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Notes

Coordination and Oxidation of *N,N'*-Bis(*o*-mercaptophenyl)ethylenediamine (HS*NN*SH) by VO^{2+}: {V($^-$*SNNS*$^-$)}$_4$(μ-O)$_4$ and Tetrabenzotetrathiatetraazacycloeicosane

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Introduction

Vanadate (under physiological conditions $H_2VO_4^-$), which is involved in a manifold of enzymatic phosphorylation reactions,[1] is reduced in the intracellular medium to vanadyl (VO^{2+}) by reducing agents such as ascorbate, NADH, or glutathione. The inhibition of enzymes containing thiol groups in the active center has been traced back to, inter alia, a redox reaction between vanadate and the sulfhydryl. In the case of glyceraldehyde 3-phosphate dehydrogenase, such a reaction, resulting in the inhibition of glycolysis, has been verified.[2] More recently, it was suggested that intracellular reduction to the $\mathrm{V^{III}}$ state may occur.[3] This possibility is supported by the size of the redox potential[4] and by the occurrence of $\mathrm{V^{III}}$ in several vanadate-metabolizing organisms.[5] The interaction of vanadyl with thiolates is further of interest in the view of the use of $\mathrm{V^{IV}}$ compounds as catalysts in the oxidation of organic sulfides to sulfoxides[6] and a possible catalytic role of $\mathrm{V^{IV}}$ in dehydrosulfurization of crude oil and also in the context of an approach toward structural models of the cofactor vanadium site in vanadium nitrogenase.[7]

On the basis of these considerations, we have investigated the reactivity of $\mathrm{V^{IV}}$ toward hybrid ligands containing *OS* (e.g. *o*-mercaptopyridine *N*-oxide[8]) and *NS* ligand sets. Here, we describe a noteworthy reaction of VO^{2+} with the tetradentate ligand *N,N'*-bis(*o*-mercaptophenyl)ethylenediamine (HS*NN*SH, H_2-**1**[9]), the coordination behavior of which toward metal ions such as $\mathrm{Fe^{II}}$, $\mathrm{Mo^{II}}$, and $\mathrm{Ru^{II}}$ has been reported earlier.[10] Reported examples of vanadium complexes with alternate *NS*-functional ligands are the $\mathrm{V^{III}}$ complexes V(*NS*$^-$)$_3$ (H*SN* = *o*-mercaptopyridine and *o*-mercaptoaniline[11a]), the $\mathrm{V^{IV}}$ complex VO($^-$*SNNS*$^-$)' ((HS*NNS*H)' is the double Schiff base derived from ethylenediamine and thiosalicycladehyde[11b]), and the dinuclear $\mathrm{V^{IV}}$ complex V_2O_2(*NS*$^-$)$_4$ with H*NS* = *o*-mercaptopyridine.[11c]

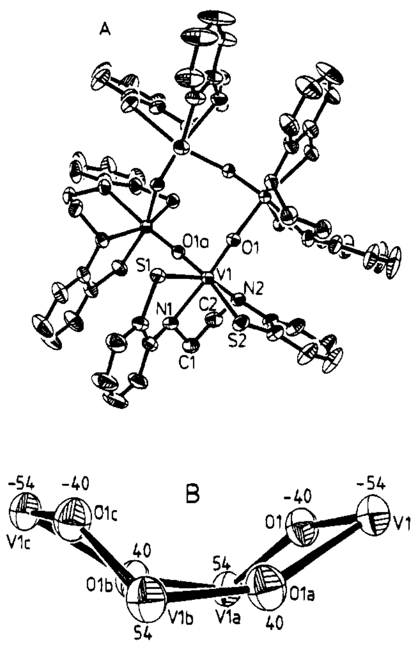

Figure 1. ORTEP drawing (50% probability ellipsoids) of **2**: (A) view of the complete tetramer; (B) central V_4O_4 ring (S_4 point symmetry) in side view with deviations (in pm) of the atoms from the ideal plane. Selected bond distances (Å) and angles (deg): V1–O1 1.652(3), V1–O1a 2.014(3), V1–N1 2.263(4), V1–N2 2.145(4), V1–S1 2.387(2), V1–S2 2.343(1); O1a–V1–S2 165.28(9), S2–V1–O1 100.1(1), S2–V1–S1 90.06(5), S2–V1–N1 89.4(1), S2–V1–N2 84.1(1).

Results and Discussion

Reaction of Na_2-**1** with $VOCl_2(thf)_2$ yields (cf. Scheme 1) the tetranuclear $\mathrm{V^{IV}}$ complex {V($^-$*SNNS*$^-$)}$_4$(μ-O)$_4$, **2** (maximum yield 73%), along with an oxidation product of the ligand, tetrabenzo[*c,i,m,s*][1,2,11,12]tetrathia[5,8,15,18]tetraazacycloeicosane (**3**) in minimum yields of 8%. Oxidation occurs at the thiolate groups, leading to a connection of two of the dianions **1** via disulfide bridges to form **3**. This oxidation hence corresponds to the enzymatic and nonenzymatic oxidation of thiols (cysteine residues) to disulfides (cystine bridges) in biological systems. Since the reaction was carried out under strict exclusion of air, $\mathrm{V^{IV}}$ is the only oxidant available. Furthermore, in the presence of air but absence of $\mathrm{V^{IV}}$, oxidation of **1** does not lead to **3**. We have not established the formation of $\mathrm{V^{III}}$ unambiguously. However, we have been able to show

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[4] $E°$ for V^{3+}/VO^{2+} in water is 0.309 V (Fiore, M.; Orecchio, S.; Romano, V.; Zingales, R. *J. Chem. Soc., Dalton Trans.* **1993**, 799). In the context of the role of sulfhydryl groups, the reversible redox pair $[\mathrm{V^{III}}(pec)_2]^-/\mathrm{V^{IV}}(pec_2)$ (0.24 V; pec = penicillaminate(1−)) is of interest (Maeda, H.; Kanamori, K.; Michibata, H.; Konno, T.; Okamoto, K.; Hidaka, J. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 790).

[5] Vanadium-accumulating sea squirts mainly on the genus *Phleobranchia* (Brand, S. G.; Hawkins, C. J.; Marshall, A. T.; Nette, G. W.; Parry, D. L. *Comp. Biochem. Physiol., B* **1989**, *93*, 425) and the fan worm *Pseudopotamilla occelata* (Ishii, T.; Nakai, I.; Numako, C.; Okoshi, K.; Otake, T. *Naturwissenschaften* **1993**, *80*, 268). Moreover, $\mathrm{V^{III}}$ is formed in the course of bacterial reduction of vanadate by *Pseudomonas vanadiumreductans* (Lyalikova, N. N.; Yukova, N. A. *Geomicrobiol. J.* **1992**, *10*, 15).

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Scheme 1

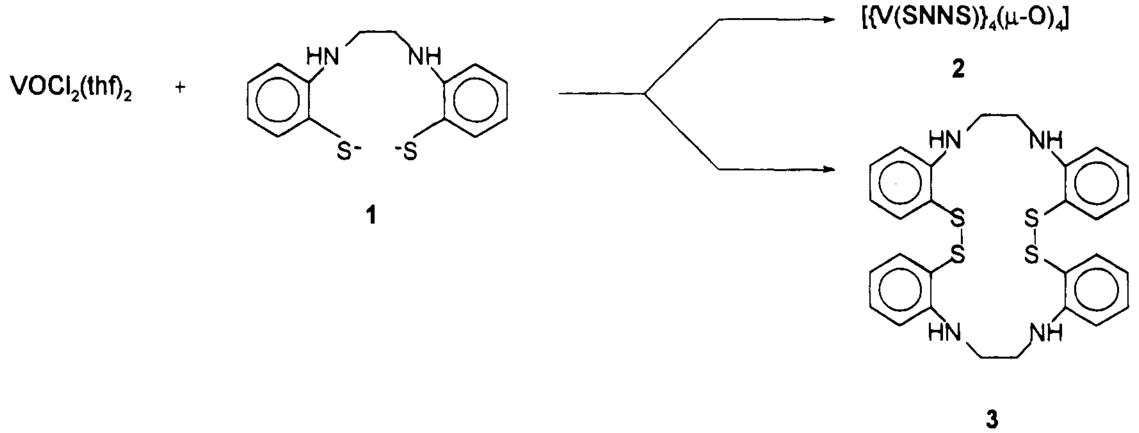

Table 1. Crystallographic Data for **2** and **3**

compd	**2**	**3**
chem formula	$C_{56}H_{56}N_8O_4S_8V_4$	$C_{28}H_{28}N_4S_4$
a, Å	13.693(4)	16.445(2)
c, Å	31.189(12)	19.389(4)
V, Å^3	5848(3)	5243.5(14)
Z	4	4
fw	1365.32	548.78
space group	$I4_1/a$	$I4_1/a$
T, °C	−100	−100
λ, Å	1.541 78 Å	1.541 78 Å
μ, cm^{-1}	83.1	35.3
ϱ_{calcd}, cm^{-1}	1.551	1.390
R1[a] ($F > 4\sigma(F_o)$)	0.0853	0.0484
wR2[b] (all data)	0.1473	0.1247

[a] $R1 = \sum_h[F_o(h) - F_c(h)]/\sum_h F_o(h)$. [b] $wR2 = \sum_h w[F_o(h)^2 - F_c(h)^2]^2/\sum_h w[F_o(h)^2]^2$.

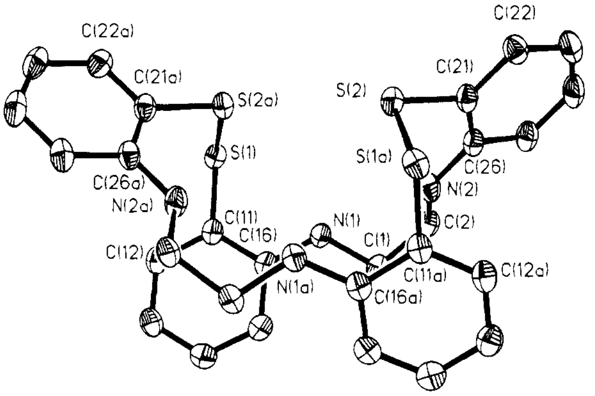

Figure 2. ORTEP drawing (50% probability ellipsoids) of **3**. Selected distances (Å) and angles (deg): S1−S2a 2.0829(7), S1−C11 1.764(2), S2−C21 1.772(2), N1−C16 1.379(2), N1−C1 1.456(2), N2−C26 1.361(3), N2−C2 1.441(3); C11−S1−S2a 104.77(6), C21−S2−S1a 104.18(6), C16−N1−C1 122.3, C26−N2−C2 124.6(2).

Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters (Å^2 × 10^3) for **2**

	x	*y*	*z*	U_{eq}[a]
V1	6725(1)	7109(1)	1078(1)	24(1)
S1	6609(1)	7833(1)	383(1)	30(1)
S2	7835(1)	5957(1)	811(1)	34(1)
O1	5739(2)	6420(2)	1122(1)	27(1)
N1	7947(3)	8217(3)	1114(1)	33(1)
N2	7378(3)	6772(3)	1685(1)	29(1)
C1	8605(3)	7970(4)	1477(2)	39(1)
C2	7968(3)	7619(4)	1839(2)	37(1)
C11	7821(3)	8272(4)	339(2)	39(1)
C12	8213(4)	8493(5)	−62(2)	58(2)
C13	9173(4)	8788(6)	−91(2)	79(2)
C14	9741(4)	8905(6)	268(2)	85(3)
C15	9367(4)	8711(5)	671(2)	59(2)
C16	8406(3)	8397(4)	704(2)	39(1)
C21	8167(3)	5415(3)	1303(2)	35(1)
C22	8681(4)	4532(4)	1314(2)	54(2)
C23	8938(5)	4117(5)	1698(2)	70(2)
C24	8672(5)	4543(5)	2083(2)	64(2)
C25	8161(4)	5419(4)	2079(2)	44(1)
C26	7923(3)	5849(3)	1695(2)	33(1)

[a] U_{eq} was calculated as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor. $\mathbf{U}_{ij}$ has the form $-2\pi^2[(ha^*)^2U_{11} + ... + 2hka^*b(U_{12}]$.

Table 3. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters (Å^2 × 10^3) for **3**

	x	*y*	*z*	U_{eq}[a]
S1	2881(1)	2799(1)	925(1)	27(1)
S2	6118(1)	1898(1)	326(1)	27(1)
N1	3968(1)	1757(1)	1848(1)	27(1)
N2	5216(1)	809(1)	1290(1)	31(1)
C1	4316(1)	1087(1)	2241(1)	28(1)
C2	4633(1)	444(1)	1751(1)	28(1)
C11	3176(1)	2995(1)	1780(1)	26(1)
C12	2888(1)	3706(1)	2087(1)	30(1)
C13	3068(1)	3891(1)	2766(1)	33(1)
C14	3552(1)	3358(1)	3142(1)	31(1)
C15	3846(1)	2648(1)	2848(1)	28(1)
C16	3667(1)	2447(1)	2161(1)	25(1)
C21	6136(1)	821(1)	322(1)	27(1)
C22	6594(1)	404(1)	−169(1)	32(1)
C23	6591(1)	−441(1)	−187(1)	37(1)
C24	6113(1)	−860(1)	284(1)	38(1)
C25	5645(1)	−462(1)	770(1)	33(1)
C26	5650(1)	397(1)	807(1)	27(1)

[a] U_{eq} was calculated as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor. $\mathbf{U}_{ij}$ has the form $-2\pi^2[(ha^*)^2U_{11} + ... + 2hka^*b^*U_{12}]$.

in a side experiment that V^{III} and Na_2-**1** form a complex of composition VCl($^-$*SNNS*$^-$) **4** (see Experimental Section).

The molecular structures of **2** and **3** are shown in Figures 1 and 2. Crystallographic data and the data collection parameters are given in Table 1; atomic positional parameters, in Tables 2 and 3. **2** is a neutral, tetranuclear complex, in which four V($^-$*SNNS*$^-$) fragments are bridged asymmetrically by oxo groups. The central $V_4(\mu\text{-}O)_4$ unit with an approximate boat conformation has S_4 symmetry (Figure 1B) and hence is a new structural element in tetranuclear vanadium clusters.[12] Known to this date have been $V_4(\mu\text{-}O)_4$ units with a puckered eight-membered ring (D_{2d} in $V_4O_{12}{}^{4-}$ [13a] and $HV_4O_{12}{}^{3-}$ [13b] or C_{4v} as in the carboxylato complexes $V_4O_4(\mu\text{-}O/OH)_4(\mu\text{-}O_2CR)_4$[13c,d]) and a planar eight-membered ring (D_{4h} in $[t\text{-}BuNH_3]_4[V_4O_{12}]$[13e]). The bridging oxygens in **2** essentially are vanadyl oxygens. The

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[12] Klemperer, W. G.; Marquart, T. A.; Yaghi, O. M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 49.

V=O double bond length d(V=O), commonly 1.57 Å, is lengthened to 1.65 Å, corresponding to a rather low V=O stretching band at 874 cm^{-1}. A comparable lengthening of d(V=O) has also been observed for vanadyl oxygen involved in a hydrogen bond network.[14] The distance d(V−O) to the second vanadium, 2.01 Å, lies in the upper range of V−O single-bond lengths. Each of the vanadium centers is in a distorted octahedral geometry. Vanadium, the doubly bonded oxygen, the two nitrogens, and one of the sulfurs span the plane; the second sulfur and the singly bound oxygen from the adjacent vanadium center form the (kinked; ∠S−O−V = 165.3°) axis of the octahedron. The bond distances d(V−S) and d(V−N2) are within the range commonly observed, while d(V−N1) (2.263(4) Å) is rather long due to the position of N1 *trans* to the vanadyl oxygen.

The compound shows perfect paramagnetic behavior down to 2 K, following the Curie−Weiss law with $C = 3.1 \times 10^{-5}$ and $\Theta = 0.1554$. The magnetic moment is 4.43 μ_B for the tetramer.

The heteroeicosane **3** attains the cage conformation (C_2 symmetry; Figure 2). N1, the ethylene bridge (C1 and C2), and two of the benzo substituents (C11−C16) form the base of this cage, which is flanked by N2, the S_2 bridges, and the remaining benzo moieties (C21−C26). The angles between the aryls and the disulfide groups amount to 79.6° (C11−C16/C11,CS1,S2a) and 94.7° (C21a−C26a/C21a,S2a,S1) and hence lie in the same range as those found for other aryl disulfides with an electron-donating *o*-substituent[15] (compare, e.g., (o-$NH_2C_6H_4)_2S_2$: 83.6°). The dihedral angle S1,S2a,C21a/S1,S2a,C11 of 105.7° is widened with respect to those of other disulfides (82.1 ± 5.4°); the angles at sulfur atoms S1 and S2 (104.77(6) and 104.18(6)°) and d(S1−S2) (2.0829(7) Å) compare to the mean values found for other disulfides (103.0 ± 0.4° and 2.072 ± 0.8 Å, respectively).

Experimental Section

General Procedures and Preparations. All reactions were carried out under inert-gas atomsphere. Susceptibility measurements were performed in the temperature range 300−2 K on a Biomagnettic Technologies variable-temperature SQUID magnetometer, VTS 905. The ligand Na_2−**1** was prepared as described in ref 7.

A 210 mg (0.66 mmol) sample of Na_2-**1** suspended in 10 mL of THF was treated with 180 mg (0.64 mmol) of $VOCl_2(thf)_2$ dissolved in 10 mL of THF. After 2 days of stirring, 70 mL of pentane was added and the precipitate of **2** and other, unidentified products were filtered off. **3** crystallized from the filtrate within 1 day. Yield: 15−37 mg (8−20%). ^{1}H NMR ($CDCl_3$, 200 MHz): 3.03 (2H, s; CH_2), 4.96 (1H, s; NH), 6.50−7.39 ppm (4H, m; aromatic H). IR (KBr): 3371 (ν(N−H)), 1283 (wagging CH_2−S), 412 cm^{-1} (ν(S−S)). MS (70 eV): $m/z = 516$ (M^+ − S), 274 (M/2).

For the isolation of **2**, the precipitate was extracted with 20 mL of CH_2Cl_2, the extract filtered, and the solvent removed by evaporation. The residue was redissolved in 20 mL of THF. A 100 mL portion of pentane was added, and the precipitate was filtered off and washed with H_2O/C_2H_5OH, 1/1 v/v, until the initially green filtrate became colorless (ca. 200 mL of the solvent mixture was needed). (V^{III} complexes, eventually formed from a redox reaction between **1** and $VOCl_2$, are destroyed under these conditions of workup.) The remaining residue on the filter plate was washed once with a small amount of ether and dried. Extraction with CH_2Cl_2, evaporation to dryness, and drying under vacuum yielded **2** as a brown-violet powder. Yield: 105−160 mg (48−73%). ^{1}H NMR (CD_2Cl_2, 200 MHz): 3.04 (2H, s; CH_2), 4.94 (1H, s; NH), 6.52−7.54 ppm (4H, m; aromatic H). IR (Nujol): 3216 ($\nu(N-H)_{as}$), 3055 ($\nu(N-H)_s$), 874 cm^{-1} (ν(V=O)). CV (CH_2Cl_2, relative to SCE): irreversible oxidation steps at 0.54, 0.96, and 1.34 V. Anal. Calcd for $C_{56}H_{64}N_8O_4S_8V_4$ ($M_r = 1365.41$): C, 49.26; H, 4.31; N, 8.21. Found: C, 49.56; H, 4.69; N, 8.02.

For the preparation of VCl($^-$*SNNS*$^-$) (**4**) 240 mg (0.64 mmol) of $VCl_3(thf)_3$ and 230 mg (0.64 mmol) of Na_2-**1** were mixed and dissolved in 20 mL of THF. After 1 h of stirring, the mauve reaction mixture was concentrated to one-third of its original volume and filtered, and the filtrate was treated with 50 mL of pentane. The resulting violet precipitate was filtered off and dried under high vacuum. Yield: 280 mg (70%). IR (Nujol): 3171 ($\nu(N-H)_{as}$), 3058 cm^{-1} ($\nu(N-H)_s$). The ν(V=O) typical of **2** is lacking. Anal. Calcd for $C_{14}H_{16}ClN_2S_2V$ (M_r = 362.82): C, 46.35; H, 4.45; N, 7.72. Found: C, 46.61; H, 4.23; N, 7.84.

X-ray Structure Determinations. Suitable crystals of **2** crystallized from a solution of **2** in THF/pentane, 4/1, at 2 °C; suitable crystals of **3** separated from the filtrate of the reaction mixture as described above. Data collection was performed out on a CAD-4 diffractometer at 173 K, Cu Kα (λ = 1.541 78 Å) in the 2θ scan mode. The solution and refinement of the structures were carried out with the program packages SHELXS-86 and SHELXL-93. An absorption correction was applied. In the case of **2**, the hydrogens on N1 and N2 were found. The other H atoms of **2** and the H atoms of **3** were calculated into idealized positions and isotropically refined in the last cycle. Non-hydrogen atoms were refined anisotropically. For data cf. Table 1.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft.

Supplementary Material Available: A listing of crystallographic data and solution and refinement parameters, cell drawings (2 pages), and tables of bond distances and angles, anisotropic displacement factors for the non-hydrogen atoms, and H atom coordinates and isotropic displacement parameters for **2** and **3** (9 pages). Ordering information is given on any current masthead page.

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