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Oxovanadium(IV) complexes of ligands containing phosphonic acid moieties

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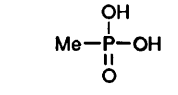
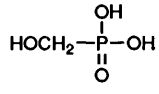
Complex formation between oxovanadium(IV) and phosphonate ligands was investigated by pH potentiometric and spectroscopic (EPR and electronic absorption) techniques showing that, in contrast to monophosphate, which is able to bind the metal ion forming four-membered chelated rings, methylphosphonate acts only as a monodentate ligand so that hydrolysis sets in at very low pH. Other ligands have also been considered, phosphonoformic acid, its higher homologue phosphonoacetic acid, methylenediphosphonic acid and 1-hydroxy(methyl)methylenediphosphonic acid, which adopt a chelating behaviour and form much more stable complexes. Spectroscopic and potentiometric evidence for the binding of methylenediphosphonic and 1-hydroxy(methyl)methylenediphosphonic acid by oxovanadium(IV) yielding trinuclear species similar to the well-characterized analogue formed by diphosphate has been obtained.

The chemistry of vanadium in biological systems highlights the role played by biogenic ligands stabilizing oxovanadium(IV) inside the cell, after the metal has been adsorbed as vanadate(V) and been reduced. In doing so, they provide important mechanisms for preventing the toxic effects of the higher oxidation state. Phosphate and its derivatives, *e.g.* nucleoside-phosphates, play a major role in the intracellular complexation of vanadium. Continuing our research on the complexing properties of phosphate ligands towards the oxovanadium(IV) ion, we have turned our attention to some phosphonate ligands and compared them with the analogous carboxylates.

Phosphonic acids, containing physiologically stable P–C bond(s), are of considerable interest as metal-complexing agents potentially active in living systems. Metal-complexing properties of phosphonates and their derivatives, mainly aminophosphonates, have been studied with metal ions such as copper(II), calcium(II), zinc(II), *etc.*[1] To the best of our knowledge, studies for oxovanadium(IV) complex formation in solution are still lacking.


Methylphosphonic acid (H_2L^1)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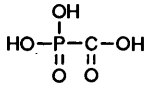
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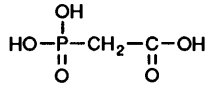
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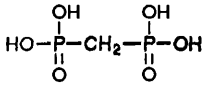
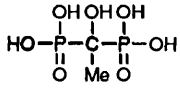

Methylenediphosphonic acid (H_4L^5)


1-Hydroxy(methyl)methyle acid (H_4L^6)

The phosphonates used were Aldrich, Alfa or Fluka products of puriss. quality. Their purity was checked and the exact concentration of solutions determined by the Gran method.[2] A stock solution of VO^{2+}, prepared as described in ref. 3, was standardised for metal concentration by permanganate titration and for hydrogen-ion concentration by potentiometry using the appropriate Gran function. The ionic strength was adjusted to 0.2 mol dm^{-3} KCl. In all cases, the temperature was 25.0 ± 0.1 °C.

Potentiometric measurements

Stability constants were determined by pH-metric titration of 25.0 cm^3 samples. The phosphonate concentration was 0.004 and 0.002 mol dm^{-3} and the phosphonate-to-metal ion molar ratio 8:1, 4:1, 2:1 and 1:1. Titrations were performed over the range pH 2–10 with KOH solution of known concentration (*ca.* 0.2 mol dm^{-3}) under a purified argon atmosphere. In some cases pH equilibrium could not be reached within 10 min due to either precipitation or very slow complex formation reactions. These titration points were omitted from further evaluation. The reproducibility of titration points included in the evaluation was within 0.005 pH unit in the whole pH range.

The pH was measured with a Radiometer pHM 84 instrument equipped with a GK 2322C combined electrode, calibrated for hydrogen-ion concentration according to Irving *et al.*[4] The difference between pH-meter readings and $-\log [H^+]$ was constant in the ranges pH 2–4 and 10–11.6. Thus the junction potential proved to be constant, although not negligible, as discussed previously.[4] The concentration stability constants $\beta_{pqr} = [M_pA_qH_r]/[M]^p[A]^q[H]^r$ were calculated with the aid of the PSEQUAD computer program.[5] The formation of hydroxo complexes of $V^{IV}O$ was taken into account in the calculations. The following species were assumed: $[VO(OH)]^+$ ($\log \beta_{1-1} = -5.94$), $[\{VO(OH)\}_2]^{2+}$ ($\log \beta_{2-2} = -6.95$), with stability constants calculated from the data of Henry *et al.*[6] and corrected for the different ionic strengths by use of the Davis equation, and $[VO(OH)_3]^-$ ($\log \beta_{1-3} = -18.0$), taken from ref. 7.

Spectroscopic measurements

Isotropic and anisotropic X-band EPR spectra (9.15 GHz) were recorded at 298 or 120–140 K, respectively, on aqueous solutions using a Varian E-9 spectrometer. As usual, the samples for low-temperature measurements were added with a

Table 1 Protonation constants (log K) and oxovanadium(IV) complex formation constants (log β) of several phosphonic acids at $I = 0.20$ mol dm^{-3} (KCl) and 25 °C

	H_2L^1	H_2L^2	H_3L^3	H_3L^4	H_4L^5	H_4L^6
log K						
$K_{PO_3^{2-}}$	7.42(1)	6.81(1)	7.39(1)	7.78(2)	10.00(2)	10.69(3)
$K_{PO_3^{2-}}$					6.78(1)	6.60(1)
$K_{CO_2^-}$			3.16(2)	4.71(2)		
$K_{PO_3H^-}$	2.13(4)	1.5(1)	< 1	1.2(2)	1.2(2)	< 1
$K_{PO_3H^-}$					< 1	< 1
log β						
$VOAH_2$					21.64(6)	
VOAH	9.55(6)	10.14(9)	11.53(6)	12.99(2)	19.03(5)	19.27(3)
VOA	5.87(3)	6.59(9)	9.20(3)	9.28(1)		
$VOAH_{-1}$			2.73(3)	2.52(2)		
$VOAH_{-2}$	−5.98(4)	−6.39(24)				
VOA_2H_2				23.76(9)		
VOA_2H			18.35(15)	19.86(4)		
VOA_2			15.22(5)	15.13(2)	19.75(9)	
VOA_2H_{-1}		4.24(19)				
$(VOAH_{-1})_2$	6.72(5)	7.69(19)				
$(VO)_3A_3$					53.29(9)	54.73(9)
pH Range	2–6	2–6	2–7.5	2–7.5	2–9.5	2–9.5
No. of points	171	200	192	168	208	179
Fitting*	0.010	0.013	0.013	0.010	0.013	0.011

* Fitting = average differences in the calculated and experimental titration curves expressed in cm^3 of the titrant.

few drops of dimethyl sulfoxide to ensure good glass formation in frozen solutions. Electronic absorption spectra were obtained on a Beckman Acta MIV spectrophotometer.

Results and Discussion

Methylphosphonic acid

The acid (H_2A) exhibits two dissociation steps with pK_a values of 2.13 and 7.42. Potentiometric data (Table 1) indicate 1:1 complexes $[VOAH]^+$ and [VOA]. Bis(complexes) are rejected by the data fitting, at least over the range of ligand-to-metal ratios from 2:1 to 8:1 and up to pH *ca.* 7, where slow hydrolytic processes start.

The constant for the equilibrium $VO^{2+} + HA^- \rightleftharpoons [VOAH]^+$ ($10^{2.24}$) is in the range of the values reported so far for the monodentate species $[VO(H_2PO_4)]^+$ ($10^{1.49}$ and $10^{3.20}$), $[VO(H_2P_2O_7)]$ ($10^{2.23}$) and $[VO(MeCO_2)]^+$ ($10^{1.86}$).[8–11] On this basis, there is little doubt that HA^- behaves as a monodentate ligand co-ordinating through one of its oxygens. A remarkably higher value ($10^{5.87}$) is measured for the analogous constant of [VOA]. The pK_{VOAH} value for the deprotonation of the co-ordinated ligand is 3.79, more than three orders of magnitude lower than that for the free ligand. This may either imply an electron withdrawing effect due to metal co-ordination or a chelating mode for the ligand.

The EPR results support that, at ligand-to-metal molar ratios from 1:1 to 100:1, complex formation starts at pH values as low as 2. The EPR parameters, slightly but significantly different from those of the aqua ion, characterize $[VOAH]^+$ and [VOA], although, as expected for complexes of weak O-donor ligands, no clear distinction between the two species is possible. However, a bidentate chelation of the phosphonate group in [VOA] is less likely since no ^{31}P splitting is observed which, usually, characterizes four-membered O–P–O or S–P–S chelation.[12–14] The EPR data listed in Table 2 are those measured at 100:1 ligand-to-metal molar ratio, so they could have contributions from bis(complexes) which are likely to be formed at such a high ligand excess.

A monodentate behaviour is also supported by the hydrolysis which is complete above pH 5 and yields $[VOAH_{-1}]^-$. Actually, this complex is a dihydroxo-bridged dimer $[(VOAH_{-1})_2]^{2-}$ which is EPR inactive at room temperature. In comparison, the bis(chelated) complexes formed by the polyphosphate chains of ADP and ATP underwent hydrolysis only above pH 8.[15] In very basic media the EPR-active monomeric species $[VO(OH)_3]^-$ is formed.

Hydroxymethylphosphonic acid

The alcoholic function of the ligand (H_2A) may assist phosphonate in five-membered ring chelation. The ability of $V^{IV}O$ to co-ordinate alcoholic functions is well documented.[16]

In the species $[VOAH]^+$ and [VOA] the assistance of undissociated hydroxyl groups in co-ordination is supported by the magnitude of the stability constants. They are significantly higher than the corresponding ones measured for the analogous methylphosphonic acid complexes. The co-ordination sets PO_3H^-, OH and PO_3^{2-}, OH may be assigned to $[VOAH]^+$ and [VOA] respectively. Again, the deprotonation of the PO_3H^- group is strongly favoured in comparison with the free ligand (pK_{VOAH} = 3.55 *vs.* pK_{PO_3H} = 6.81), supporting that in the methylphosphonic acid system such an effect is not due to a switch of the bonding mode from monodentate to bidentate. Although $V^{IV}O$ is able to promote dissociation and co-ordination of alcoholic groups,[16] this behaviour is not exhibited by hydroxymethylphosphonic acid, at least in acidic solution, and the hydrolysed species $[(VOAH_{-1})_2]^{2-}$ is predominant above pH 5.

The formation of $[VOAH]^+$ and [VOA] is indicated by EPR spectroscopy, from pH 2 to 4.5, through a continuous increase in linewidth. Simultaneously, there is a decrease in intensity of hyperfine resonances. Above pH 5 the solution is EPR silent at room temperature.

A different trend is observed at ligand excesses as high as 100:1. Hydrolysis is strongly suppressed and the EPR spectrum observed at pH 7 is likely due to a 2(PO_3^{2-}, OH) bis(chelated) $[VOA_2]^{2-}$ species. Upon increasing pH the deprotonation of alcoholic groups is supported. In fact, at pH 8 a minor component, assigned with $[VOA_2H_{-1}]^{3-}$ composition and a PO_3^{2-}, OH; PO_3^{2-}, O^- donor set, is substantiated. Its EPR parameters are noticeably different from those of the aqua ion, indicating a rather strong donor like the alcoholate group. Above pH 9 another species is predominant, $[VOA_2H_{-2}]^{4-}$, where two alcoholate groups assist phosphonates in metal chelation. The bis(chelated) nature of such species is supported

Table 2 Spectral data for the complexes

Ligand	Species	$g_{\|\|}$	$10^{-4}A_{\|\|}(^{51}V)/cm^{-1}$	Donor set	λ_{max}[a]/nm
H_2O	$[VO(H_2O)_5]^{2+}$	1.933	183		630(8) (sh), 770(18)
OH^-	$[VO(OH)_3]^-$	1.955	162		410(114), 520(28) (sh)
Methylphosphonic acid	VOAH	1.932[b]	179	PO_3H^-	
	VOA			PO_3^{2-}	665(10) (sh), 840(19)[b]
	VOA_2[c]			$2\,PO_3^{2-}$	
	$(VOAH_{-1})_2$			PO_3^{2-}, 2(μ-OH^-)	640(18), >850 (≈12)
Hydroxymethylphosphonic acid	VOAH	1.932	178–179	PO_3H^-, OH	660(8) (sh), 830(17)
	VOA			PO_3^{2-}, OH	
	VOA_2[c]			$2(PO_3^{2-}$, OH)	635(12), 850 (13)
	VOA_2H_{-1}	1.940	171	PO_3^{2-}, OH; PO_3^{2-}, O^-	
	VOA_2H_{-2}[d]	1.958	160	$2(PO_3^{2-}$, $O^-)$	415(18) (sh), 570(11), 750(16)
	$(VOAH_{-1})_2$			PO_3^{2-}, O^-; 2(μ-OH^-)	630(18), 810(17)
Phosphonoformic acid	VOAH	1.933	179	PO_3H^-, CO_2^-	
	VOA	1.937	177	PO_3^{2-}, CO_2^-	630(9) (sh), 790(23)
	VOA_2	1.936	175	$2(PO_3^{2-}$, $CO_2^-)$	400(9), 585(13), 760(27)
Phosphonoacetic acid	VOAH	1.936	178	PO_3H^-, CO_2	
	VOA	1.940	175	PO_3^{2-}, CO_2^-	615(8), 815(30)
	VOA_2	1.942	173	$2(PO_3^{2-}$, $CO_2^-)$	410(3), 600(9), 835(34)
Methylenediphosphonic acid	$VOAH_2$	1.932	181	PO_3H^-, PO_3H^-	650(7) (sh), 800(21)
	VOAH	1.934	178	PO_3^{2-}, PO_3H^-	660(8) (sh), 810(23)
	$(VO)_3A_3$	See text			350(5), 615(6), 825(16)
	VOA_2	1.940	174	$2(PO_3^{2-}$, $PO_3^{2-})$	400(4), 620(8), 810(22)
1-Hydroxy(methyl)methylene-diphosphonic acid	$VOAH_2$	1.930	182	PO_3H^-, PO_3H^-	
	VOAH	1.935	179	PO_3^{2-}, PO_3H^-	650(8), 835(21)
	$(VO)_3A_3$	See text			370(4), 620(6), >850(~18)
	VOA_2[c]	1.938	175	$2(PO_3^{2-}$, $PO_3^{2-})$	370(6), 620(8), >850(~25)
	VOA_2H_{-1}[d]	1.943	168	PO_3^{2-}, PO_3^{2-}; PO_3^{2-}, O^-	
	VOA_2H_{-2}[d]	1.951	159	$2(PO_3^{2-}$, $O^-)$	410(12), 565(5), 815(7)

[a] Values of ε (mol^{-1} dm^3 cm^{-1}) shown in parentheses are referred to the total metal concentration and to the maximum extent of formation of the species. [b] Measured at ligand-to-metal molar ratio of 100:1 and pH 4. [c] Species not detected at the ligand-to-metal molar ratios used in potentiometry. [d] Species not detected by potentiometry over the pH range examined.

by thermodynamic and spectral evidence. In fact, in such basic conditions, only bis(chelate) complexes are stable enough to resist hydrolysis. On the other hand, the comparison with the EPR parameters of complexes of hydroxycarboxylic ligands support the proposed donor sets. For instance, with *meso*-tartaric acid the CO_2^-, O^- and $2(CO_2^-, O^-)$ bonding modes to VO^{IV} yield the data sets $g_{||} = 1.939$, $A_{||} = 168 \times 10^{-4}$ cm^{-1} and $g_{||} = 1.949$, $A_{||} = 155 \times 10^{-4}$ cm^{-1}, respectively.[17] At this ligand excess, complete hydrolysis takes place only above pH 11.5 and directly yields $[VO(OH)_3]^-$.

A comparison with analogous systems allows an improvement in our knowledge of the complexing features of phosphonates. In these ligands, unfavourable steric and electrostatic factors hinder the formation of bis(complexes) which facilitates hydrolysis. In comparison with the carboxylic glycolic ligand the formation of bis(chelated) $2(CO_2^-, OH)$ species is almost complete at pH 3.5 and the $2(CO_2^-, O^-)$ bonding mode is dominant at pH 7.[16] Nevertheless, the assistance of alcoholic groups favours bis(complexes) and, at a ligand molar excess of 100:1, the $2(PO_3^{2-}, O^-)$ species of hydroxymethylphosphonic acid are stable even in rather basic conditions.

Phosphonoformic and phosphonoacetic acid

The carboxylic groups of these ligands (H_3A) may co-ordinate to the metal ion even in acid solution, providing very effective chelating properties below pH 7. These species could be detected by potentiometry in the $V^{IV}O$–phosphonoformic acid system (Fig. 1). A [VOAH] complex is formed at pH 2. It is distinctly more stable than the analogous complexes of methyl- and hydroxymethyl-phosphonic acid in spite of the weaker basicity of the PO_3H^- group. Therefore, it is probably a PO_3H^-, CO_2^- chelated species. Actually, the constant for the equilibrium $VO^{2+} + HA^{2-} \rightleftharpoons [VOAH]$ is $10^{4.14}$. The complex loses a proton with $pK_a = 2.33$ leading to the PO_3^{2-}, CO_2^- bonding mode in the mono(chelated) $[VOA]^-$. The

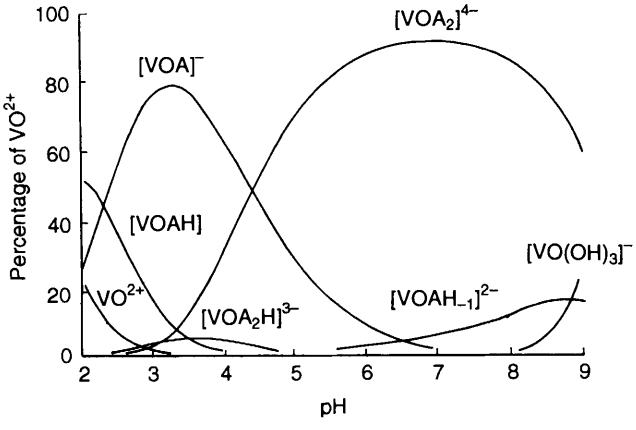


Fig. 1 Concentration distribution curves for the complexes formed in the oxovanadium(IV)–phosphonoformic acid system as a function of pH; $c_{VO^{2+}} = 0.002$ and $c_{ligand} = 0.004$ mol dm^{-3}

$[VOA_2]^{4-}$ species, which involves two such chelated rings, is the predominant complex formed between pH 5 and 9. As inferred by the rather high value of $\log(K_{VOA}/K_{VOA_2}) = 3.18$, the co-ordination of the second phosphonate molecule is rather hindered, most likely because of the unfavourable electrostatic effects expected for the formation of a complex with a charge of 4−. The PO_3^{2-}, CO_2^- chelation mode protects the metal ion from hydrolysis, at least over the acidic pH range. In fact, even with a moderate excess of ligand, formation of hydroxo species starts only above pH 9, as indicated by a decrease in the intensity of the EPR signals.

The complexation scheme can be followed distinctly by isotropic EPR spectroscopy (Fig. 2). At a 2:1 ligand-to-metal molar ratio, pH *ca.* 2, the magnitude of the ^{51}V hyperfine coupling constant (103×10^{-4} cm^{-1}) is small compared with that of the aqua ion (106×10^{-4} cm^{-1}) indicating the onset of

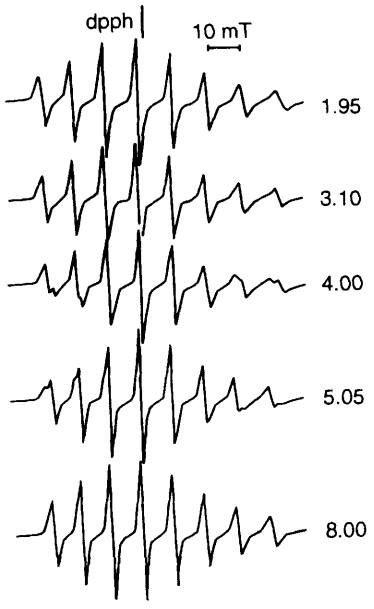


Fig. 2 X-Band EPR spectra recorded at room temperature on aqueous solutions of VO^{2+} (0.002 mol dm $^{-3}$) and phosphonoformic acid at the ligand-to-metal molar ratio of 2:1 with varying pH

metal complexation. Distinct resonances may be attributed to the complex predominating around pH 3 ($g_0 = 1.966$ and $A_0 = 101 \times 10^{-4}$ cm^{-1}) and to a major species existing from pH 4 to 9 ($g_0 = 1.969$ and $A_0 = 95 \times 10^{-4}$ cm^{-1}).

Frozen-solution EPR spectra are much more complicated. The species [VOAH] is hard to distinguish due to the overlap with the aqua ion; reliable parameters may be measured at a ten-fold ligand excess and pH 2. Besides the resonances due to the major species $[VOA]^-$ and $[VOA_2]^{4-}$, signals are observed which can be ascribed to a polynuclear species. The magnitude of the hyperfine splitting, about half of that expected for a monomeric complex, is indicative of a dinuclear VO^{IV} complex. In such a case two sets of 15 equispaced lines, separated by $2D$ (D is the zero-field splitting value) are expected. The measured EPR parameters are: $g_{\|} = 1.939$, $A_{\|} = 79 \times 10^{-4}$ cm^{-1} and $2D = 81 \times 10^{-4}$ cm^{-1}. If D is considered of pure dipolar origin, which is reasonable for weak magnetic interactions, by use of Stevens equation [18] one can calculate a V–V distance of 6.7 Å in an axially symmetric dimer (collinear O=V ··· V=O moieties). Instead, by assuming an angle of 45° between V–V and V=O, the D value is consistent with an intermetallic distance of 5.3 Å. Most likely, the dinuclear entity, for which no evidence is obtained at room temperature, is formed by the dimerization of $[VOA_2]^{4-}$ upon lowering the temperature. The intermetallic distance, as calculated by assuming a 45° angle between V=O and V–V, is in accord with a structure where two $[VOA_2]^{4-}$ units interact with each other through the apical involvement of a phosphonate oxygen.

The PO_3^{2-}, CO_2^- chelation mode of phosphonoacetic acid leads to a six-membered ring. The electron-releasing properties of the methylene bridge make the donor groups stronger, compared to phosphonoformic acid, and stabilize protonated species like [VOAH] and $[VOA_2H]^{3-}$. The situation is well reflected in the isotropic EPR spectra through a continuous decrease of the hyperfine constant with increasing pH, indicating the coexistence of more than one species. Only above pH 6 do the g_0 and A_0 values become constant and show no further changes up to pH 9 ($g_0 = 1.936$ and $A_0 = 97 \times 10^{-4}$ cm^{-1}). Monitoring the spectra of frozen solutions allows the complexation processes to be followed more easily. At 2:1 ligand-to-metal molar ratio, pH 2.5, the EPR parameters ($g_{\|} = 1.936$ and $A_{\|} = 178 \times 10^{-4}$ cm^{-1}) are different from those of the aqua ion. A composite hyperfine pattern is measured at pH 3.6 which indicates a further species exhibiting $g_{\|} = 1.940$ and $A_{\|} = 175 \times 10^{-4}$ cm^{-1}. This reaches a maximum concentration at pH *ca.* 4.6. From pH 6 to 9, a third complex is predominant with $g_{\|} = 1.942$ and $A_{\|} = 173 \times 10^{-4}$ cm^{-1}. Above pH 4, a broad band which may be attributed to polynuclear species reaching the maximum extent of formation around pH 7, is detected. Such species are not observed in the isotropic spectra, which do not exhibit a decrease in intensity, and are disfavoured by increasing ligand excess. Therefore, they can be explained by segregation processes taking place in frozen solution. Hydroxo binding is effective at pH ≈ 10 and $[VO(OH)_3]^-$ is formed at pH > 11.

The EPR results are in accordance with the calculated speciation curves. The main complexes detected by EPR are [VOAH], $[VOA]^-$ and $[VOA_2]^{4-}$, whereas the minor component $[VOA_2H]^{3-}$ is not distinguished. Equilibrium data confirm that the formation of $[VOA_2]^{4-}$ is disfavoured, *cf.* log $(K_{VOA}/K_{VOA_2}) = 3.43$, in comparison with both $V^{IV}O$ phosphonoformate and malonate systems. The closure of two rings by CO_2^-, PO_3^{2-} donor sets is somewhat less favourable in phosphono-acetic than -formic acid because of the lower acidity of the dissociable groups and the larger size of the chelated rings. On the other hand, in comparison to the malonate system, the weaker acidity of the phosphonic group and the greater negative charge of the complex are likely the critical factors.

A further conclusion can be drawn from analysis of the EPR data. Significantly different ^{51}V hyperfine constants are measured for complexes provided with the same donor sets, *e.g.* the $2(CO_2^-, PO_3^{2-})$ species. A similar anomaly has already been observed in the oxalate and malonate bis(chelated) complexes, which exhibit A_0 values of 97 and 94 $\times 10^{-4}$ cm^{-1}, respectively.[19] Exactly the same trend, a decrease of A_0 and $A_{\|}$, is observed on replacing phosphono-formic by -acetic acid, indicating that the effect is attributable to the electron-releasing properties of the methylene bridge which makes the donor groups more basic. The same effect could also be detected upon comparing $V^{IV}O$–diphosphate[10] and $V^{IV}O$–methylenediphosphonate systems (see below). Again, the replacement of the electron-withdrawing oxygen by the electron-releasing CH_2 produces an increase in $g_{\|}$ and a decrease in $A_{\|}$.

On the whole, the results of these systems support the coordination of phosphonic and carboxylic groups to $V^{IV}O$ yielding stable PO_3H^-, CO_2^- or PO_3^{2-}, CO_2^--chelated species. Each of these groups, on its own, is not strong enough to hinder hydroxo species formation even in acidic solution. Their cooperative involvement shifts the onset of hydrolysis into the basic pH range.

Methylenediphosphonic and 1-hydroxy(methyl)methylenediphosphonic acid

Methylenediphosphonic acid (H_4A) bears a phosphonic group in the place of the carboxylic moiety of phosphonoacetic acid. 1-Hydroxy(methyl)methylenediphosphonic acid (H_4A) is an α-hydroxyl derivative of methylenediphosphonic acid. Over the measurable pH range three out of four deprotonation processes may be detected for methylene- and two for 1-hydroxy-(methyl)methylene-diphosphonic acid.

These geminal diphosphonates exhibit a complexation scheme different from those of the monophosphonates. In the range pH 3.5–10, the isotropic EPR spectra of the $V^{IV}O$–methylenediphosphonic acid system consist of a broad band (g_0 *ca.* 1.97) to which weak hyperfine components with a splitting of *ca.* 30×10^{-4} cm^{-1} are superimposed. These features, similar to those reported for the cyclic trimer $[(VO)_3A_3]^{6-}$ of diphosphate(4−) which exhibit 22 equally spaced hyperfine lines ($g_0 = 1.965$ and $A_0 = 34 \times 10^{-4}$ cm^{-1}), are as expected for the interaction of an unpaired electron with three equivalent metal nuclei.[10,20–22] Anisotropic spectra (Fig. 3) display a

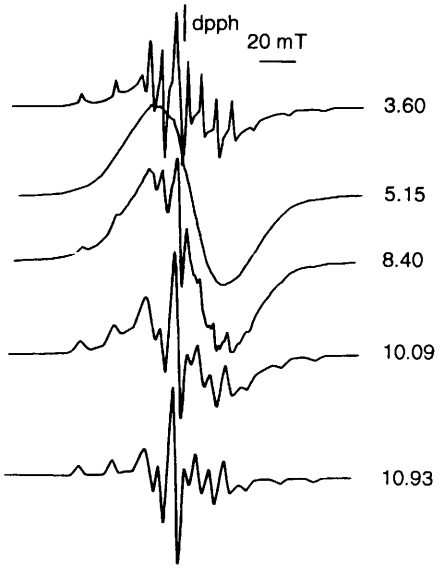


Fig. 3 X-Band EPR spectra recorded at 120 K on aqueous solutions of VO^{2+} (0.002 mol dm^{-3}) and methylenediphosphonic acid at a ligand-to-metal molar ratio of 2:1 with varying pH

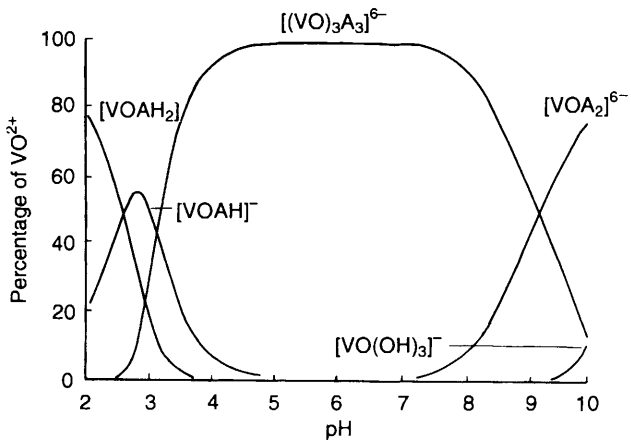


Fig. 4 Concentration distribution curves for the complexes formed in the oxovanadium(IV)–methylenediphosphonic acid system as a function of pH; $c_{VO^{2+}} = 0.002$ and $c_{ligand} = 0.004$ mol dm^{-3}

broad resonance at *g ca.* 2, as in the few cases of $V^{IV}O$ trimers reported so far.[10,23]

Potentiometric data are fitted by taking into account a very stable species $[(VO)_3A_3]^{6-}$ where A is the fully deprotonated methylenediphosphonate(4−) ligand. The species has a cyclic structure with the ligand adopting chelating and bridging modes through the four oxygen atoms.

As shown in the speciation diagram in Fig. 4, mononuclear species $[VOAH_2]$ and $[VOAH]^-$ ($pK_{VOAH_2} = 2.61$) are formed by the protonated forms of the ligand and both of them are chelated. Values of pH higher than 9 favour the $2(PO_3^{2-}, PO_3^{2-})$ bis(chelated) $[VOA_2]^{6-}$ species. It is also seen in Fig. 4 that complex formation is nearly complete at acidic pH and no free VO^{2+} ion is present at the starting pH. In spite of this, reasonable and fairly accurate overall stability constants can be obtained from pH-metric data as the equilibrium system is 'fixed' in the high pH range to the hydroxo species $[VO(OH)_3]^-$.

The constant for the equilibrium $VO^{2+} + H_2A^{2-} \rightleftharpoons [VOAH_2]$ is $10^{4.86}$, a value which can be characteristic for a PO_3H^-, PO_3H^- chelated species. The EPR features of this species are slightly different from those of the aqua ion, as found in the mono(chelated)complexes of ATP and ADP.[15] More different are the parameters of the PO_3^{2-}, PO_3H^- chelated species $[VOAH]^-$, for which an increase in $g_{\|}$ and a decrease in $A_{\|}$ are observed. The $2(PO_3^{2-}, PO_3^{2-})$ donor arrangement in $[VOA_2]^{6-}$ reinforces this trend, analogously for the bis(complexes) of ATP and ADP.[15]

1-Hydroxy(methyl)methylenediphosphonic acid interacts with VO^{2+} even at pH 1.3. A well defined species is observed at pH 2.4–3.6 ($g_{\|} = 1.935$ and $A_{\|} = 179 \times 10^{-4}$ cm^{-1}). Between pH 4 and 9, even at a 10:1 molar excess of ligand, a cyclic trimer is detected (g_0 *ca.* 1.97, A_0 *ca.* 34×10^{-4} cm^{-1}). A mononuclear species analogous to the $[VOA_2]^{6-}$ complex of methylenediphosphonic acid is formed above pH 10 at high ligand excess.

Potentiometric measurements distinguish only a mononuclear $[VOAH]^-$ and a polynuclear $[(VOA)_n]^{2n-}$ species over the range pH 2–9. Again, the best fit was obtained by assuming a trinuclear $[(VO)_3A_3]^{6-}$ species with a stability comparable with that of the corresponding methylenediphosphonic acid complex.

The co-ordination of alcoholate group(s) is detected by EPR spectroscopy in more basic solutions (pH 12–14), where two further monomeric species are sequentially formed. The former, $[VOA_2H_{-1}]^{7-}$, involves two chelated, PO_3^{2-}, PO_3^{2-} and PO_3^{2-}, O^-, rings and upon deprotonation yields $[VOA_2H_{-2}]^{8-}$ with $2(PO_3^{2-}, O^-)$ co-ordination. Noteworthy, the alcoholic group of 1-hydroxy(methyl)methylenediphosphonic acid undergoes deprotonation at pH values significantly higher than those of the methylene analogue. Besides electrostatic factors due to the different charge of the ligands, the high stability of the $2(PO_3^{2-}, PO_3^{2-})$ chelation set could be responsible for this behaviour. The species $[VOA_2H_{-1}]^{7-}$ and $[VOA_2H_{-2}]^{8-}$ are also rather stable and this may be an effect of the size of the five-membered PO_3^{2-}, O^- chelated ring and the rather strong basicity of the alcoholate donor groups. However, this conclusion does not exclude the possibility of tridentate co-ordination for one of the AH_{-1} ligands.

Conclusion

This study confirms the need for combined equilibrium and spectroscopic studies for a complete and unambiguous description of VO^{2+} complex formation processes. In particular, polyprotic phosphonic and phosphate ligands may yield anions able to bind the metal ion in rather acidic solution. Due to the involvement of weak donors, extracting structural information on such species on the exclusive basis of spectroscopic data may be difficult and only the complete deprotonation of the ligand yields spectral parameters distinct enough from those of the aqua ion. However, as observed previously with phosphate complexes,[10] some distinctive spectral trends may be found. For instance, in all systems examined herein the onset of complex formation may be seen in the electronic spectra through a bathochromic shift of the low-energy absorption maximum typical of the aqua ion (Table 2). On the other hand, spectroscopy is powerful in assigning the nuclearity of the species and in following complex formation at rather high ligand excess and in very basic solution.

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