First (Peroxo)vanadium(V) Complex with Heteroligand Formed in Reaction System − Synthesis, Structure and Reactivity of K[VO(O$_2$)(*omeida*)]·H$_2$O {*omeida* = *N*-[2-(2-oxomorpholine-4-yl)ethyl]iminodiacetato(2−)}

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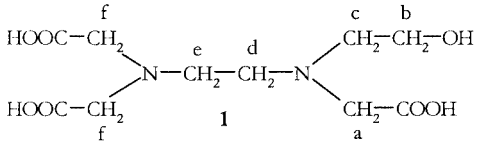
The crystalline peroxo complex of vanadium(V), K[VO(O$_2$)(*omeida*)]·H$_2$O, where *omeida* is a δ-lactone derivative, *N*-[2-(2-oxomorpholine-4-yl)ethyl]iminodiacetate(2−), has been obtained by reaction of vanadate with H$_2$O$_2$ and *N*-(2-hydroxyethyl)ethylenediaminetriacetic acid (*HEDTA*) in acidic aqueous solution at pH = 3 and 278 K. X-ray analysis revealed a distorted pentagonal-bipyramidal coordination around the vanadium atom, with a typical *cis* arrangement of oxo and peroxo ligands in apical and equatorial positions, respectively. Two amino nitrogen atoms of the tetradentate *omeida*(2−)-N^1,N^2,O^1,O^2 ligand occupy the neighbouring equatorial positions of the pentagonal plane, and two oxygen atoms of carboxymethyl groups bound to the same N1 nitrogen atom are in equatorial and apical positions. The six-membered lactone ring in *omeida* was formed in the reaction solution from carboxy and hydroxy groups not involved in coordination with the vanadium atom. The ^{51}V NMR spectra of K[VO(O$_2$)(*omeida*)]·H$_2$O, and of peroxovanadate/*HEDTA*/H$_2$O and vanadate/*HEDTA*/H$_2$O solutions, as well as the ^{1}H NMR spectrum of *HEDTA*, proved that lactone ring closure proceeds only in peroxovanadate but not vanadate solutions. Spectroscopic investigation of the oxygen transfer reaction from the peroxo ligand in [VO(O$_2$)(*omeida*)]$^-$ to the thiolato sulfur atom in [Co(*en*)$_2${S(CH$_2$)$_2$NH$_2$}]$^{2+}$ or [Co(*en*)$_2$(*cyst*)]$^+$, and of the oxidation of *N*-acetyl-L-cysteine by K[VO(O$_2$)(*omeida*)]·H$_2$O, revealed much more complicated reaction mechanisms than those of other (amino-polycarboxylato)monoperoxo complexes of vanadium(V).

Introduction

Monoperoxo complexes of vanadium(V) with polydentate heteroligands *L* providing an N$_x$O$_y$ donor set[1−7] are structural and functional models for the peroxo form of vanadium haloperoxidase, and are also studied for the insulin mimetic properties of vanadium(IV,V) complexes. They are useful models for the peroxo form of the enzyme despite the differing coordination numbers of the vanadium atom in the enzyme and in synthesized monoperoxo complexes. In the active site of the peroxo form, the five-coordinate vanadium atom, in a distorted tetragonal-pyramidal arrangement, is bound to the imidazole nitrogen atom of His496, two non-protein oxygen atoms and two peroxo oxygen atoms of the η^2-peroxo ligand.[8] In previous structurally characterized neutral, anionic or cationic monoperoxo complexes with predominantly seven-coordinate vanadium atom, [VO(O$_2$)*L*], and in anionic diperoxo complexes with six- or seven-coordinate vanadium atom, [VO(O$_2$)$_2$*L*]$^{n-}$, the mono- or polydentate heteroligand *L* used in the synthesis and the ligand bound to the vanadium atom are identical. We describe here the first (peroxo)vanadium(V) complex with heteroligand formed in situ. The reaction of vanadate(V) with H$_2$O$_2$ and *HEDTA* (**1**) in acidic aqueous solution did not result, as expected, in the formation and isolation of an oxo(peroxo)(*hedta*) complex of vanadium(V), but the monoperoxo complex with coordinated *N*-[2-(2-oxomorpholine-4-yl)ethyl]iminodiacetate(2−) (*omeida*) (**2**), K[VO(O$_2$)(*omeida*)]·H$_2$O, crystallized out.



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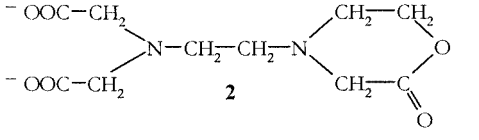

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The reactivity of (peroxo)vanadium(V) complexes as oxidants can be studied in the reaction with a thiolato or cysteinato complex of Co^{III}, in which the peroxo oxygen atom is transferred to the coordinated sulfur atom, while a sulfen-

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ato complex is formed. We have previously determined the rate constants for this reaction using a series of structurally characterized monoperoxo complexes of vanadium(v) that have single-signal ^{51}V NMR spectra in aqueous solution.[6]

The interaction of vanadate with *HEDTA* in the absence of hydrogen peroxide was investigated by Crans et al.[9] Based on ^{51}V and ^{13}C NMR measurements they found that two species exist in aqueous vanadate/*HEDTA* solutions, in which the tetradentate *hedta* ligand coordinates to the vanadium atom either via two amino nitrogen atoms, and carboxylic and alkoxy oxygen atoms in alkaline solutions, or via nitrogen atoms and two carboxylic oxygen atoms in acidic or slightly alkaline solutions.

Results and Discussion

The IR spectrum of K[$VO(O_2)$(*omeida*)]·H_2O exhibits the characteristic bands observed for mono(peroxo)vanadium(v) complexes with coordinated deprotonated polycarboxylato ligands:[3,6,10–12] $\nu(V-O_p)$ at 562 (O_p = peroxo oxygen atom), $\nu(O_p\text{-}O_p)$ at 928, $\nu(V=O)$ at 947, $\nu_s(COO^-)$ at 1399, $\nu_{as}(COO^-) + \delta(H_2O)$ at 1616–1670 cm^{-1}. Moreover, it contains a sharp intense band at 1754 cm^{-1}, which is too high for the stretching vibration in uncoordinated COOH groups (1700–1720 cm^{-1}) – strongly indicating the presence of a "new" short C=O bond in the complex. This was confirmed by X-ray structure analysis which, surprisingly, showed that the heteroligand bound in the complex is not the anion of **1** but a derivative of morpholin-2-one (**2**). Thus, the IR band at 1754 cm^{-1}, which corresponds with the range 1747–1737 cm^{-1} reported for free δ-lactones,[13] and with 1750 cm^{-1} for 4-methylmorpholin-2-one,[14] can be assigned to a C=O stretching vibration in the coordinated *omeida* ligand [*d*(C8–O9) = 1.203(3) Å, Table 1].

Figure 1 illustrates the molecular structure of the [$VO(O_2)$(*omeida*)]$^-$ anion and Table 1 lists selected bond lengths and angles. The structure of [$VO(O_2)$(*omeida*)]$^-$ is mononuclear, with a distorted pentagonal-bipyramidal arrangement around the vanadium atom. The *omeida* dianion is coordinated as tetradentate ligand, providing an N_2O_2 donor set, and forming three five-membered chelate rings. Two carboxylate oxygen atoms, O4 and O6, are in *cis* positions of the bipyramid. Unlike in the [$VO(O_2)$(H*edta*)]$^{2-}$ ion,[15] these deprotonated and coordinated carboxylic oxygen atoms originate from carboxymethyl groups bound to the same N1 nitrogen atom. The pentagonal plane is formed by O2, O3 oxygen atoms of the η^2-peroxo ligand, N1, N2 nitrogen atoms occupying the *cis* positions, and carboxylic O4 oxygen atom. The apical positions of the bipyramid are occupied by doubly bonded oxo ligand O1 and deprotonated carboxylic O6 oxygen atoms. The average standard deviation of atoms from the pentagonal plane is 0.0515 Å. The vanadium atom is displaced from the plane towards the apical O1 oxygen atom by 0.2045(9) Å. This is less than the average value, 0.236 Å, found for other mono(peroxo)vanadium(v) complexes with polydentate aminopolycarboxylates.[3,6,16,17]

Table 1. Selected bond lengths [Å] and angles [°] for K[$VO(O_2)$(*omeida*)]·H_2O

In coordination polyhedron:			
V1–O1	1.605(2)	O1–V1–O3	104.98(9)
V1–O3	1.866(2)	O1–V1–O2	104.40(9)
V1–O2	1.868(2)	O3–V1–O2	45.08(8)
V1–O4	2.048(2)	O1–V1–O4	95.85(8)
V1–O6	2.106(2)	O1–V1–O6	164.80(8)
V1–N1	2.197(2)	O3–V1–O6	89.98(8)
V1–N2	2.282(2)	O2–V1–O6	87.98(8)
O2–O3	1.431(3)	O4–V1–O6	83.78(7)
		O1–V1–N1	88.63(8)
		O4–V1–N1	74.98(7)
		O6–V1–N1	76.57(7)
		O1–V1–N2	88.23(8)
		O6–V1–N2	85.24(7)
		N1–V1–N2	77.53(7)
In coordinated 2-oxomorpholine:			
O8–C8	1.339(3)	C8–O8–C9	120.8(2)
O8–C9	1.460(3)	C10–N2–C7	106.2(2)
O9–C8	1.203(3)	N2–C7–C8	115.9(2)
N2–C10	1.484(3)	O9–C8–O8	118.6(3)
N2–C10	1.484(3)	O9–C8–C7	120.7(3)
N2–C7	1.486(3)	O8–C8–C7	120.6(2)
C7–C8	1.511(4)	O8–C9–C10	113.5(2)
C9–C10	1.510(4)	N2–C10–C9	111.3(2)

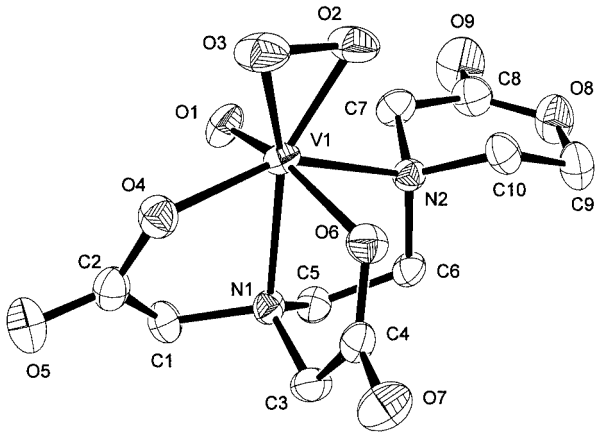


Figure 1. X-ray crystal structure of the anionic complex [$VO(O_2)$(*omeida*)]$^-$, showing the atomic numbering scheme; hydrogen atoms are omitted for simplicity; the ORTEP plot is drawn at a 50% probability

The generally observed *trans* effect, i.e. the elongation of the apical V–O6 bond *trans* to the short V–O1 bond when compared with the equatorial V–O4 distance, given by $\Delta d(V-O)$ = 0.058 Å, is also much less significant than in other polycarboxylato complexes with ligands that provide an NO_3 donor set [$\Delta d(V-O)$ = 0.073–0.200 Å],[6] and even in the (carboxymethyl)histidinato(2–) complex, K[$VO(O_2)$(*cmhist*)]·H_2O,[18] with $\Delta d(V-O)$ = 0.099 Å. The latter complex was previously the only structurally well-characterized peroxo complex with the same arrangement of N_2O_2 donor set atoms around the vanadium atom as in the complex studied here. Both in K[$VO(O_2)$(*cmhist*)]·H_2O and K[$VO(O_2)$(*omeida*)]·H_2O, the N2 atoms are from the heterocycles imidazole and morpholin-2-one, respectively.

The pentagonal bipyramid in $[VO(O_2)(omeida)]^-$ is not symmetric: the O2, O3 peroxo oxygen atoms deviate from the O1,V1,N1,O6 plane by 0.6354(29) and 0.7952(29) Å, respectively. Two glycinate rings, the almost planar "apical" one formed by V1, N1, C3, C4, O6 atoms (deviation of fitted atoms 0.0725 Å) and the "equatorial" one formed by V1, N1, C1, C2, O4 atoms (deviation of fitted atoms 0.2318 Å), are perpendicular (89.92°). Only one hydrogen bond between the oxygen atom of a water molecule and the uncoordinated O7 carboxylic oxygen atom with $d(H_w-O7)$ = 1.990(60) and $d(O_w-O7)$ = 2.797(3) Å has been found. Similarly, as in the (carbamoylethyl)iminodiacetato complex, $K[VO(O_2)(ceida)]\cdot 2H_2O$,[6] the potassium cation in $K[VO(O_2)(omeida)]\cdot H_2O$ is coordinated by seven oxygen atoms, one of a water molecule, three end-bonded carboxylic oxygen atoms (O5, O5, O7) of three different anions, and two carboxylic (O4, O6) and an O3 peroxo oxygen atoms coordinated to the same vanadium atom. The K−O distances range from 2.667(2) to 3.007(2) Å. The distance to the eighth oxygen atom, 3.428 Å, exceeds the 3.25 Å of any other higher coordination number.[19]

^{51}V NMR Measurements

All ^{51}V NMR spectra were measured at 278 K, the same temperature at which $K[VO(O_2)(omeida)]\cdot H_2O$ was synthesized. The ^{51}V NMR spectrum of a 0.015 M aqueous solution of $K[VO(O_2)(omeida)]\cdot H_2O$ (Figure 2, a), measured 7 min after dissolution, exhibits a single peak at δ = −515 ppm ($W_{1/2}$ = 450 Hz). This shift is unusually low for a heteroligand mono(peroxo)vanadate and it occurs in the region where, mostly, the chemical shifts for heteroligand dioxo complexes of vanadium(v) are observed.[20−23] However, the UV/Vis spectrum of the same solution exhibits the peroxo-to-vanadium CT band at λ_{max} = 439 nm (ε = 357 $mol^{-1}\cdot dm^3\cdot cm^{-1}$), which is within the 410−460 nm range typical for monoperoxo complexes of vanadium(v).[24,25] The chemical shift δ = −515 ppm can thus be assigned to the $[VO(O_2)(omeida)]^-$ ion **I** (Scheme 1). The presence of a single peak allows us to suggest that the molecular structure of the complex anion is maintained on dissolution. After 24 h, 95% of the vanadium is still in solution in the form of **I**, as well as a minor species with $\delta(^{51}V)$ = −567 ppm ($W_{1/2} \approx$ 260 Hz) (Figure 2, b), which we assign to an isomeric peroxo(*omeida*) complex **II**, because no absorbance decrease due to peroxo ligand decomposition was observed in the UV/Vis spectrum. The smaller $W_{1/2}$ value for **II** is in accordance with its higher symmetry when compared with **I** (Scheme 1). Further evidence for the assignment of **I** and **II** was provided by the ^{51}V NMR spectra of aqueous peroxovanadate/*HEDTA*, vanadate/*HEDTA* and peroxovanadate/*HEDTA*/*OMEIDA* solutions (*OMEIDA* = *N*-[2-(2-oxomorpholin-4-yl)ethyl]iminodiacetic acid), measured at the same pH as used in the synthesis.

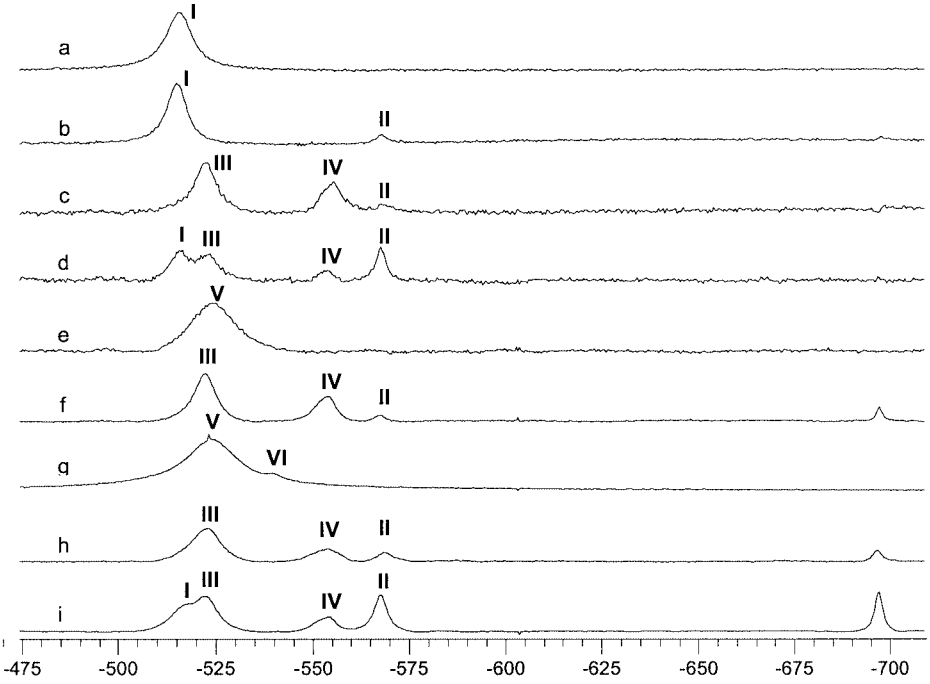
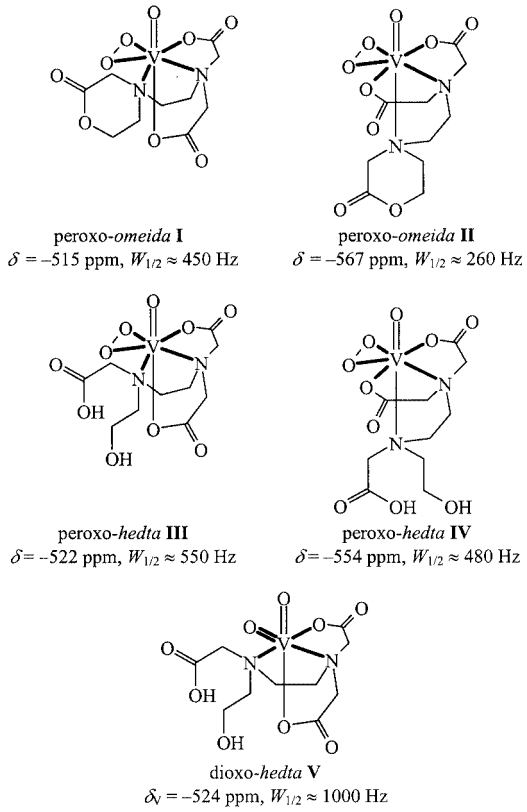


Figure 2. Selected ^{51}V NMR spectra of aqueous solutions at 278 K; a, b: 0.015 M $K[VO(O_2)(omeida)]\cdot H_2O$, (a) 7 min, (b) 24 h after dissolution; c, d: peroxovanadate/*HEDTA* solutions, (c) 15 min, (d) 5 d after preparation, concentrations: see Table 2; e, f: vanadate/*HEDTA* solutions, (e) 8 min to 70 h after preparation, (f) after addition of 1 mmol H_2O_2 to the solution (e) prepared 70 h before addition; g: vanadate/*HEDTA*/*OMEIDA* solutions, c(**3**ii) = 0.15 M, $c(KVO_3)$ = 0.075 M; h: peroxovanadate/*HEDTA*/*OMEIDA* (**3**i) solutions, c(**3**i) = 0.15 M, $c(KVO_3)$ = 0.075 M, $c(H_2O_2)$ = 0.225 M; i: peroxovanadate/*HEDTA*/*OMEIDA* (**3**ii) solutions, c(**3**ii) = 0.15 M, $c(KVO_3)$ = 0.075 M, $c(H_2O_2)$ = 0.225 M; pH(c−i) = 3.0



Scheme 1. ^{51}V NMR spectral characteristics and proposed structures of dioxo(*hedta*)-, monoperoxo(*hedta*)- and monoperoxo(*omeida*)vanadates formed in vanadate/*HEDTA*/H_2O and peroxovanadate/*HEDTA*/H_2O solutions

Peroxovanadate/HEDTA/H_2O Solutions (pH = 3)

Preparation: 0.225 mmol of H_2O_2 (0.022 mL, w = 30%) was added to 0.15 mmol of KVO_3, dissolved in H_2O (5 mL), and 0.3 mmol of *HEDTA* was then dissolved in the resultant solution. Before making up to the total volume of 10 mL, the pH was adjusted with 0.5 M KOH. Changes in the ^{51}V NMR spectrum of the peroxovanadate/*HEDTA*/H_2O solution with time allowed us to observe the formation of the peroxo(*hedta*) species and their subsequent transformation into the peroxo(*omeida*) complexes **I** and **II**. The spectrum measured 15 min after preparation of the solution (Figure 2, c) exhibits shifts of two dominant species at δ = −522 ppm (**III**) (I_{rel} = 63%, $W_{1/2}$ ≈ 550 Hz) and −554 ppm (**IV**) (I_{rel} = 31%, $W_{1/2}$ ≈ 480 Hz), and two minor species with shifts at δ = −567 ppm (I_{rel} ≈ 3%) and −697 ppm, the latter being the shift of the heteroligand-free diperoxo ion $[VO(O_2)_2(H_2O)_x]^-$.[26,27] We assign the major species **III** and **IV**, to isomeric monoperoxo(*hedta*) complexes (Scheme 1) formed immediately after mixing the solutions, which then undergo the lactone ring closure, while the monoperoxo(*omeida*) complexes **I** and **II** are formed. After 20 h, the peak at δ = −515 ppm corresponding to complex **I**, with known solid structure, appeared (I_{rel} = 11%), which after 5 d became the predominant species (I_{rel} = 40%). The increase of I_{rel}(**I** + **II**) for the monoperoxo(*omeida*) species with time is proportional to the decrease of I_{rel}(**III** + **IV**) for the monoperoxo(*hedta*) complexes (Table 2). This indicates that lactone formation under such mild conditions proceeds on the ligand coordinated to the $VO(O_2)^+$ moiety. Under same conditions, free *HEDTA* does not undergo cyclization, as evidenced by its unchanged ^{1}H NMR spectrum.

Table 2. Dependence of I_{rel} on time for monoperoxo(*omeida*) (**I**, **II**) and monoperoxo(*hedta*) (**III**, **IV**) complexes formed in peroxovanadate/*HEDTA*/H_2O solutions at pH = 3; conditions: T = 278 K, concentrations: 0.015 M vanadate, 0.03 M *HEDTA*, 0.023 M H_2O_2

Species	δ [ppm]	$W_{1/2}$ [Hz]	I_{rel} [%][a]					
			15 min	90 min	20 h	24.5 h	2 d	5 d
I	−515	ca. 520	–	–	11[b]	12[b]	19.5[b]	40[b]
II	−567	ca. 260	3	5.5	13	15.5	19	22.5
III	−522	550	63	60	48[b]	45[b]	39[b]	23[b]
IV	−554	480	31	29	24	20	18.5	13

[a] Difference between the sum of I_{rel} for **I**−**IV** and 100% corresponds to I_{rel} for $[VO(O_2)_2(H_2O)x]^-$. [b] Values obtained by deconvolution.

Vanadate/HEDTA/H_2O Solutions (pH = 3)

Preparation: 1 mmol of *HEDTA* was dissolved in 0.1 M KOH (4 mL), 0.5 mmol of KVO_3 (1 mL, 0.5 M) and 0.5 M KOH (0.4 mL) were added, and the total volume made up to 10 mL. Relevant data on the formation of the dioxo- and monoperoxo(*omeida*) complexes were also provided by changes in the ^{51}V NMR spectra of the vanadate/*HEDTA*/H_2O solutions with time, and spectra of the same solutions to which 1 mmol of H_2O_2 (0.1 mL, w = 30%) was added just before NMR measurements. The spectrum of the vanadate/*HEDTA*/H_2O solution, measured 8 min to 70 h after preparation of the solutions, remained unchanged (Figure 2, e). It exhibits a very broad single peak with δ = −524 ppm ($W_{1/2}$ ≈ 1200 Hz), which is similar to data observed for the $[VO_2(Hedta)]^{2-}$ ion (δ = −518 ppm, $W_{1/2}$ ≈ 1000 Hz).[23] We consider the species with δ = −524 ppm to be the dioxo(*hedta*) complex **V**, $[VO_2(hedta)]^{n-}$, which is identical to the species found by Crans[9] in vanadate/*HEDTA* solutions at 298 K in the pH range 5−9 (δ = −520 ppm, $W_{1/2}$ = 710 Hz). The shift by 4 ppm and the signal broadening (710 → 1200 Hz) is caused by the lower temperature in our measurements. In the complex **V**, the *hedta* ligand was proposed to be bound via two amino nitrogen atoms and two carboxylic oxygen atoms.[9] However, when H_2O_2 was added after 8 min, or after 8, 24 and 70 h to the prepared vanadate/*HEDTA*/H_2O solutions, the spectra (Figure 2, f) exhibited, besides the shift of $[VO(O_2)_2(H_2O)_x]^-$ (I_{rel} ≈ 4%), three peaks with identical chemical shifts and $W_{1/2}$ values to those for **II**, **III** and **IV** (Table 2). The small change in chemical shifts (−524 → −522 ppm) but the significant change in $W_{1/2}$ (1200 → 540 Hz), both evidently occurring in all spectra after the addition of H_2O_2, confirmed the formation of the dioxo- and peroxo(*hedta*) species before and after the addition of hydrogen peroxide, respectively. The relative intensities for

II−**IV** do not significantly change with the time of addition of H_2O_2, and were approx. 62% for **II**, 29% for **III**, and 5% for **IV**. Monoperoxo(*omeida*) complex **I** was not observed, even when H_2O_2 was added after 70 h to the vanadate/*HEDTA*/H_2O solution, i.e. after a time when a significant amount of **I** has formed in the peroxovanadate/*HEDTA*/H_2O solution (Table 2). Thus, lactone ring closure and the formation of peroxo(*omeida*) complex **I** from *HEDTA* is, under the given conditions, a slow process that proceeds only in the peroxovanadate solution.

Alkaline Solution of K[VO(O$_2$)(omeida)]·H$_2$O (pH = 8.5)

Preparation: 0.5 M KOH (0.2 mL) was added to 0.15 mmol of the complex, dissolved in H_2O (8 mL), and the volume made up to 10 mL. Generally, lactone rings open in alkaline media and, indeed, ring opening was observed in the NMR spectrum of a 15 mM aqueous solution of K[$VO(O_2)$(*omeida*)]·H_2O measured just 12 min after preparation. The spectrum's six peaks correspond to monoperoxo(*omeida*) complexes **I**, **II** (I_{rel} = 67, 7.5%, respectively), monoperoxo(*hedta*) complexes **III**, **IV** (I_{rel} = 11, < 1%, respectively), and two minor species with signals at δ = −499 ppm (I_{rel} = 3.5%) and −750 ppm (I_{rel} = 6%). The δ = −499 ppm shift corresponds to $[VO_2(hedta)]^{n-}$, with *hedta* coordinated in alkaline solutions (pH = 7−11) via the alkoxy group,[9] and the δ = −750 ppm shift to the diperoxovanadate species which exhibit, over a wide pH range (0.5−11), a strong pH dependence of δ values (−690 to −765 ppm).[26,28] After 8 h, I_{rel}(**I** + **II**) decreased to 33% and I_{rel}(**III** + **IV**) increased to 61%, whereas I_{rel} for the diperoxovanadate remained almost constant. These and previous measurements show that the pH change between 3.0 and 8.5 has no influence on the chemical shifts for **I**−**IV**. These constant chemical shifts over a wide pH range provide an additional indirect confirmation of the assignment for **III** and **IV**, because the shifts for mono- or dimeric vanadates with chemical shifts δ = −550 to −570 ppm, which could be also present in solution as uncomplexed vanadium forms, exhibit a pH dependence in the region discussed.[26]

Vanadate/HEDTA/OMEIDA/H$_2$O and Peroxovanadate/HEDTA/OMEIDA/H$_2$O solutions (pH = 3)

In a further series of experiments that confirmed the above conclusions, we measured the ^{51}V NMR spectra of vanadate and peroxovanadate solutions with *HEDTA*/*OMEIDA* heteroligand solution (**3**) prepared by: (i) refluxing for 20 h the 0.7 M aqueous solution of *HEDTA* (pH = 1, acidified with 1 M $HClO_4$) or (ii) refluxing the same solution for 25 h after it had stood for 3 weeks at room temperature. In such solutions, the formation of *OMEIDA* is expected, as the cyclization of chelating aminopolycarboxylic acids is favored by higher temperature and lower pH.[29] The vanadate/*HEDTA*/*OMEIDA*/H_2O solution for NMR measurements was prepared as follows; to avoid, in the absence of H_2O_2, the formation of $H_xV_{10}O_{28}^{(6-x)-}$ ions which have a poor complex formation ability, solution **3** (2 mL, 0.7 M) was mixed with 1.5 mL of alkalized 0.5 M KVO_3 (prepared by dissolving the metavanadate in 0.1 M KOH). The pH of the resulting solution was then adjusted to 3 by addition of 0.2 mL of 0.5 M KOH. The spectrum of vanadate/*HEDTA*/*OMEIDA*/H_2O solution prepared from **3**(i) exhibits a single shift at δ = −524 ppm ($W_{1/2}$ ≈ 1200 Hz). The spectrum of the same solution, however, prepared using the heteroligand solution **3**(ii) (Figure 2, g) gave on deconvolution two shifts, at δ = −524 ppm ($W_{1/2}$ ≈ 1250 Hz, I_{rel} = 86%) due to dioxo(*hedta*) complex **V**, and at δ = −539 ppm ($W_{1/2}$ ≈ 355 Hz, I_{rel} = 14%), which we assign to a dioxo(*omeida*) complex **VI**, $[VO_2(omeida)]^-$. The spectra of the peroxovanadate/*HEDTA*/*OMEIDA*/H_2O solutions (prepared in the same way but with addition of 0.23 mL of 30% H_2O_2) showed (Figure 2, h and i) that, with increased reaction time for lactone formation in **3**(i), with respect to **3**(ii), the sum of I_{rel} for monoperoxo(*omeida*) complexes (**I**, **II**) increased from 12 to 43%, while I_{rel} for the monoperoxo(*hedta*) species (**III**, **IV**) decreased from 81 to 41%. These results showed that *HEDTA* in solutions **3** was not completely transformed into *OMEIDA*, i.e. the lactone closure does not proceed easily in the absence of peroxovanadate even at high temperatures and long reaction times. *OMEIDA* has not yet been synthesized as a pure solid; only its dimethyl and diethyl esters are known.[30]

Reactivity of K[VO(O$_2$)(*omeida*)]·H$_2$O

Previously,[6,31] we investigated the kinetics of oxygen transfer reaction from the peroxo ligand in a series of (amino-polycarboxylato)- or (pyridinecarboxylato)monoperoxovanadates, $[VO(O_2)L]$, to the thiolato sulfur atom in $[Co(en)_2\{S(CH_2)_2NH_2\}]^{2+}$ as a pseudo-monomolecular reaction in excess of the vanadium complex [Equation (1)].

$$[VO(O_2)L] + [Co(en)_2\{S(CH_2)_2NH_2\}]^{2+} \rightarrow VO_2L + [Co(en)_2\{SO(CH_2)_2NH_2\}]^{2+} \quad (1)$$

The first-order rate constants at 298 K lead to the following sequence of increasing reactivity: $[VO(O_2)(ada)]^- < [VO(O_2)(ceida)]^- < [VO(O_2)(nta)]^{2-} < [VO(O_2)(quin)_2]^{3-} < [VO(O_2)(H_2O)_2(pic)]$, which correlates with the charge-transfer energy and temperature of active oxygen release. However, Equation (1) with $[VO(O_2)(omeida)]^-$ as oxidant provided some unexpected results. Under both pseudo-mono- and bimolecular reaction conditions, a linear increase of the sulfenato complex concentration with time was found, as is known for zero-order reactions. The same course of concentration change was also observed in a reaction solution from which dissolved dioxygen was bubbled out by nitrogen, and also in a solution kept out of the cell compartment, i.e. not irradiated by 371 nm light. The participation of molecular oxygen in the reaction, or photochemical effects, can thus be excluded. Even the 1:1 reaction of $[VO(O_2)(omeida)]^-$ with the cysteinato complex, $[Co(en)_2(cyst)]^+$, could not be evaluated as a bimolecular reaction, as the relationship between absorbance and time is given by $1/A = a - b \times \ln t$ (Figure 3).

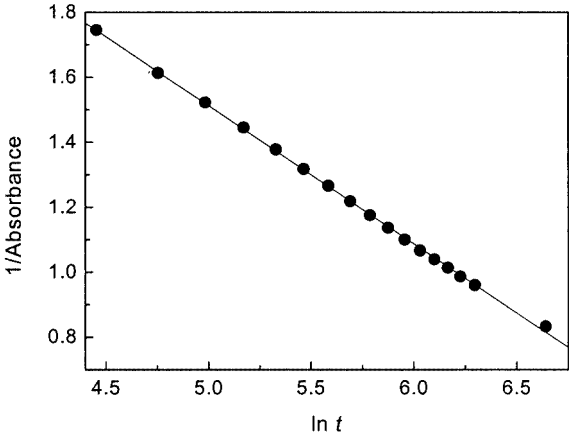


Figure 3. Reciprocal absorbance at 371 nm vs. ln[function of time] for 1:1 aqueous solution of $[VO(O_2)(omeida)]^-$ (**I**) and $[Co(en)_2(cyst)]^+$; c = 0.0007 M, T = 298.2 K, measured in a closed 1-cm cell under nitrogen

We further investigated the interaction of $[VO(O_2)(omeida)]^-$ with *N*-acetyl-L-cysteine at 37 °C. This is of interest with respect to the insulin mimetic properties of vanadium(IV) and -(V) complexes, which include (carboxymethyl)aspartato(3−) complex, $K_2[VO(O_2)(cmaa)(H_2O)]$, prepared according to the literature[32,33] and which have been recently studied in vitro by Rehder et al.[34] The biological activity of *N*-acetyl-L-cysteine, which, for example, inhibits the phosphorylation of tyrosine in cellular proteins caused by peroxovanadates,[35] has an important effect in chronic bronchitis[36] or improves by increased oxygen delivery the survival of patients with hepatic failure.[37] The changes in the UV/Vis spectrum of a 1:5 solution of $[VO(O_2)(omeida)]^-$ and N-acetyl-L-cysteine with time showed that about one-third of the $[VO(O_2)(omeida)]^-$ was decomposed in 6 h. The concentration decrease with time is linear even in this reaction (Figure 4).

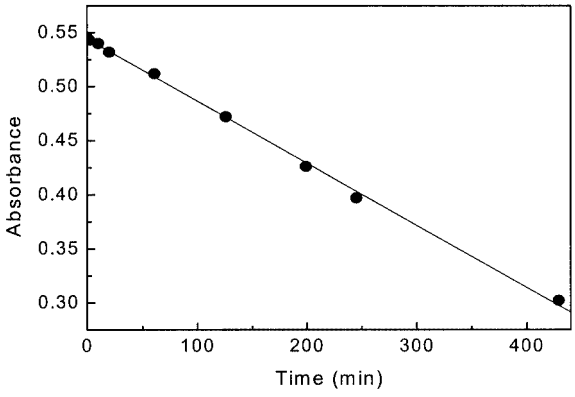


Figure 4. Absorbance at 440 nm vs. time for 1:5 aqueous solution of $[VO(O)_2(omeida)]^-$ (**I**) and *N*-acetyl-L-cysteine; c = 0.0015 and 0.0075 M, respectively; T = 310 K, measured in closed 1-cm cell under nitrogen

The absorbance changes linearly up to a high degree of conversion, i.e. for more than just the initial phase of reaction, where linearity of the measured property is common. These reactions obviously exhibit "mixed kinetics", i.e. the observed absorbance change corresponds to several reaction types. The mechanism of oxidation, both of Co^{III} complexes and *N*-acetyl-L-cysteine by $[VO(O_2)(omeida)]^-$, is thus more complicated than that found for other heteroligand monoperoxo complexes of vanadium(V).[31] A detailed kinetic study is needed to elucidate the reaction mechanism.

Conclusions

The reaction of aqueous peroxovanadate with *HEDTA* resulted in the formation and isolation of a crystalline monoperoxo complex of vanadium(V) with the dianion of *OMEIDA*, $K[VO(O_2)(omeida)]\cdot H_2O$. The crystal structure determination revealed that the vanadium atom in $[VO(O_2)(omeida)]^-$ is in a typical distorted pentagonal-bipyramidal arrangement, and is coordinated by oxygen atoms of the oxo and η^2-peroxo ligands, and by N_2O_2 donor set atoms of the tetradentate *omeida* heteroligand. ^{51}V NMR measurements showed that the heteroligand is formed in situ (pH = 3, 278 K) only in peroxovanadate but not vanadate solutions. The ^{51}V NMR spectra revealed two isomeric monoperoxo(*hedta*) complex anions and their transformation into isomeric monoperoxo(*omeida*) complexes. The $VO(O_2)(omeida)]^-$ ion as oxidant in the reaction with thiolato or cysteinato complexes of Co^{III} and with *N*-acetyl-L-cysteine, both under pseudo-mono- or bimolecular conditions, showed unusual kinetic behaviour: linear concentration changes with time. The elucidation of the reaction mechanism requires a further kinetic study.

Experimental Section

General Remarks: The FT IR spectrum (Nujol mull) was registered with a Nicolet Magna 750 spectrometer. The NMR spectra were recorded with a Varian Gemini 2000 spectrometer (300 MHz for ^1H). ^{51}V NMR spectra were recorded at 78.879 MHz in a 5-mm diameter NMR vial and with a capillary with D_2O immersed in the measured aqueous solution. Typical parameters were: sweep width 32 kHz, line broadening factor 20 Hz, acquisition time of 63 ms with a relaxation delay 10 ms. The chemical shifts are related to $VOCl_3$ as external standard. The V NMR 6.1 program was used to deconvolute spectra between δ = −490 and −530 ppm. The ^1H NMR spectra in D_2O were obtained by using standard parameters. The UV/vis spectral and kinetic measurements were performed with a Hewlett−Packard 8452 spectrometer with a thermostatted (±0.1 °C) compartment. ^1H NMR data of *HEDTA*: (278 K, c = 0.01 M): δ = 3.873 (s, a), 3.831 (t, b), 3.495 (t, c), 3.337 (t, e), 3.723 (s, f) (lettered according to formula **1**).

Synthesis of $K[VO(O_2)(omeida)]\cdot H_2O$: KVO_3 (0.28 g, 2 mmol), prepared from V_2O_5 and KOH at pH ≈ 8, was dissolved under heating in water (10 mL). The solution was then ice-cooled and H_2O_2 (0.3 mL, 30%; Slavus, Slovakia) was added. To the resulting red peroxovanadate solution, *HEDTA* (0.56 g, 2 mmol; Aldrich) was added in small portions whilst stirring. The pH was adjusted to 3.0 with 2 M KOH, and ethanol (15 mL) was added dropwise to initiate the crystallization. The small amount of initially formed orange

precipitate dissolved within 24 h. From the refrigerated solution (5 °C), kept in closed vessel, very dark red crystals of K[VO(O_2)(*omeida*)]·H_2O crystallized out within 2 weeks. Yield: 0.26 g, 31.5%. Monocrystals suitable for X-ray analysis were obtained by crystallization from the first filtrate. After isolation, the product was washed with cooled ethanol (5 °C) and dried over silica gel at 5 °C. The peroxo complex formed is very stable in the reaction solution: we have obtained identical products even on subsequent crystallization from the mother solution within three months. The repeated CHN analysis and IR spectra showed that the solid complex is stable for several months when kept at 5 °C. $C_{10}H_{16}KN_2O_{10}V$ (414.3): calcd. C 28.96, H 3.89; K 9.44, N 6.76, O_2^{2-} 7.72; found C 28.66, H 3.77, K 8.98, N 6.44, O_2^{2-} 7.62. C, H and N contents were determined with a Carlo−Erba 1106 analyzer, peroxide by iodometric titration and potassium by flame photometry (Flapho 4, Zeiss Jena). IR: $\tilde{\nu}$ = 422 vw, 431 w, 494 m, 530 m, 562 s, 596 w, 657vw, 730 m, 743 m, 814 m, 883 s, 928 vs, 947 vs, 972 w, 987 m,1010 w, 1077 w, 1064 w, 1064 vw, 1094 s, 1115 w,1129 vw, 1167 vw, 1222 s, 1248 w, 1265 s, 1283 m, 1300s, 1318 s, 1339 m, 1353 s, 1399 vs, 1488 w, 1616 vs, 1643 vs, 1671 vs sh, 1731 m, 1754 vs, 3367 s, 3544 m cm^{-1}.

Kinetic Measurements: Oxidation of the thiolato and cysteinato complexes, $[Co(en)_2\{S(CH_2)_2NH_2\}]^{2+}$ and $[Co(en)_2(cyst)]^+$, was monitored at 371 nm, corresponding to absorption maximum for the sulfenato complex formed. $[Co(en)_2\{S(CH_2)_2NH_2\}](ClO_4)_2$ and $[Co(en)_2(cyst)]ClO_4$ were synthesized according to published procedures.[38,39] The reaction with *N*-acetyl-L-cysteine was monitored at the wavelength of absorption maximum for $[VO(O_2)(omeida)]^-$ (440 nm).

X-ray Crystallographic Study: The X-ray measurements were taken at 293 K with a KUMA CCD diffractometer with graphite-monochromated Mo-K_α radiation by using the ω-2θ scan technique. No significant decay of the intensity was observed. The data were not corrected for absorption effects. Some 2246 reflections with $I > 2\sigma_I$, of all unique reflections obtained, were classified as observed. Crystallographic data for K[VO(O_2)(*omeida*)]·H_2O: dark red crystals, 293(2) K, $KVC_{10}H_{16}N_2O_{10}$, M_r = 414.29, monoclinic, a = 18.0558(12), b = 6.9241(4), c = 12.0978(8) Å, β = 99.695°, V = 1490.9(2) $Å^3$, Z = 4, space group $P2_1/c$, $D_{calcd.}$ = 1.846 g/cm^3, λ = 0.71073 Å, $R1$ = 0.0323, $wR2$ = 0.0866, $R1 = F_o - F_c/F_o$, $wR2 = \{[w(||F_o|^2 - |F_c|^2|)^2]/[w(F_o^4)]\}^{1/2}$. CCDC-178735 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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