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Chiral oxovanadium(V) complexes with a 6-amino-6-deoxyglucopyranoside-based Schiff-base ligand: Catalytic asymmetric sulfoxidation and structural characterization

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ABSTRACT

Two new chiral oxovanadium(V) complexes [VO(OMe)(L)] (**1**) and [VO(Osal)(L)] (**2**) derived from the Schiff-base ligand 6-*N*-[(3,5-di-*tert*-butyl-salicylidene)amino]-6-deoxy-1,2,3-tri-*O*-methyl-α-D-glucopyranose (H_2L) were synthesized via two different routes. The reaction of the Schiff-base ligand H_2L with ammonium metavanadate in hot methanol as well as with tris(isopropoxy)oxovanadium(V) in diethyl ether at room temperature leads to a mixture of complexes **1** and **2**, which can be isolated by means of fractional crystallization. The complexes were characterized with elemental analysis, ^{51}V, ^{1}H and ^{13}C NMR, IR spectroscopy, MS and in case of **1** by X-ray diffraction. Complex **1** crystalizes in the orthorhombic space group $P2_12_12_1$ with a distorted trigonal bipyramidal geometry at the vanadium center ($\tau = 0.58$). Under hydrolytic conditions **1** forms the *cis*-dioxovanadium(V) complex [VO_2(MeOH)(HL)] (**3**) which can be monitored by NMR spectroscopy. Complexes **1** and **2** were tested as catalysts for sulfoxidation of different sulfide substrates PhSR (R = Me, Bz) utilizing hydrogen peroxide or *tert*-butyl hydroperoxide (TBHPO) as oxidant in dichloromethane as solvent. The yield as well as the enantiomeric excess were found to strongly depend on the catalyst, substrate and oxidant used.

1. Introduction

Optically active sulfoxides are an interesting class of compounds widely used in the pharmaceutical industry and academia as chiral auxiliaries in asymmetric syntheses of biologically active compounds [1]. In particular metal catalysts have been employed in the enantioselective oxidation of sulfides to generate chiral sulfoxides. These metal catalysts are mainly based on titanium, vanadium, and manganese complexes [2]. Less is known for metal catalysts based on molybdenum and iron, which have nevertheless proven to efficiently catalyze the oxidation of sulfide substrates by peroxides [3].

A particular focus has been placed on vanadium complexes, not only because of their catalytic properties [4–6], but also because of the fact that vanadium haloperoxidase enzymes facilitate the enantioselective catalytic oxidation of sulfides by hydrogen peroxide [7]. The active site of vanadium haloperoxidases consists of a vanadate moiety with a trigonal bipyramidal geometry covalently bound to a histidine residue [8], with the reactivity attributed to the presence of an extensive hydrogen bonding network [9]. This can be modeled by vanadium(V) complexes with an appropriate ligand [10] or host–guest system based on cyclodextrin [11], where the latter case can provide chiral information through the employed sugar host.

A straightforward approach to generate suitable systems for applications in asymmetric catalysis is the utilization of carbohydrate-based ligands [12]. Over the past two decades an intense exploration has been focused on the functionalization of the sugar backbone with amides, amines, imines, and carboxylic groups to accomplish a stronger metal-ion complexation [13]. In this context particularly Schiff-base ligands have been addressed due to their common availability via condensation of amino sugars with aldehyde moieties [14,15,16]. Vanadium(V) complexes with this type of Schiff-base ligands are rather limited [16,17]. To our knowledge only one case was reported were such a Schiff-base ligand was utilized as a chiral carbohydrate-based auxiliary in vanadium-promoted enantioselective catalysis [18].

In this paper, we report the catalytic properties and characterization of two new oxovanadium(V) complexes derived from 6-amino-6-deoxy-1,2,3-tri-*O*-methyl-α-D-glucopyranoside.

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2. Experimental

2.1. Materials and general procedures

The Schiff-base ligand 6-*N*-[(3,5-di-*tert*-butyl-salicylidene) amino]-6-deoxy-1,2,3-tri-*O*-methyl-α-D-glucopyranose (H_2L) was obtained in a six-step synthesis according to published procedures [15]. All other chemicals and reagents were obtained from commercial sources and used without further purification unless stated otherwise. If required, solvents were further purified by standard methods [19]. Column chromatography was performed using MN silica gel 60 (70–230 mesh) purchased from Macherey-Nagel. NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer. The IR spectra were measured on a Bruker IFS55/Equinox. Mass spectrometric measurements were carried out on a MAT95XL Finnigan instrument for electron spray ionization (negative and positive mode) and MATSSQ-710 Bruker instrument for FAB measurements. Elemental analyses were made with a LECO CHN/932 elemental analyzer. HPLC measurements were made with a Jasco-MD 1515 instrument equipped with a WHELK-O 1 column and a UV-diode array multiwavelength detector.

2.2. Synthesis of [VO(OMe)(L)] (**1**) and [VO(Osal)(L)] (**2**)

2.2.1. Method A

The Schiff-base ligand H_2L (0.400 g, 0.91 mmol) was dissolved in 15 mL methanol and NH_4VO_3 (0.106 g, 0.91 mmol) was added to this solution. The resulting suspension was stirred at 65 °C. After 6 d one equivalent of ethylene glycol (0.060 mL, 0.97 mmol) was added and after additional stirring for 3 d at 65 °C the resulting clear brown solution was filtered hot and allowed to stand for crystallization at room temperature. Fractional crystallization first yields a very small portion of complex **1** as red crystals (yield <1%) and subsequently dark purple crystals of **2** (0.086 g, 0.12 mmol). Yield: **1** <1%; **2** 13%.

2.2.2. Method B

A suspension of the Schiff-base ligand H_2L 2(0.265 g, 0.61 mmol), NH_4VO_3 (0.071 g, 0.61 mmol), and ethylene glycol (0.037 g, 0.61 mmol) in 10 mL methanol was heated under reflux for 2 d until all metavanadate was dissolved. The brown solution was filtrated hot and allowed to stand at room temperature for crystallization. Fractional crystallization afforded first a first crop of red crystals of complex **1** (0.183 g, 0.34 mmol) and a second crop of dark purple crystals of **2** (0.012 g, 0.02 mmol). Yield: **1** 56%; **2** 3%.

2.2.3. Method C

To a solution of the Schiff-base ligand H_2L (0.440 g, 1.00 mmol) in 15 mL dry diethyl ether VO(O*i*Pr)$_3$ (0.260 g, 1.07 mmol) was slowly added dropwise under an atmosphere of argon. The resulting brown solution was kept with gentle stirring for 3 d. Subsequently the solvent was removed to dryness under reduced pressure. The crude product (0.450 g) was redissolved in 17 mL dry methanol and kept under an atmosphere of argon. After a few days red crystals of complex **1** (0.190 g, 0.36 mmol) could be isolated from this solution. Yield: **1** 36%. Upon exposure of the mother liquor to air for several days a small crop of complex **2** (0.040 g, 0.05 mmol) could be isolated as purple crystals.

2.2.4. Data for [VO(OMe)(L)] (**1**)

Anal. calcd for $C_{25}H_{40}NO_8V$ (533.53): C, 56.28; H, 7.56; N, 2.63. Found: C, 56.38; H, 7.42; N, 2.47. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 9H, C(C*H*$_3$)$_3$), 1.43 (s, 9H, C(C*H*$_3$)$_3$), 3.33–3.37 (m, 2H, H-2 and OC*H*$_3$), 3.42 (s, 3H, OC*H*$_3$), 3.43–3.54 (m, 2H, H-5), 3.55 (s, 3H, OC), 3.64 (s, 3H, OC*H*$_3$), 3.79–3.97 (m, 1H, H-6eq), 4.43 (td, $^2J_{6ax6eq} = {}^3J_{6ax5}$ = 11.4 Hz, $^4J_{6ax4}$ = 1.6 Hz, 1H, H-6ax), 4.86 (d, $^3J_{12}$ = 2.7 Hz, 1H, H-1), 5.02 (s, 3H, VOC*H*$_3$), 5.18–5.29 (m, 1H, H-4), 7.16 (d, ^4J = 2.6 Hz, 1H, Ar), 7.55 (d, ^4J = 2.6 Hz, 1H, Ar), 8.37 (s, 1 H, C*H*=N) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.3, 31.0 (2 × C(*C*H$_3$)$_3$), 33.9, 34.8 (2 × *C*(CH$_3$)$_3$), 55.1, 59.2, 60.6 (3 × OCH$_3$), 66.4 (C-6), 68.5 (C-5), 70.4 (VOCH$_3$), 80.8, 82.9 (C-2, C-3), 92.5 (C-4), 98.0 (C-1), 118.6 (Ar-*C*), 127.0 (Ar-*C*H), 130.0 (Ar-*C*H), 138.2 (Ar-*C*), 141.5 (Ar-*C*), 160.7 (Ar-*C*), 165.6 (*C*H=N) ppm. ^{51}V NMR (105 MHz, $CDCl_3$): δ = −535 ppm ($\nu_{1/2}$ = 170 Hz). IR (KBr): 2954 (s), 2907 (m), 2870 (m), 2831 (w), 2798 (w), 1632 (s), 1562 (m), 1466 (m), 1418 (m), 1392 (w), 1363 (w), 1299 (w), 1278 (w), 1199 (m), 1157 (m), 1134 (w), 1065 (s), 1050 (s), 1000 (s), 961 (m), 818 (w), 683 (m), 558 (w) cm^{-1}. MS-FAB (NBA): *m*/*z* (%) = 502 [V(OH)(L)]$^+$ (90), 471 (30), 438 (40), 372 (80), 341 (100).

2.2.5. Data for [VO(Osal)(L)] (**2**)

Anal. calcd for $C_{39}H_{58}NO_9V$ (735.82): C, 63.66; H, 7.94; N, 1.90. Found: C, 64.53; H, 8.05; N, 1.69. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (s, 9H, C(C*H*$_3$)$_3$), 1.24 (s, 9H, C(C*H*$_3$)$_3$), 1.28 (s, 9H, C(C*H*$_3$)$_3$), 1.57 (s, 9H, C(C*H*$_3$)$_3$), 2.92 (s, 3H, OC*H*$_3$), 3.15 (t, $^3J_{31} = {}^3J_{32}$ = 9.0 Hz, 1H, H-3), 3.32 (dd, $^3J_{23}$ = 9.5 Hz, $^3J_{21}$ = 3.7 Hz, 1H, H-2), 3.42 (s, 3H, OC*H*$_3$), 3.48 (s, 3H, OC*H*$_3$), 3.69 (m, 1H, H-5), 3.69 (ddd, $^3J_{56ax}$ = 12.0 Hz, $^3J_{56eq}$ = 4.0 Hz, $^3J_{54}$ = 8.9 Hz, 1H, H-5), 3.94 (dd, $^2J_{6eq6ax}$ = 12.0 Hz, $^3J_{6eq5}$ = 4.0 Hz, 1H, H-6eq), 4.37 (td, $^2J_{6ax6eq} = {}^3J_{6ax5}$ = 12.0 Hz, $^4J_{6ax4}$ = 1.3 Hz, 1H, H-6ax), 4.85 (d, $^3J_{12}$ = 3.6 Hz, 1H, H-1), 5.68 (t, $^3J_{43} = {}^3J_{45}$ = 8.9 Hz, 1H, H-4), 7.14 (d, ^4J = 2.6 Hz, 1H, Ar), 7.21 (d, ^4J = 2.6 Hz, 1H, Ar), 7.42 (d, ^4J = 2.2 Hz, 1H, Ar), 7.59 (d, ^4J = 2.6 Hz, 1H, Ar), 8.41 (s, 1H, C*H*=N), 9.10 (s, 1H, C*H*=O) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4, 29.7, 31.2, 31.4 (4 × C(*C*H$_3$)$_3$), 34.2, 34.3, 35.0, 35.4 (4 × *C*(CH$_3$)$_3$), 55.3, 59.6, 59.8 (3 × OCH$_3$), 66.5 (C-6), 69.0 (C-5), 80.4 (C-2), 83.4 (C-3), 96.6 (C-4), 98.4 (C-1), 120.8 (Ar-*C*), 124.0 (Ar-*C*), 127.2 (Ar-*C*H), 129.4 (Ar-*C*H), 130.6 (Ar-*C*H), 131.9 (Ar-*C*H), 137.1 (Ar-*C*), 138.1 (Ar-*C*), 140.4 (Ar-*C*), 142.3 (Ar-*C*), 161.7 (Ar-*C*), 164.7 (Ar-*C*), 164.9 (*C*H=N), 192.8 (*C*H=O) ppm. ^{51}V NMR (105 MHz, $CDCl_3$): δ = −539 ppm ($\nu_{1/2}$ = 500 Hz). IR (KBr): 2952 (vs), 2905 (s), 2867 (m), 1651 (vs), 1626 (vs), 1558 (m), 1543 (m), 1464 (m), 1438 (m), 1411 (m), 1392 (m), 1363 (m), 1274 (m), 1254 (s), 1170 (w), 1069 (vs), 1053 (vs), 954 (s), 846 (s), 776 (w), 753 (m), 722 (w), 680 (s), 551 (s) cm^{-1}. MS-ESI (MeOH): *m*/*z* (%) = 1494 [2M + Na]$^+$ (20), 758 [M + Na]$^+$ (100), 736 M$^+$ (10).

2.3. NMR data for the hydrolysis product [VO_2(MeOH)(HL)] (**3**)

NMR tube experiments were performed to examine the hydrolytic stability of complexes **1** and **2**. Only complex **1** was found to be susceptible to hydrolysis leading to the complex [VO_2(MeOH)(HL)] (**3**).

^{1}H NMR (400 MHz, DMSO): δ = 1.27 (s, 9H, C(C*H*$_3$)$_3$), 1.42 (s, 9H, C(C*H*$_3$)$_3$), 3.00 (s, 3H, OC*H*$_3$), 3.00–3.07 (m, 2H, H-2 and H-4), 3.16 (d, ^3J = 5.2 Hz, 3H, C*H*$_3$OH → V), 3.21 (t, $^3J_{32} = {}^3J_{34}$ = 9.2 Hz, 1H, H-3), 3.28 (s, 3H, OC*H*$_3$), 3.20–3.30 (m, 1H, H-5), 3.46 (s, 3H, OC*H*$_3$), 3.92 (td, $^2J_{6ax6eq} = {}^3J_{6ax5}$ = 9.8 Hz, $^4J_{6ax4}$ = 2.1 Hz, 1H, H-6ax), 4.06 (q, ^3J = 5.3 Hz, 1H, CH$_3$O*H* → V), 4.29 (dd, $^2J_{6eq6ax}$ = 9.8 Hz, $^3J_{6eq5}$ = 2.1 Hz, 1H, H-6eq), 4.68 (d, $^3J_{12}$ = 3.4 Hz, 1H, H-1), 5.36 (d, ^3J = 6.4 Hz, 1H, O*H* at C-4), 7.25 (d, ^4J = 2.4 Hz, 1H, Ar), 7.44 (d, ^4J = 2.4 Hz, 1H, Ar), 8.34 (s, 1H, C*H*=N) ppm. ^{13}C NMR (100 MHz, DMSO): δ = 29.2, 31.3 (2 × C(*C*H$_3$)$_3$), 33.8, 34.8 (2 × *C*(CH$_3$)$_3$), 48.6 (*C*H$_3$OH → V), 53.9, 57.3, 60.1 (3 × OCH$_3$), 66.2 (C-6), 66.7 (C-6', C-5), 72.3 (C-4), 81.0 (C-2), 82.5 (C-3), 96.2 (C-1), 118.3 (Ar-*C*), 127.8 (Ar-*C*H), 129.0 (Ar-*C*H), 137.9 (Ar-*C*), 138.0 (Ar-*C*), 161.8 (Ar-*C*), 169.1 (*C*H=N) ppm. ^{51}V NMR (105 MHz, DMSO-d_6): δ = −519 ppm.

2.4. Catalysis

The appropriate vanadium(V) complex (0.01 mmol) and alkyl phenyl sulfide (1.0 mmol) were dissolved in dichloromethane

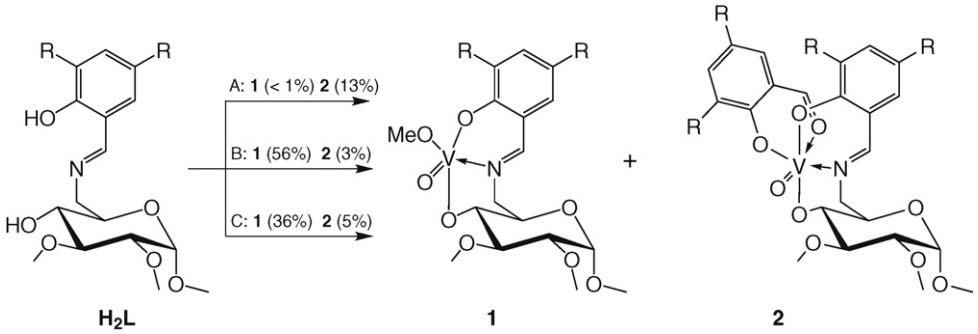


Fig. 1. Reagents and conditions for the synthesis of complexes **1** and **2**: (A) (i): NH_4VO_3/MeOH, 6 d, 65 °C (ii): ethylene glycol/MeOH, 3 d, 65 °C; (B) NH_4VO_3, ethylene glycol/MeOH, 2 d, 65 °C; (C) $VO(iPrO)_3/Et_2O$ (under argon), RT.

(10 mL) together with 1,3,5-trimethoxybenzene as an internal standard. This solution was cooled to 0 °C, and the oxidant hydrogen peroxide (1.25 mmol, 35%, w/w) or *tert*-butyl hydroperoxide (TBHP, 1.2 mmol) were added. Subsequently the reaction mixture was allowed to warm up to room temperature and the progress of the reaction was monitored by TLC (diethyleter/*n*-hexane = 9/1). After the appropriate reaction time, fractions of 0.2 mL (or 2 mL in the case of TBHP) were quenched with 2 mL sodium sulphite (0.1 M) solution (or 5 mL di-*n*-butyl sulfide in the case of TBHP). The resulting aqueous solution was extracted three times with 4 mL dichloromethane. From the combined organic phases all volatiles were removed in vacuo. Conversion and selectivity were determined by ^{1}H NMR spectroscopy of the obtained residual material in $CDCl_3$. After separation of the sulfoxide by column chromatography (silica gel, diethyleter/*n*-hexane = 9/1), the enantiomeric excess value (ee) was determined with HPLC on a chiral column.

2.5. Crystal structure analysis of [VO(OMe)(L)] (*1*)

The crystallographic data was collected with a Nonius KappaCCD diffractometer, using graphite-monochromated Mo-Kα radiation of 71.073 pm. The structure was solved by direct methods and refined by the full-matrix least-squares techniques against F^2 with SHELXTL [20]. All non-hydrogen atoms were refined anisotropically. The positions of hydrogen atoms were calculated and treated as riding atoms with fixed thermal parameters. Selected crystal collection and refinement parameters: formula = $C_{25}H_{40}NO_8V$, formula mass = 533.52 g/mol, crystal system = orthorhombic, space group = $P2_12_12_1$, a = 837.52(2), b = 1323.48(3), c = 2438.34(5) pm, V = 2.7027(10) nm^3, Z = 4, $\rho_{calcd.}$ = 1.311 g/cm^3, T = 183(2) K, reflections measured = 18879, unique reflections (R_{int} = 0.051) = 6171, reflections observed ($I > 2\sigma(I)$) = 5019, parameters = 316, flack parameter = −0.02(2), R_1 = 0.040, wR_2 = 0.094, goodness of fit = 1.023. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 680708 for **1**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K., at www.ccdc.cam.ac.uk/conts/retrieving.html or deposit@ccdc.cam.ac.uk.

3. Results and discussion

3.1. Synthesis of complexes

Two new chiral oxovanadium(V) complexes with the Schiff-base ligand H_2L were synthesized as depicted in Fig. 1. The ligand H_2L is derived from Schiff-base condensation of the aminosugar 6-amino-6-deoxy-1,2,3-tri-*O*-methyl-α-D-glucopyranoside and 3,5-di-*tert*-butylsalicylaldehyde [15]. The oxovanadium(V) complexes [VO(OMe)(L)] **1** and [VO(Osal)(L)] **2** were obtained according to two basic reaction schemes starting from either ammonium metavanadate or tris(isopropoxy)oxovanadium(V).

When H_2L is heated under reflux together with a suspension of ammonium metavanadate in methanol only a slow reaction is observed as indicated by the presence of the vanadium precursor. After a reaction time of 6 d ethylene glycol was added to support the dissolution of the vanadium precursor (Fig. 1, route A), which is known as a general feature for protic chelating ligands [21]. Due to the long reaction times a partial hydrolysis of the Schiff-base ligand occurs and as a consequence the formation of complex **2** is observed. Addition of ethylene glycol directly at the beginning of the reaction (Fig. 1, route B) affords considerably shorter reaction times and therefore leads to a significantly larger amount of complex **1**. The two resulting oxovandium(V) complexes can be separated and isolated by fractional crystallization. From the reactions in methanol solution solely the ester derivatives of the oxovanadium(V) complexes could be isolated. This is in agreement with earlier results obtained from reactions of *N*-salicylidenehydrazide ligands with ammonium metavanadate as precursor, where the formation of *cis*-dioxovanadium(V) complexes only was observed for reactions in aprotic solvent like DMF [22].

Alternatively the ligand H_2L can also be reacted with tris(isopropoxy)oxovanadium(V) in diethyl ether at room temperature (Fig. 1, route C). This leads to a cleaner conversion, as no adventitious water is generated during the course of the reaction. Nevertheless, after exposure to ambient air also in this case a small amount of complex **2** can be isolated.

3.2. Structure of complex *1*

The chiral complex **1** crystalizes in the orthorhombic space group $P2_12_12_1$. Fig. 2 shows the molecular structure. The coordination geometry at the vanadium(V) center can be considered as distorted trigonal bipyramidal with the imine nitrogen atom (N) and the methanolic oxygen atom O2M in the apical positions. Whereas the equatorial plane is constituted by the oxo group (O1) and the phenolic (O3) as well as the C-4 alcoholic oxygen atoms (O4). The resulting stereochemistry at the trigonal bipyramidal vanadium(V) center is anti-clockwise (TBPY-5-45-A). The Schiff-base ligand H_2L coordinates as tridentate chelate in its dianionic form with the imine nitrogen atom (N) and the deprotonated oxygen atoms of the phenolic (O3) and the sugar C-4 hydroxy groups (O4) as donors. The stereochemical requirements given by the sugar backbone afford a considerable distortion from planarity for the tridentate chelate ligand. The resulting O3–V–O4 bond angle of 134° is responsible for the observed trigonal bipyramidal geometry with a τ value of 0.58 (τ = 0.58; with τ = 1 for trigonal bipyramidal and τ = 0 for square pyramidal).

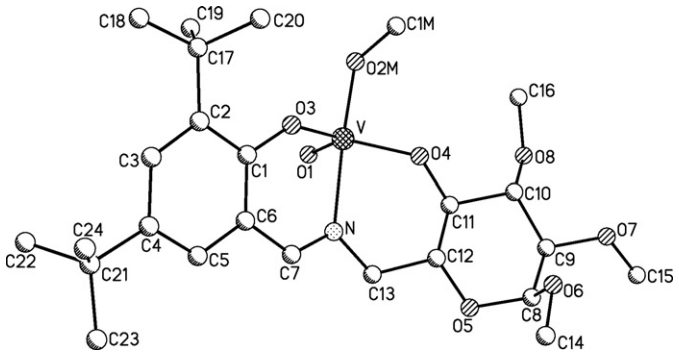


Fig. 2. Molecular structure and numbering scheme for **1** (hydrogen atoms are omitted for clarity). Selected bond lengths (pm) and angles (°): V–O1 158.17(17), V–O2M 180.38(17), V–O3 187.03(16), V–O4 180.71(16), V–N 218.15(18), O1–V–O2M 102.09(9), O1–V–O3 112.15(9), O1–V–O4 111.43(9), O1–V–N 88.92(8), O2M–V–O3 91.88(7), O2M–V–O4 92.95(8), O2M–V–N 168.78(8), O3–V–N 81.82(7), O3–V–O4 133.98(8), O4–V–N 84.92(7).

3.3. NMR spectroscopy

Complexes **1** and **2** posses a favorable solubility in organic solvents due to their *tert*-butyl groups at the aromatic fragment. This allows NMR spectra to be taken for a broad range of solvents including chloroform and DMSO. The ^{51}V, ^{1}H and ^{13}C NMR spectral data are summarized in Section 2. Although the solid samples of complexes **1** and **2** are both analytically pure, for solutions of complex **1** two species can be detected with varying ratio dependent on the solvent and its water content. Whereas for complex **2** in all cases solely one species is present in solution. This suggests that only complex **1** is susceptible to hydrolysis under these conditions and probably forms a *cis*-dioxovanadium(V) complex.

For **1** and **2** the typical coordination-induced shift (CIS) for the relevant resonances is observed [23,24]. As expected the ^{1}H resonances for imine protons of the Schiff-base ligand show only small downfield shifts of about 0.1 ppm upon coordination to the oxovanadium(V) centers [25]. Also the CIS values for the ^{13}C resonances of the carbon atoms C-4 and C-6 of the sugar chelate ring at the vanadium center with about 25 and 6.5 ppm, respectively, are in the expected range. With the value for C-6 clearly suggesting that this chelate ring is in an equatorial arrangement with respect to the orientation of the V=O group [26]. Moreover, also the CIS values for the ^{1}H resonances of the H-4 proton of the sugar backbone with 1.6 and 2.0 ppm for complexes **1** and **2**, respectively, clearly indicate its cisoid orientation with respect to the V=O group [26]. This is further corroborated by the distinct differences of the CIS values for the two methylene protons at the C-6 carbon atom of the sugar backbone, which is due to the anisotropic effect of the V=O group [26]. Overall the NMR spectral data are consistent with the configuration of the sugar-based chelate ring present in the crystal structure of **1**, which is depicted in Fig. 3.

In complex **2** the methoxy group is substituted by the salicylic aldehyde derived from the partial hydrolysis of the Schiff-base ligand. The additional coordination of the carbonyl group is suggested by the observed CIS value of −4.5 ppm for the relevant ^{13}C resonance which is similar to what is observed for the imino group of the corresponding Schiff-base ligand (−2.9 ppm).

As mentioned above complex **1** is susceptible toward hydrolysis leading to the corresponding *cis*-dioxovanadium(V) complex (see Fig. 4). Therefore depending on the solvent and water content two sets of signals can be observed and assigned to the methoxy substituted oxovanadium(V) complex **1** and the in situ formed *cis*-dioxovanadium(V) complex **3**. The ^{1}H NMR spectrum of the fresh prepared reddish solution of **1** in DMSO-d_6 with adventitious water

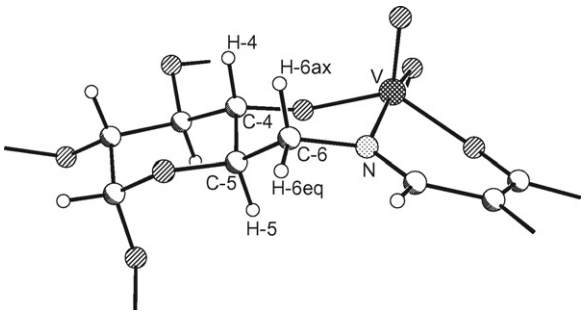


Fig. 3. Configuration of the sugar backbone with the related chelate ring at the vanadium center, taken from the crystal structure of **1**; numbering scheme corresponds to the conventional carbohydrate nomenclature.

shows within minutes a considerable amount of the hydrolysis product **3** (see in Fig. 5a). This solution changes within one hour to a yellow solution with an almost quantitative conversion to the *cis*-dioxovanadium(V) complex **3** as detected by NMR (see in Fig. 5b). Most significant are the changes related to the protonation of the methoxy group and the C-4 hydroxy group of the sugar backbone leading to coordinated alcoholic oxygen donors. This is consistent with the higher hydrolytic stability of phenolate coordinated at vanadium(V) centers [24]. The disappearing ^{1}H resonance for the methoxy group (VOMe at 4.88 ppm) in **1** is replaced by two new resonances for the coordinated methanol molecule, a doublet for the methyl protons at 3.16 ppm and a quartet for the hydroxy proton at 4.06 ppm. The additional oxo group with its anisotropic effect [26] together with the rearrangement at the vanadium(V) center of **3** is also reflected by the alteration of the CIS for the axial and the equatorial methylene proton at C-6, with the latter more downfield in the case of **3**.

3.4. Sulfoxidation

We have tested the oxovanadium(V) complexes **1** and **2** for their ability to catalyze the oxidation of prochiral sulfides using methyl phenyl sulfide (thioanisol) and phenyl benzyl sulfide as model substrates. As oxidants hydrogen peroxide or *tert*-butyl hydroperoxide (TBHPO) were used in a slight excess of 1.20–1.25 equivalents based on the sulfide substrate. The basic reaction conditions are similar to those described in the literature [4]. Reactions are run with 1 mol% of catalyst based on the model substrate. Apolar dichloromethane was used as solvent, as it is well known that sulfoxidation in aprotic solvents tend to give better results concerning the enantioselectivity of the reaction [5].

The results obtained are summarized in Table 1 and show, that the observed yield and enantiomeric excess (ee) strongly depend on the nature of the catalyst, substrate and peroxide used. Nevertheless, as a general feature the formation of the corresponding sulfone as potential side product due to further

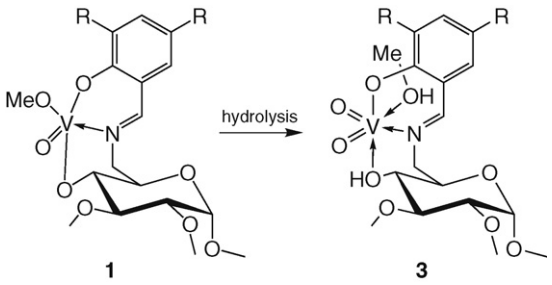


Fig. 4. Hydrolysis of complex **1** in DMSO forming the *cis*-dioxocomplex **3**.

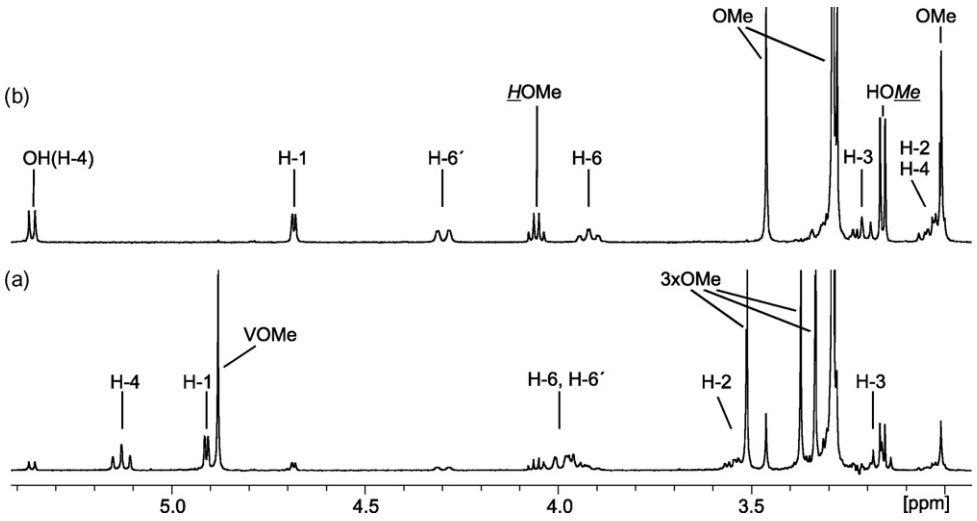


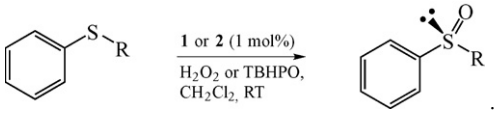
Fig. 5. ^{1}H NMR spectra for the hydrolysis of **1** in DMSO-d_6: (a) immediately after dissolution; (b) 1 h after dissolution almost exclusively the hydrolysis product **3** is present.

oxidation of the sulfoxide could not be observed for all tested reactions.

The best results have been obtained for complex **1** as catalyst in the oxidation of methyl phenyl sulfide with hydrogen peroxide as oxidant (Table 1, entry 1). In this case an overall yield of 91% within 2 h reaction time and a 26% ee of the R-configured sulfoxide was obtained (Table 1, entry 1). Increasing the steric demand of the substrate on going from methyl phenyl sulfide to phenyl benzyl sulfide leads to a decrease in both the overall yield of sulfoxide to 77% and the ee of the corresponding R-configured product to a value of 16% (Table 1, entry 2). Additional increase of the steric demand at the reactive center of complex **1** by employing the bulkier oxidant TBHPO leads to an even more pronounced decrease in reactivity, as the oxidation of methyl phenyl sulfide as substrate is concerned. A conversion of 93% of the substrate is observed after 15 h, but without any detectable stereochemical induction (Table 1, entry 3).

The catalytic activity was also tested for complex **2**. The substitution of the methoxy group by the bulkier phenolic group of 3,5-di-*tert*-butylsalicylaldehyde leads to considerably larger steric demand at the vanadium(V) center as compared to complex **1**. Moreover, an additional weakly coordinated sixth ligand also leads to an increase in coordination number a the vanadium atom. For both substrates employed an enormous increase of the reaction time is observed. With hydrogen peroxide as oxidant in the sulfoxidation reaction, for methyl phenyl sulfide 61% were converted within 5 d, whereas in the case of phenyl benzyl sulfide only 35% conversion was observed after 7 d (Table 1, entry 4 and 5). In neither of both these case any steric induction could be detected.

Table 1
Results for the catalytic oxidation of thioethers PhSR (R = Me, Bz) by peroxides (H_2O_2 or TBHPO) in CH_2Cl_2.



Entry	Catalyst	Substrate	Oxidant	Yield (%)	*t* (min)	ee (%)
1	**1**	PhSMe	H_2O_2	91	120	26(R)
2	**1**	PhSBz	H_2O_2	77	120	16(R)
3	**1**	PhSMe	TBHPO	93	900	0
4	**2**	PhSMe	H_2O_2	61	7200	0
5	**2**	PhSBz	H_2O_2	35	9960	0

The overall performance of complex **2** is indicative of a drastically reduced catalytic activity. This can be attributed to the fact that the vanadium atom in complex **2** is well shielded through the bulky 3,5-di-*tert*-butyl-salicylaldehyde. Nevertheless, the conversion for a control reaction without catalyst (methyl phenyl sulfide: 16% in 5 d; phenyl benzyl sulfide: 12% in 7 d) clearly shows some remaining activity.

To elucidate the potential formation of peroxo species, which are assumed to be the active oxidant during the course of reaction, NMR spectra for complexes **1** and **2** in the presence of a 100-fold excess of hydrogen peroxide have been measured. The ^{1}H and ^{51}V NMR spectra taken for complex **2** in $CDCl_3$ solution give no evidence for the formation of any kind of peroxo species. Moreover, the spectra clearly show that the structural integrity of complex **2** is retained under these conditions. The latter can be attributed to the usually observed pronounced stability of phenolate substituted oxovanadium(V) complexes [24]. Overall the NMR experiments are consistent with the low catalytic activity found for complex **2**.

The situation is quite different in the case of complex **1**. NMR spectra of $CDCl_3$ solutions with hydrogen peroxide (100-fold excess) show significant changes in ^{1}H and ^{51}V NMR spectra due to the formation of a peroxo complex [$VO(O_2)(HL)$]. In the ^{51}V NMR spectra of freshly prepared solutions a new resonance at −693 ppm can be detected. Even after 1 h the majority of the formed peroxo species is still present in solution. For an extended time window (about 2 h) the peroxo species starts to disappear at the expense of two new resonances at −508 and −526 ppm (see Fig. 6). This is consistent with the observed catalytic activity of complex **1**.

The catalytic properties of the 6-aminoglucose-based complexes **1** and **2** can be compared to those of similar 2-aminoglucose Schiff-base ligands which have been prepared in situ from vanadyl acetylacetonate and the appropriate ligand [18]. In general, the in situ generated catalysts based on 2-aminoglucose derivatives react faster and with higher enantiomeric excess but of the S-configured sulfoxide than what is observed for complexes **1** and **2**. In addition to the altered enantioselectivity the complexes **1** and **2** show a more pronounced chemoselectivity than their 2-aminoglucose counterparts, as for the latter a considerable amount of sulfone as oxidative side product is observed. It is tempting to attribute the lower stereoselectivity of complexes **1** and **2** to the presence of a larger chelate ring which transfers the chiral information of the sugar onto the catalytic vanadium center. Nevertheless, this comparison is disputable and certainly has its limits, as neither any kind of molecular

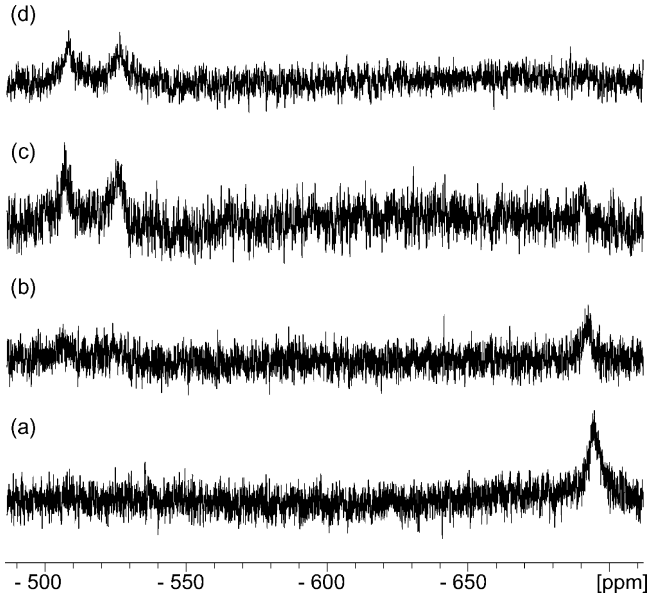


Fig. 6. ^{51}V NMR spectra of **1** in $CDCl_3$ with H_2O_2 in 100-fold excess: (a) immediately, (b) 1 h, (c) 2 h, (d) 3 h after mixing.

structure nor a defined speciation for the reactive species in the case of the in situ generated catalyst is known.

4. Conclusion

We have characterized two new chiral oxovanadium(V) complexes derived from a 6-aminoglucose-based Schiff-base ligand and tested their catalytic properties towards the oxidation of sulfides. The two chiral complexes **1** and **2** differ in their steric demand with respect to the employed alcoholate coordinated to the vanadium(V) center. It was found that an increased steric demand at the catalyst leads to a considerably reduced reactivity towards sulfoxidation. A similar effect is also found for increasing steric demand originating from either the substrate or the oxidant. The highest enantiomeric excess with 26% of the R-configured sulfoxide was obtained for complex **1** as catalyst in the oxidation of the less sterically demanding substrate and oxidant (methyl phenyl sulfide and hydrogen peroxide). For complex **2** very long reaction times are observed, indicative for the absence of any significant catalytic activity.

For complex **1** an anti-clockwise configuration of the substituents at the vanadium(V) center is observed in the crystal structure. NMR spectra indicate that the orientation of the oxo group at the vanadium atom is retained for the solution structure. This becomes particularly evident form the pronounced downfield shifts of the appropriate chelate ring protons due to the anisotropy effect of the V=O group.

Complex **1** is susceptible to hydrolysis which leads to the corresponding *cis*-dioxovanadium(V) complex **3**. Whereas for complex **2** the formation of hydrolysis product could not be detected. This difference also reflects in the reactivity of complexes **1** and **2** which is attributed to the increasing steric demand at their vanadium(V) centers in the given order.

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