have shown how combined potentiometric, spectrophotometric, $^{51}V$ and $^{17}O$ NMR methods were used to resolve the complex equilibria in aqueous solution involving vanadium(v) and *N*-hydroxyacetamide ($CH_3CONHOH$, usually known as acetohydroxamic acid, abbreviated below to "aha"). The stoichiometry and formation constants of the resulting complexes were established and their probable structures discussed.[8] Since then the structures of two of these complexes have been theoretically studied using density functional theory. Besides, vibrational analysis of one of them has been performed.[9] The hydroxamic acid group of an organic molecule, after deprotonation, behaves as a typical bidentate donor and *N*-hydroxyacetamide represents the simplest of these organic molecules.

We have now completed a similar study involving aqueous vanadium(v) and 2-amino-*N*-hydroxypropanamide ($NH_2CH_2CH_2CONHOH$, also known as β-alaninehydroxamic acid, hereafter designated as βalaha) which besides the hydroxamic acid has also an amino group. The neutral form of this β amino substituted hydroxamic acid, differently from the α ones, exists in aqueous solution mainly as the zwitterion ($^+H_3NCH_2CH_2CONHO^-$).[10] Our results suggest that only the hydroxamate group is capable of bonding to vanadium, but it can do so even while the amino group remains protonated.

## 2 Experimental

We have carried out potentiometric (pH titrations), spectrophotometric and $^{51}V$ NMR measurements on aqueous solutions containing mixtures, in several different ratios, of vanadium(v) and β-alaninehydroxamic acid (at 25 °C, in 0.10 mol $dm^{-3}$ $NaClO_4$ medium). Measurements were carried out in the pH range 2.5–10.5.

### NMR measurements

The $^{51}V$ NMR spectra were obtained at 105.2 MHz with a Bruker DRX400 spectrometer. Typical spectra required 1024 transients, obtained in *ca.* 10 min and were referenced to capillary $VOCl_3$. Solutions were prepared in 0.10 mol $dm^{-3}$ $NaClO_4$ medium, prepared with 10% $D_2O$, with [V] being 7.16, 8.23 and 13.2 mmol $dm^{-3}$ and ligand to metal ratios equal to 5.5, 7.8 and 13.2 : 1, respectively. All baselines were corrected by spline fitting before integration of the spectra.

### Potentiometric measurements

Potentiometric measurements were carried out by the addition of NaOH to acidified mixtures of vanadium(v) and HL, in the following proportions. [HL] = 0.0251 mol $dm^{-3}$ held constant plus [V] = 0.908, 1.82, 2.72 and 3.63 mmol $dm^{-3}$. A Metrohm 670 Titroprocessor was used to measure the electromotive force. Solutions were added using a Metrohm Dosimat 665 autoburette, except for the ligand solutions which were added using a volumetric pipette. The ionic strength was adjusted to 0.10 mol $dm^{-3}$ with $NaClO_4$ solution and the temperature held at 25.0 ± 0.1 °C by circulating thermostatted water. A Metrohm 649 magnetic stirrer was used, and all measurements were done under $N_2$. Standardised, carbonate-free NaOH solutions were used throughout.

The electrode system was calibrated for $[H^+]$ before and after each series of measurements, by titration of $HClO_4$ with

standardised NaOH, or *vice versa*, at an ionic strength of 0.10 mol $dm^{-3}$. A critical evaluation of the parameters ($E°$, $RT/F$, $A_j$, $B_j$) which resulted from the potentiometric calibration procedure was always made. The values of $-\log[H^+]$ (represented by the symbol pH) were then obtained by a computerised extrapolation.

### Spectrophotometric measurements

The solutions undergoing titration were also circulated, by a peristaltic pump, through a continuous flow quartz cuvette, installed in a model 8451A Hewlett-Packard spectrophotometer. This allowed simultaneous measurement of the volume of NaOH added, of pH and of the absorbance of the solution. The time interval between subsequent titrant additions as well as the volume increments were both pre-set to obtain both a spectrum and a pH value after each addition.

### Chemicals

All solutions were prepared using deionised water. Carbonate free NaOH solutions were prepared from saturated solutions and standardised with potassium hydrogenphthalate. Solutions of β-alaninehydroxamate hydrochloride (Sigma) were always prepared just before use and their concentrations checked by direct potentiometric titrations with NaOH solutions. Stock solutions of vanadium were prepared by dissolving vanadium pentaoxide (Reagen) in perchloric acid[11] or by dissolving $NaVO_3$ (Carlo Erba) in an excess of a standardised $HClO_4$ solution.

### Computer calculations

The protonation and formation constants were refined by a rigorous least squares and non-linear routine using the computer programs SUPERQUAD[12] and KALKULA,[13] respectively. A low standard deviation computed by these programs (which refers to random errors only) was used as evidence of the presence of that species and of the adequacy of the equilibrium model proposed. Species distribution diagrams were calculated using the program SCECS.[14] Approximate $pK_a$ values were obtained from the NMR data by fitting the shift *vs.* pH data using the Henderson–Hasselbalch equation. Formation constants were calculated by fitting the observed integrals by the standard equilibrium constant equations.

After recording, the NMR spectra were quantitatively evaluated using the Bruker software computer program 1D WIN-NMR,[15] to obtain both chemical shifts and precise integrals from overlapping peaks.

## 3 Results and discussion

### $^{51}V$ NMR

Figs. 1 and 2, obtained using 8.27 mmol $dm^{-3}$ vanadium(v) and 65.3 mmol $dm^{-3}$ HL solutions and going from pH 2.3 up to 10.6, show basically two $^{51}V$ NMR resonances originating from V–βalaha complexes. The stoichiometries of the products which give rise to these two peaks were found by varying the vanadium(v) and ligand concentrations, while keeping constant the pH and the ligand to metal ratio of a series of solutions. In the first spectrum of Fig. 1 (pH 2.3) the peak with $\delta$ −520 (A) has been attributed to a 1:1 ligand:metal ratio complex $[VO_2H_pL]^p$ ($p = 1$ to $-2$), while the second peak with $\delta$ −450 (B) is due to a 2:1 ligand:metal complex $[VO_2H_pL_2]^{p-1}$ ($p = 3$ to 0). Both of these peaks are pH dependent as shown in these two figures and they remain in existence over a wide pH range, even though they tend to overlap in the pH range 4 to 7. Beginning at pH 6.7, as shown in the spectrum of Fig. 1, a new peak (E) starts to appear. It remains at $\delta$ around −435 up to pH 9.7, overlapping with peak B in between pH 8 and 9. This peak can be attributed to an oligomeric species, not accounted for in the present study. Species resulting from the hydrolysis of

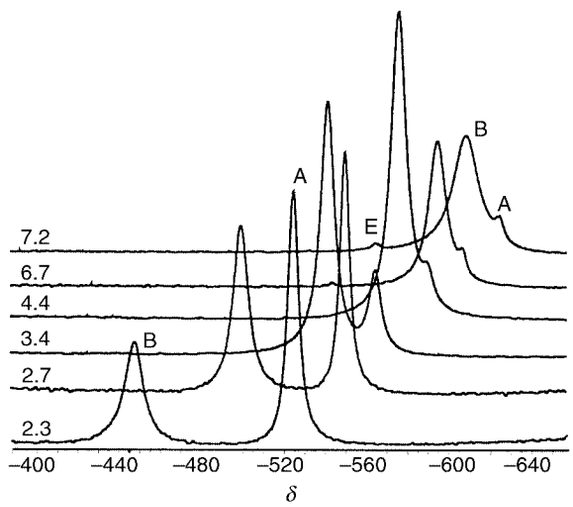



**Fig. 1** The $^{51}V$ NMR spectra of aqueous solutions of vanadium(v) (8.30 mmol $dm^{-3}$) and βalaha (65.3 mmol $dm^{-3}$) at different pH. Peak A = 1:1 and B = 2:1 ligand:metal complexes. In both Fig. 1 and 2 the spectra have been displaced to aid visualisation, the observed values are represented in Fig. 4.

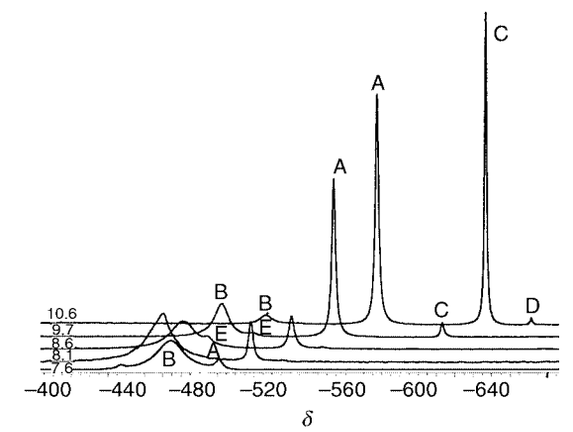



**Fig. 2** The $^{51}V$ NMR spectra of aqueous solutions of vanadium(v) (8.30 mmol $dm^{-3}$) and βalaha (65.3 mmol $dm^{-3}$) at different pH. Peak A = 1:1, B = 2:1 ligand:metal complexes, C = $H_2VO_4^-/HVO_4^{2-}$ and D = $V_2O_7^{4-}$.

vanadium are observed starting at pH 9.7 (Fig. 2). The peak with $\delta$ around −540 (C) is typical of the $H_2VO_4^-/HVO_4^{2-}$ equilibrium mixture; $HVO_4^{2-}$ is the predominant species at pH 12.2 (spectrum not shown). The species $V_2O_7^{4-}$ gives rise to peak D, starting at pH 10.6 with $\delta$ *ca.* −560.

Computer treatment had to be used to separate peaks A and B in order to calculate peak integrals and shifts. It then became unmistakable that A first diminishes as the pH increases to just above 4, remains almost constant from pH 4 to about 7 and then starts to enlarge again, reaching a maximum around pH 10. With peak B the reverse is seen, *i.e.* it first grows up to pH 4, remains practically constant from that point up to pH 7 and then starts to diminish, as shown in Fig. 3, which shows the $^{51}V$ NMR integrals for the monomeric vanadium complex species found in the spectra of Figs. 1 and 2. The $^{51}V$ NMR shifts as a function of pH of the monomeric species complexes are illustrated in Fig. 4. Peak A indicates deprotonation steps around pH 3–4 and 7–8, while B does the same between pH 2–4 and 6–9.

### Formation constants

All the experimental data that have been gathered regarding the complex equilibria between vanadium(v) and β-alaninehydroxamic acid (HL), *i.e.* potentiometric and NMR data, can be represented by the general equation (1) where $\beta_{pqr}$ represents

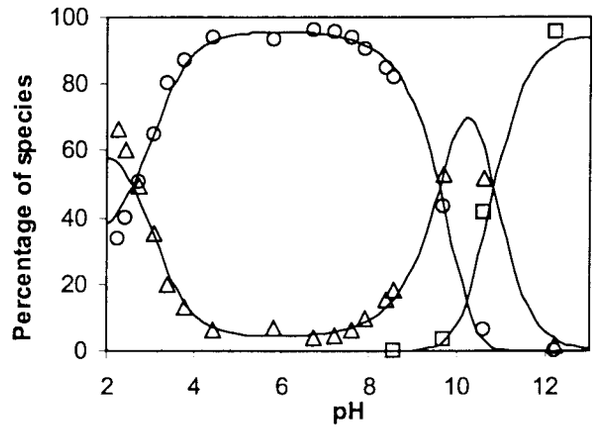



**Fig. 3** Dependence on pH of the concentrations of the main species deduced from $^{51}$V NMR integrals. Concentrations: vanadium(v), 8.30; βalaha, 65.3 mmol dm$^{-3}$. Solid line calculated as percentages of: Δ, $\Sigma[VO_2H_nL]$; ○, $\Sigma[VO_2H_nL_2]$ and □, ($H_2VO_4^- + HVO_4^{2-}$).

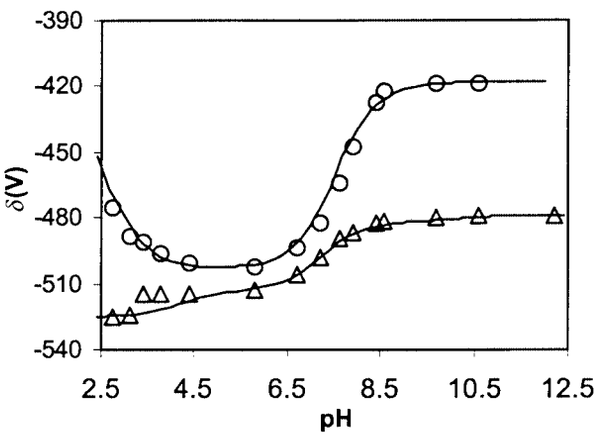



**Fig. 4** Dependence on pH of the $^{51}$V NMR shifts for the main species, concentrations as in Fig. 3. Δ, 1:1; ○, 2:1 ligand:metal ratio complexes. Solid line calculated as: $\delta_A = (\Sigma\delta_n[VO_2H_nL])/(\Sigma[VO_2H_nL])$ and $\delta_B = (\Sigma\delta_n[VO_2H_nL_2])/(\Sigma[VO_2H_nL_2])$.

$$pH^+ + qVO_2^+ + rL^- \overset{\beta_{pqr}}{\rightleftharpoons} [(H^+)_p(VO_2^+)_q(L^-)_r]^{p+q-r} \quad (1)$$

the formation constant of the complex species with different $p$, $q$ and $r$ values. Protons can either be added to form a complex species, in which case $p$ has a positive value, or can be lost, giving a negative $p$ value. This representation of the complexation equilibria starting from $VO_2^+$ and the actual ligand ($L^-$) differs from our previous one involving $V^V$ and acetohydroxamic acid,[8] which was based on the prevailing vanadium(v) species in dilute neutral solutions, *i.e.* the vanadate ion ($H_2VO_4^-$). Having adopted this new representation, we consequently had to represent in the same manner the protonation constants of the β-alaninehydroxamate anion, which were redetermined by us and are listed in Table 2, and the hydrolysis constants of the $VO_2^+$ cation. These hydrolysis constants were calculated from data reported by Pettersson and co-workers[4] and are shown in Table 1.

The stoichiometry of the complexes has been determined from NMR experiments as already described but it has proved impossible to determine all the $\beta_{pqr}$ constants from one single method. Final results are shown in Table 2. Some of the p$K_a$ values were too close for determination from the NMR shifts alone. Conversely, some parts of the potentiometric titration curves were insufficiently sensitive to the relative proportions of the species present. However, very good data were obtained by combining the two methods.

When solutions of sodium metavanadate ($NaVO_3$, which hydrolyses to form $H_2VO_4^-$) and β-alaninehydroxamate hydrochloride are mixed there is no significant change in the hydrogen ion concentration, the pH remaining between 5 and 6. It is therefore evident that the resulting 1:1 and 2:1 complex species formed in this region are simply the result of an association of $H_2VO_4^-$ with one and two molecules of protonated βalaha ($H_2L^+$), forming a neutral 1:1 complex and a positively charged 2:1 one. Simple NMR peak integrations in this pH region were then used to calculate the formation constants of the species $[VO_2L]$ (log $\beta = 14.2 \pm 0.2$) and $[VO_2H_2L_2]^+$ (log $\beta = 34.9 \pm 0.2$). Similarly, using simple peak integrations at pH 9.7, formation constants of the species $[VO_2H_{-1}L]^-$ (log $\beta = 6.98 \pm 0.05$) and $[VO_2L_2]^-$ (log $\beta = 18.15 \pm 0.05$) were calculated. Finally, two deprotonation constants were calculated from the chemical shifts of peak A (p$K_{a1} = 4.27$ and p$K_{a2} = 7.34$) for the 1:1 species and three from the shifts of peak B (p$K_{a1} = 2.6$, p$K_{a2} = 7.5$ and p$K_{a3} = 9.2$) for the 2:1 species. By fixing the formation constants of species 4, 7 and 10 of Table 2, which were determined using NMR and the $VO_2^+$ hydrolysis constants listed in Table 1, the constants for the remaining species were determined from potentiometric data alone using the programs SUPERQUAD[12] and KALKULA.[13] Fig. 5 shows the resulting almost perfect agreement between experimental and calculated potentiometric data. Besides, the values of p$K_a$ calculated from NMR data alone and the ones which resulted from this simultaneous calculation of all constants are in quite adequate agreement, as shown in Table 2.

All species of this vanadium(v)–βalaha system, except $[VO_2H_{-2}L]^{2-}$ and $[VO_2L_2]^-$, have much larger formation constants than the corresponding ones in the aha system. We have recalculated the previously reported[8] formation constants of the $V^V$–aha species, according to the same formulation we are now using. For the 1:1 species we have: $[VO_2L]$ (log $\beta = 9.74$), $[VO_2H_{-1}L]^-$ (log $\beta = 4.90$) and $[VO_2H_{-2}L]^{2-}$ (log $\beta = -3.46$). These log $\beta$ values should be compared to 14.19, 6.95 and −3.17 of the species with the same stoichiometry in the V–βalaha system (shown in Table 2). Likewise, for the 1:2 species of the $V^V$–aha system we have $[VO_2HL_2]$ (log $\beta = 20.35$), $[VO_2L_2]^-$ (log $\beta = 16.8$) and $[VO_2H_{-1}L_2]^{2-}$(log $\beta = 7.60$). The first two values should be compared with the log $\beta$ values of 27.78 and 18.15 for similar species in the V–βalaha system. However, the $[VO_2H_{-1}L_2]^{2-}$ species has not been detected in this system.

These differences in stability constants between the two systems are reflected in the species distribution diagram which has been calculated using the program SCECS[14] and shown in Fig. 6. Basically, this distribution shows that in this V–βalaha system the hydrolysis of the complex species to form $HVO_4^{2-}$ occurs at a higher pH than in the V–aha system. A similar species distribution shown in Fig. 3 has also been calculated from the NMR data, for a 8.27 mmol dm$^{-3}$ vanadium(v) and

**Table 1** Calculated hydrolysis constants of the $VO_2^+$ cation (25 °C and 0.15 mol dm$^{-3}$ NaCl medium)[a]

| Species | $p$, $q$, $r$ | Formula | log $\beta$ | p$K_a$[b] |
|---|---|---|---|---|
| 1 | −2, 1, 0 | $H_2VO_4^-$ | −7.00 | 8.17 |
| 2 | −3, 1, 0 | $HVO_4^{2-}$ | −15.17 | — |
| 3 | −4, 2, 0 | $H_2V_2O_7^{2-}$ | −11.35 | 8.50 |
| 4 | −5, 2, 0 | $HV_2O_7^{3-}$ | −19.85 | 10.34 |
| 5 | −6, 2, 0 | $V_2O_7^{4-}$ | −30.19 | — |
| 6 | −9, 4, 0 | $HV_4O_{13}^{5-}$ | −27.37 | 10.61 |
| 7 | −10, 4, 0 | $V_4O_{13}^{6-}$ | −37.98 | — |
| 8 | −8, 4, 0 | $V_4O_{12}^{4-}$ | −18.72 | — |
| 9 | −10, 5, 0 | $V_5O_{15}^{5-}$ | −23.83 | — |
| 10 | −13, 10, 0 | $H_3V_{10}O_{28}^{3-}$ | −7.07 | 1.86 |
| 11 | −14, 10, 0 | $H_2V_{10}O_{28}^{4-}$ | −8.93 | 4.17 |
| 12 | −15, 10, 0 | $HV_{10}O_{28}^{5-}$ | −13.1 | 6.62 |
| 13 | −16, 10, 0 | $V_{10}O_{28}^{6-}$ | −19.72 | — |

[a] From ref. 4. [b] $K_a$ = acid dissociation constant.

**Table 2** Stoichiometry, notation, formation (log $\beta$) constants, acidity ($pK_a$) constants and chemical shifts ($\delta_v$) calculated for the $V^V$–β-alaninehydroxamic acid system at 25 °C and $I = 0.10$ mol $dm^{-3}$

| | | | log $\beta$ | | | |
|---|---|---|---|---|---|---|
| Species | $p, q, r$ | Formula | *a* | *b* | $pK_a$ [c] | $\delta_v$ |
| 1 | 2, 0, 1 | $H_2L^+$ | — | 18.035(3) | 8.346 | — |
| 2 | 1, 0, 1 | HL | — | 9.690(3) | 9.690 | — |
| 3 | 1, 1, 1 | $[VO_2HL]^+$ | 18.5(2) | 18.72(4) | 4.3/4.5 | −525 |
| 4 | 0, 1, 1 | $[VO_2L]$ | 14.2(2) | 14.2 | 7.3/7.2 | −513 |
| 5 | −1, 1, 1 | $[VO_2H_{-1}L]^-$ | 6.98(5) | 6.95(2) | 10.1 | −482 |
| 6 | −2, 1, 1 | $[VO_2H_{-2}L]^{2-}$ | — | −3.17(6) | — | −479 |
| 7 | 3, 1, 2 | $[VO_2H_3L_2]^{2+}$ | 37.5(2) | 37.5 | 2.6/2.5 | −420 |
| 8 | 2, 1, 2 | $[VO_2H_2L_2]^+$ | 34.9(2) | 34.96(4) | 7.5/7.2 | −503 |
| 9 | 1, 1, 2 | $[VO_2HL_2]$ | 27.4(2) | 27.78(3) | 9.2/9.6 | −421 |
| 10 | 0, 1, 0 | $[VO_2L_2]^-$ | 18.15(5) | 18.15 | — | −418 |

[a] NMR results (numbers in parentheses are estimated standard deviations in the least significant digits). [b] Potentiometry results (formation constants of species 4, 7 and 10 maintained fixed while the others were refined using KALKULA and SUPERQUAD). [c] NMR/Potentiometry results.

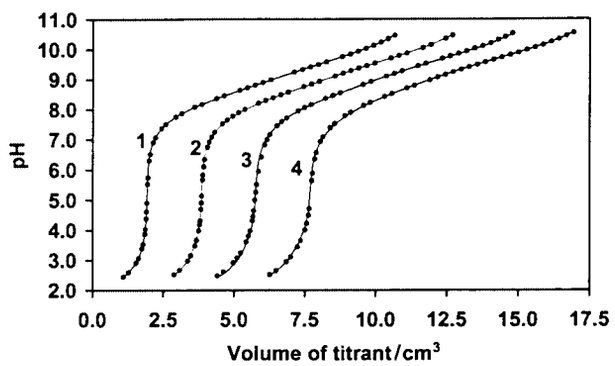



**Fig. 5** Experimental (●) and calculated (—) potentiometric titration data points corresponding to titrations of 25.1 mmol $dm^{-3}$ βalaha with (1) 0.908, (2) 1.82, (3) 2.72 and (4) 3.63 mmol $dm^{-3}$ vanadium(v).

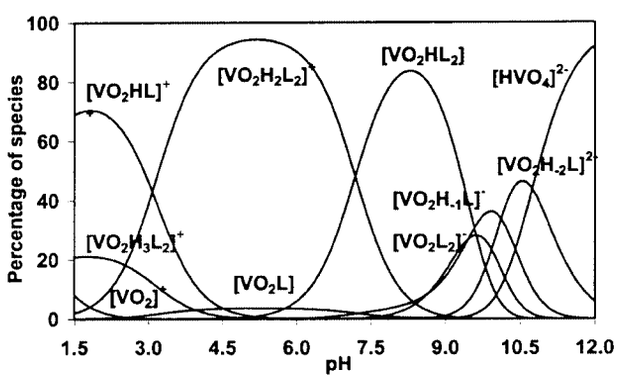



**Fig. 6** A distribution diagram for the vanadium(v)–βalaha system showing the percentages of species calculated for 8.30 mmol $dm^{-3}$ vanadium(v) and 65.3 mmol $dm^{-3}$ βalaha.

65.3 mmol $dm^{-3}$ HL solution. In this figure the sums of all the calculated 1:1 and 1:2 species are shown as lines and adequately match the experimental data points.

As shown in Fig. 6, the species $[VO_2HL]^+$ and $[VO_2H_3L_2]^{2+}$ predominate below pH 3.5 with $[VO_2HL]^+ > [VO_2H_3L_2]^{2+}$. From pH 3.5 to 7.0 the main species are $[VO_2H_2L_2]^+$ and, to a lesser extent, $[VO_2HL]^+$. Above pH 9.5 the prevailing complex species are $[VO_2H_{-1}L]^-$ and $[VO_2H_{-2}L]^{2-}$, which are finally replaced by $HVO_4^{2-}$ above pH 10.5.

## Spectrophotometry

A few spectrophotometric titration results are shown in Fig. 7. Even though it has not been possible to calculate the absorption spectrum of each species formed in this complex system, it can be seen that $[VO_2H_2L_2]^+$ can be considered as the main one responsible for the absorption at 304 nm, since it reaches a

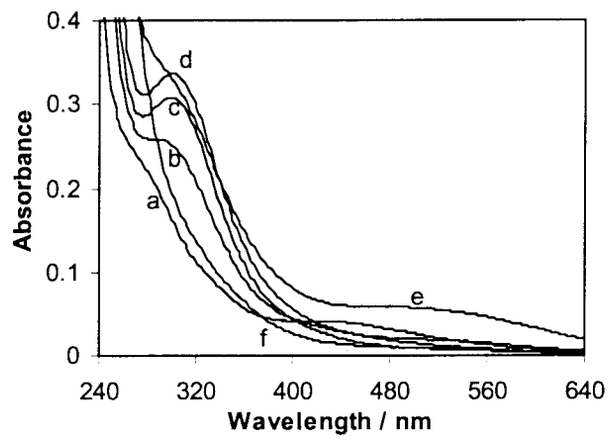
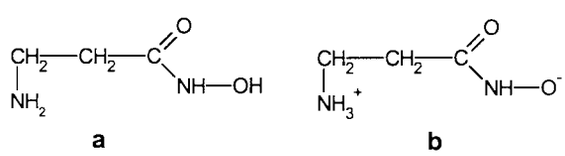



**Fig. 7** Spectrophotometric curves at pH (a) 1.69, (b) 3.45, (c) 4.17, (d) 6.47, (e) 7.63 and (f) 9.49 for a solution containing 1.80 mmol $dm^{-3}$ vanadium(v) and 16.9 mmol $dm^{-3}$ βalaha.

maximum in between pH 4 and 7, where this species predominates, as shown in Fig. 6. As for the absorption at 456 nm, its decrease from pH 2 to 4 can be related to the disappearance of $[VO_2HL]^+$ which occurs in this same region, as shown in Fig. 6, and its maximum at pH 8 coincides with a maximum in the concentration of $[VO_2HL_2]$ according to the same figure. We can therefore conclude that these spectral changes represent a valid support for the proposed equilibrium model.

## Structures

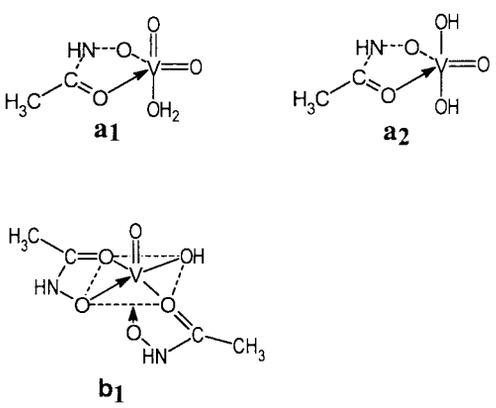
Both the β-amino and the hydroxamic acid groups present in the structure of β-alaninehydroxamic acid (structure **a**) are potentially strong metal co-ordinating groups. The amino group acts as a monodentate ligand and the hydroxamic acid, once deprotonated, as a bidentate one.




Farkas *et al.*[10] while studying the deprotonation scheme of fully protonated α and β amino substituted hydroxamic acids ($H_2L^+$), have shown that while in an α amino substituted hydroxamic acid the $NH_3^+$ group is a stronger acid than the CONHOH moiety of this molecule, the acidity sequence is the opposite for the β derivative. Consequently, the neutral form of β-alaninehydroxamic acid exists mainly as the zwitterion, shown as structure **b**. Therefore this neutral form, since it has

the hydroxamic acid group already deprotonated, is potentially capable of co-ordinating to the $VO_2^+$ cation to form a positively charged complex species.

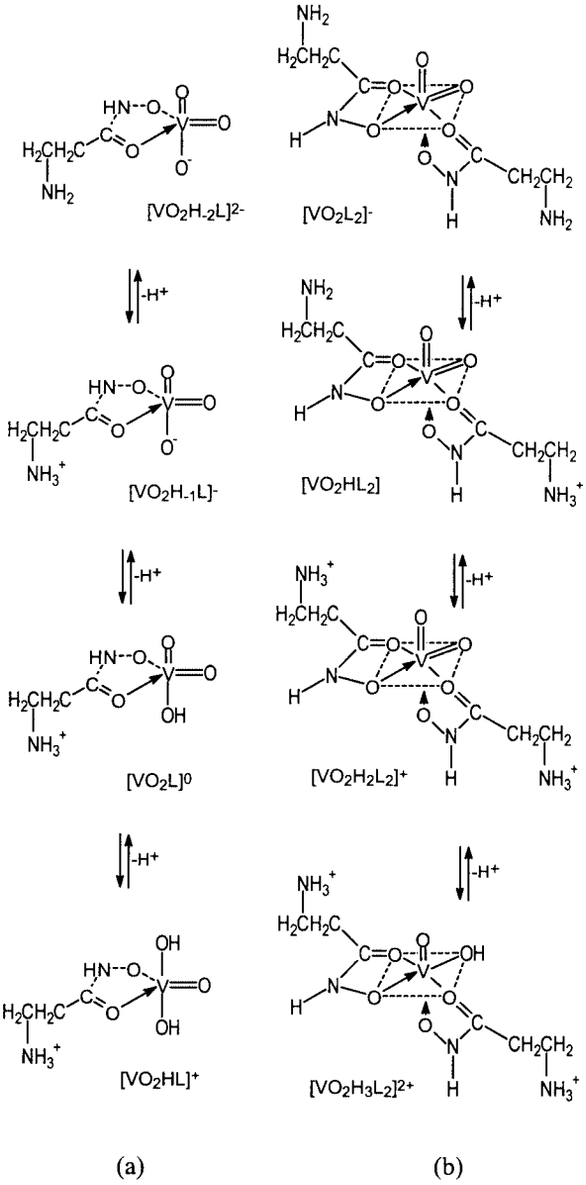
As we have shown,[8,9] acetohydroxamic acid (HL) reacts with vanadium(v) in acidic media to form a 1:1 neutral complex with the formula $[VO_2L]$. This reaction can be considered as taking place in two steps: deprotonation of aha followed by chelation of the aha anion to $VO_2^+$ forming a 5-member ring system. As a result, the two oxygen atoms of the $VO_2^+$ would remain mutually *cis* and one $H_2O$ molecule would come in to form a five-co-ordinated complex, as shown in structure $\mathbf{a}_1$. However, the theoretical, fully optimised structure of this complex shows that an intramolecular proton transfer has occurred from the $H_2O$ molecule to one of the oxo ligands.[9] Structure $\mathbf{a}_2$ depicts the result of this rearrangement, showing that as a consequence of this process the vanadium now interacts with two $OH^-$ anions rather than the less favoured $H_2O$ molecule. Deprotonation of these two OH groups can explain the existence of 1- and 2-charged species.




In this same vanadium(v)–aha system a neutral complex containing two aha ligands per vanadium, $[VO_2HL_2]$, has also been experimentally characterised.[8] Again, according to theoretical calculations, both aha ligands have lost their protons to co-ordinate to $VO_2^+$. Formation of this 2:1 species can be envisaged as the result of the addition of one uncharged aha molecule to $VO_2L$ resulting in protonation followed by substitution of one of the OH groups of structure $\mathbf{a}_2$ by the bidentate aha anion giving **b**.[9] According to calculations, the most stable conformer in this structure has one of the V–ON groups placed in a *trans* position with regard to the VO group. Once again, deprotonation of the single OH group explains the existence of only one negatively charged species in this case.

As we have pointed out, the species $[VO_2H_{-2}L]^{2-}$ and $[VO_2L_2]^-$ have quite similar formation constants both in the vanadium(v)–aha and –βalaha systems. It seems therefore quite reasonable to propose that they should have the same structure in both systems, as shown in the top of Scheme 1 for these two species. The species $[VO_2H_{-2}L]^{2-}$ supposedly is formed after two protons are released from the OH groups of structure $\mathbf{a}_2$, while $[VO_2L_2]^-$ is the result of a proton release from **b**. In both cases, the $NH_2$ groups do not participate in the co-ordination process.

All the other species of the vanadium(v)–βalaha system have larger formation constants than the ones with the same *p*, *q* and *r* values of the vanadium(v)–aha system. To account for this difference, we propose the protonation sequence shown from top to bottom in Scheme 1, according to which, for example, the species of the V–βalaha system with the stoichiometry 0,1,1 ($[VO_2L]$) instead of having vanadium(v) bonded to one $O^{2-}$, two $OH^-$ and one hydroxamate group (structure $\mathbf{a}_2$) has it bonded to two $O^{2-}$, one $OH^-$ and one hydroxamate group, as shown in Scheme 1. Likewise, for the species with the stoichiometry 1,1,2 ($[VO_2HL_2]$), instead of having $V^V$ bonded to one




**Scheme 1** Tentative structures for the 1:1 (a) and 1:2 (b) species of the vanadium(v)–β-alaninehydroxamic acid system.

$OH^-$ and two hydroxamate groups (structure **b**) has it bonded to two $O^{2-}$ and two hydroxamate groups, as shown in Scheme 1.

A final comment in favour of this proposal is the fact that α-alaninehydroxamic acid, in which the $NH_3^+$ group is a stronger acid than the hydroxamate one and therefore does not exist as the zwitterion, is not a good complexing agent for vanadium(v).

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