A Pentacoordinated Di-*N*-carboxamido-dithiolato-*O*-sulfinato-iron(III) Complex Related to the Metal Site of Nitrile Hydratase**

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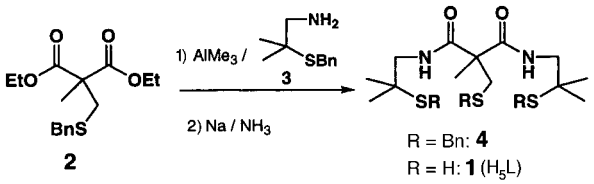
Nitrile hydratases (NHases) are enzymes that contain non-heme iron or non-corrinoid cobalt and catalyze the hydration of nitriles to amides.[1a] One NHase is used for industrial production of acrylamide.[1b] A recent X-ray structure of the active form of the NHase from *Rhodococcus* sp.R312 indicated that the iron center is bound to three cystein thiolate groups and two nitrogen atoms from peptide bonds of the protein main chain.[1c] A more precise X-ray structure of the inactive form of the NHase from *Rhodococcus* sp.N-771 provided additional information: Two of the coordinated cystein groups were posttranslationally modified to cystein sulfinic and sulfenic moieties that are both bound through sulfur, and one nitric oxide ligand occupies the sixth position.[1a] Electron nuclear double resonance (ENDOR) measurements suggested that the sixth ligand in the active form is probably a hydroxide group that was not seen at the resolution of the first structure.[1d]

Such an unusual Fe^{III} coordination sphere invites investigation to better understand its electronic properties and its catalytic activity in nitrile hydration. This, together with the mechanism of posttranslational oxidation of bound cysteins, can be achieved from the study of relevant mimetic complexes. A $(N_2S)_2Fe^{III}$ complex with two aromatic thiolato, two aromatic *N*-carboxamido, and two pyridine ligands has been reported recently,[2a] and during the writing of the current paper the same group described the bis-*S*-sulfinato derivative of this Fe^{III} complex.[2b]

To mimic the metallic site of NHase, we need a pentacoordinated Fe^{III} complex with a free sixth coordination site. Such a complex was synthesized from **1** (H_5L; see Scheme 1), a new $H_5N_2S_3$ ligand containing three aliphatic thiol groups and two aliphatic amide moieties. The coupling reaction between diethyl 2-methyl-2-benzylthiomethyl malonate (**2**)[3a] with 2-methyl-2-(benzylthio)propylamine (**3**)[3b] in toluene in the presence of trimethylaluminum gave diamide **4**. Upon subsequent reductive deprotection of the thiol groups with sodium in liquid ammonia, **1** was obtained in 72% yield (Scheme 1).



Scheme 1. Synthesis of ligand **1**. Bn = benzyl.

Coordination of iron(III) to the deprotonated ligand L^{5-} gave $(NEt_4)_2[Fe^{III}(L\text{-}O_2)]$ (**5**), whose X-ray structure shows postcoordination oxidation of the L ligand (Figure 1).[4] The intermediate complex formed before oxidation is presumably the *tris*-thiolato complex; attempts to isolate and characterize this species under argon have failed so far.

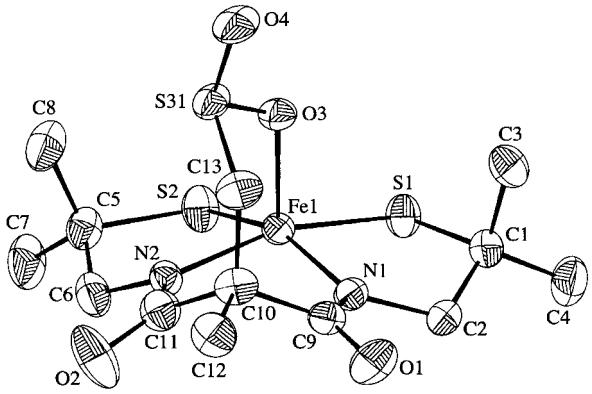


Figure 1. CAMERON representation (ellipsoid at 30% probability level) of the anion of complex **5**. The H and S32[4] atoms are omitted for clarity. Selected bond distances [Å] and angles [°]: Fe1–S1 2.223(3), Fe1–S2 2.213(3), Fe1–O3 2.005(6), Fe1–N1 1.946(7), Fe1–N2 1.957(8); S1-Fe1-S2 87.5(1), S1-Fe1-N1 86.7(2), N1-Fe1-N2 91.5(3), S2-Fe1-N2 86.2(3), S1-Fe1-O3 102.2(2), S2-Fe1-O3 107.5(2), N1-Fe1-O3 96.6(3), N2-Fe1-O3 97.6(3).

In complex **5**, the iron center is above the plane containing the two deprotonated *N*-carboxamido and two thiolato ligands, whereas the *O*-sulfinato ligand occupies the apical position. Moreover, the presence of two NEt_4^+ counterions per iron atom in the crystal lattice indicates that the iron is still in the +3 oxidation state. The Fe–N and Fe–S bond lengths are comparable to those reported for complexes showing *N*-carboxamido and thiolato coordination to Fe^{III}.[2a] The Fe^{III}–O bond from the *O*-sulfinato moiety, with a length of 2.005(6) Å, has no precedent to our knowledge.

Complex **5** is soluble in polar solvents (MeCN, DMF), yielding red solutions. The EPR spectra of **5** at 10 K in MeCN (Figure 2) or DMF glasses confirm the +3 oxidation state of iron and reveal an intermediate spin state of $S = 3/2$ with axial symmetry, in agreement with the magnetic moment of 3.8 μ_B (polycrystalline sample) between 2 and 300 K. Complex **5** is stable under reductive conditions, whereas it undergoes an irreversible oxidation at $E_{1/2} = 150$ mV vs. SCE in DMF, which might correspond to a ligand oxidation or to the formation of an Fe^{IV} complex. The *N*-carboxamido ligands are known to stabilize high oxidation states of transition metal compounds,[5] but the *cis* position of the two thiolato ligands might facilitate intramolecular disulfide formation, leading to irreversible oxidation.

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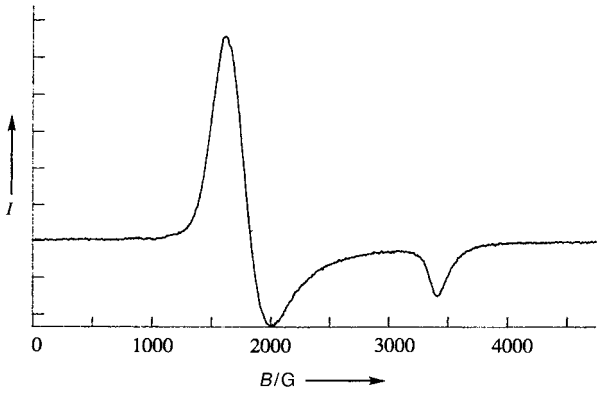

Figure 2. EPR spectrum of **5** in MeCN at 10 K ($g_\perp = 3.75$, $g_\parallel = 2.01$).

The IR spectrum (KBr pellet) of **5** shows a characteristic ν_{CO} frequency at 1575 cm^{-1} for coordinated *N*-carboxamido[2a] and a strong band at 1040 cm^{-1} corresponding to the ν_{SO} stretching of the *O*-coordinated sulfinate.[6] The UV/Vis spectrum of **5** in MeCN exhibits an absorption band at 475 nm ($\varepsilon = 5000\ L\,mol^{-1}\,cm^{-1}$), which is responsible for the red color. The resonance Raman spectrum of **5** in MeCN with an excitation at 476.5 nm shows three bands at 604 (Fe–O stretching[7]), 978, and 1160 cm^{-1} (S–O stretching[6]), which support *O*-sulfinato coordination to the iron as observed in the solid state. Moreover, the excitation profiles of the three bands in the region of 450–530 nm enable us to assign the band at 475 nm in the UV/Vis spectrum to a sulfinate-to-metal charge-transfer transition.

To our knowledge, complex **5** is the first example of an iron complex with such a mixed coordination sphere and the first example to result from air oxidation of an iron-coordinated thiolato ligand to an O-bound sulfinato ligand. Oxidation of thiolato–iron complexes by dioxygen is known to give noncoordinated disulfides or thiolato μ-oxo complexes.[8] A few examples of sulfinato–nickel complexes have been reported that result from nucleophilic attack of bound thiolate(s) on dioxygen.[9] We do not know yet whether the oxidation to give **5** starts by activation of dioxygen by the metal or by reaction of dioxygen with the bound thiolate. Very recently, dioxygen oxidation of a thiolato–Co^{III} complex to a *S*-sulfenato and *S*-sulfinato complexes was reported,[10] and a *S*-sulfinato–Fe^{III} complex has been obtained by H_2O_2 oxidation of a thiolato–Fe^{III} complex.[2b] Moreover, *O*-sulfinato complexes are known to rearrange into their more stable *S*-sulfinato form.[11] In complex **5**, the central side chain of the polydentate ligand might be too short to allow stable coordination through S. This question is under examination, as is the possible oxidation of a second thiolato ligand.

Experimental Section

All operations were carried under argon, unless mentioned otherwise, with standard Schlenk techniques. Solvents were dried and distilled before use.

1: 1) A solution of **2**[3a] (263 mg, 0.85 mmol) was added under argon at 0 °C to a mixture of **3**[3b] (500 mg, 2.56 mmol) and $AlMe_3$ (2 M in heptane, 1.7 mL) in toluene (8 mL). After the mixture was heated at reflux for one night, the reaction was quenched by HCl (2 M). Extraction with EtOAc gave a crude product, which was purified by chromatography over silica gel (EtOAc/cyclohexane 1/3) to afford **4** (410 mg, 79 %). ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.31–7.19$ (m, 17H), 3.72 (s, 2H), 3.69 (s, 4H), 3.25 (d, 4H, $J =$ 5.7 Hz), 2.97 (s, 2H), 1.48 (s, 3H), 1.26 (s, 12H); MS (CI, NH_3): *m*/*z*: 609 (MH^+). 2) To a solution of **4** (400 mg, 0.66 mmol) in THF (4 mL) and liquid ammonia (6 mL) cooled to −45 °C were added small portions of Na (≈91 mg, 4 mmol) until the blue color remained for 30 mn. After addition of solid NH_4Cl (400 mg) and evaporation of ammonia, HCl (2 M) was added (pH 1). Extraction with CH_2Cl_2 followed by chromatography over silica gel (EtOAc/cyclohexane 1/4) gave ligand **1** (203 mg, 91 %). ^1H NMR (250 MHz, DMSO): $\delta = 7.83$ (t, 2H), 3.25 (d, 4H), 3.01 (d, 2H), 2.72 (s, 2H), 2.15 (t, 1H), 1.42 (s, 3H), 1.24 (s, 12H); IR ($CHCl_3$): $\tilde{\nu} = 1675\ cm^{-1}$ (C=O); high-resolution MS (CI, CH_4): *m*/*z* calcd for $C_{13}H_{27}O_2N_2S_3$ (MH^+): 339.1235, found: 339.1234.

5: To a solution of **1** (622 mg, 1.84 mmol) and NaH (224 mg, 9.35 mmol) in DMF (11 mL) cooled to −5 °C was added a solution of $FeCl_3$ (296 mg, 1.83 mmol) in DMF (1.5 mL). The deep red solution was stirred at −5 °C for 1 h, and then solid Et_4NCl (610 mg, 3.68 mmol) was added. After addition of EtOAc (145 mL), the solution was kept at −20 °C for one night. The remaining operations were carried out in air. The red precipitate was isolated, dried under vacuum, and dissolved in CH_3CN. The solution was then filtered over celite. The solvent was evaporated to afford **5** as a highly hygroscopic, deep red solid (1.1 g, 87 %).

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[4] X-ray crystal structure analysis of **5**: A red single crystal ($0.5 \times 0.5 \times 0.5\ mm^3$) of **5**, $(C_{13}H_{21}FeN_2O_4S_3)(NEt_4)_2$, grown from DMF/$Et_2O$, was glued in araldite; Nonius CAD4 diffractometer, $T = 253$ K. Orthorhombic space group $P2_12_12_1$, $a = 10.912(4)$, $b = 17.723(6)$, $c = 18.699(7)$ Å, $V = 3616(2)$ $Å^3$, $Z = 4$, $\rho_{calcd} = 1.25\ g\,cm^{-3}$. Anomalous dispersion terms and correction of secondary extinction were applied. The structure was solved by SHELXS-86 and refined by least-squares analysis using anisotropic thermal parameters for the atoms of the anionic complex and isotropic thermal parameters for the cation Et_4N^+. The hydrogen atoms were introduced in calculated positions; 2335 reflections [$F_o > 3\sigma(F_o)$], $R_1 = 0.0727$, $wR_2 = 0.0877$, 292 least-squares parameters. The programs CRYSTALS and CAMERON were used. Two equivalent positions S_{31} and S_{32} are found in the crystal lattice due to positional disorder resulting from the coordination of either O3 or O4. Crystallographic data (excluding structure factors) for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-120197. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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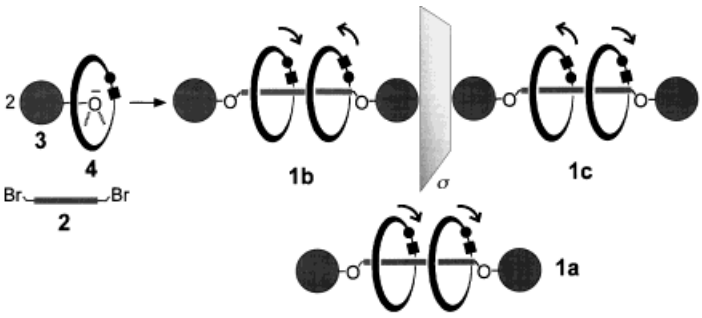


The First Cyclodiasteromeric [3]Rotaxane**

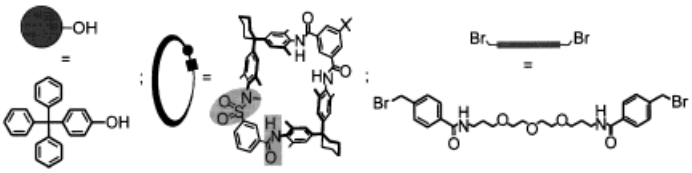
Roland Schmieder, Gosia Hübner, Christian Seel, and Fritz Vögtle*

Cycloenantiomerism in mechanically bonded molecules was first predicted by Frisch and Wassermann in 1961,[1] and the first catenanes and molecular knots displaying this property were synthesized by Sauvage et al. almost three decades later.[2, 3] As early as 1971, Schill proposed stereoisomeric [2]rotaxanes,[4] whose chiral information can be put down to a directed segment sequence in the macrocycle as well as in the axle. The axle and wheel are not chiral themselves; the mechanical connection, however, would yield a cycloenantiomeric rotaxane.

During the last decade several chiral [2]rotaxanes have been synthesized whose stereoisomerism is based on the central chirality.[5, 6] In 1997 we prepared the first cycloenantiomeric [2]rotaxanes and [1]rotaxanes as well as topologically chiral pretzelanes, which were separated into their enantiomers by means of chiral HPLC and chiroptically characterized.[6e] Recently several achiral [3]rotaxanes have been reported.[7] To our knowledge stereoisomeric [3]rotaxanes, however, have not been described yet.

We now succeeded in preparing a chiral [3]rotaxane containing two achiral wheels, which are mechanically bonded onto an achiral axle that is not directed. Analogous to the covalently linked tartaric acid, we obtained a cyclodiastereomeric compound.[8] Applying our new efficent trapping synthesis (chemical threading) for rotaxanes with diether axles,[9] we allowed the dibromide **2** to react with the stopper **3** in presence of the wheel **4**. Besides small amounts of the free axle and the [2]rotaxane (10%), the [3]rotaxane **1** was obtained in 29% yield (Scheme 1).[10]

If there is only one achiral wheel on a symmetrical axle, a [2]rotaxane with no stereoisomerism results. Rotaxanes like **1** bearing two wheels, the atomic sequences of which can be arranged clockwise or counterclockwise, should occur in a



Scheme 1. Schematic representation of the synthesis of the cylodiastereomeric [3]rotaxane as a pair of enantiomers (**1b**, **1c**) and as the *meso* form (**1a**).

meso form (**1a**) and a pair of enantiomers (**1b**, **1c**). The orientation of the macrocycles on the axle is caused by a different sequence of the three amide groups and the sulfonamide group. The two wheels **4** can have the same or opposite direction. In the case of the same orientation the *meso* compound **1a** is obtained, and the opposite direction of the wheels leads to **1b** and **1c**.

The high conformational flexibility of the molecule—in the sense of the extended translational and rotational movement of the wheels on the axle—raises the questions of whether the stereoisomers can be separated and whether chiroptical properties show significant differences. The results obtained hitherto on our separated chiral [2]- and [1]rotaxanes and catenanes indeed fueled our hopes for success. The enantiomers were successfully separated employing chiral HPLC (Chiralpak AD; Figure 1).[11, 12] First of all the (+) enantiomer was eluted in base line separation, followed by the (−) enantiomer. The retention time of the latter, however, differed only slightly from that of the *meso* form **1a** (Figure 1). Whereas the separation factor $\alpha_{(-),(+)}$ of the enan-

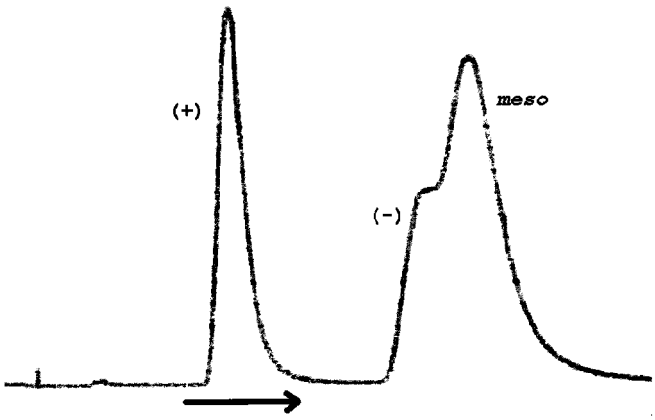


Figure 1. Chromatogram for the enantiomeric separation. Retention times: (+) enantiomer: 10.5 min, (−) enantiomer: 21.5 min, *meso* form: 23.5 min.[12]

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