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Synthesis and Structure of Novel Dinitrosyl Iron Complexes $[Fe_2(\mu\text{-}SCH_2CH_2NHR)_2(NO)_4]$

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Abstract—Two novel dinitrosyl iron complexes with thiolate bridging ligands $[Fe_2(\mu\text{-}SCH_2CH_2NHR)_2(NO)_4]$ (R = Ac, Boc), derived from the cysteamine complex $[Fe_2(\mu\text{-}SCH_2CH_2NH_3)_2(NO)_4]^{2+}$ are described. The complex with acylated cysteamine is characterized by X-ray diffraction analysis. The cysteamine complex is a convenient precursor for modification of the bridging ligand.

Keywords: coordination compounds of iron, nitrogen monoxide donors, structure, DFT calculations

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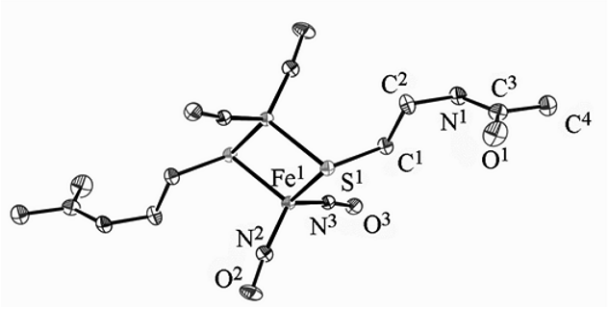
Nitrogen monoxide (NO) can have a considerable impact on the lifecycle of an organism: It affects inflammation processes [1], carcinogenesis [2], and transmission of nervous impulses [3]. The main mechanism of NO interaction with cells is covalent biding with sulfur of cystein protein residues [4]. S-Nitroso protein derivatives can further transform into various disulfides [5]. Thus, NO directly affects the thiol−disulfide cellular status [6].

At present a practically important problem is to develop means for NO delivery to biological targets. To this end, various NO donor are used [7]. Dinytrosyl iron complexes of the general formula $[Fe_2(\mu\text{-}SR)_2\cdot(NO)_4]$ [8] are promisining NO donors capable of sustained release of nitric oxide [9]. For practical application as NO donors, complexes which can selectively bind to target proteins should be developed. Therewith, the most preferred type of binding is key−lock binding via bridging ligands (μ-SR).

The cysteamine complex $[Fe_2(\mu\text{-}SCH_2CH_2NH_3)_2\cdot(NO)_4]^{2+}$ is a convenient scaffold for the synthesis of dinitrosyl iron complexes with functional μ-SR groups, as the amino group in this complex can be easily modified to allow introduction of varios substituents (Scheme 1).

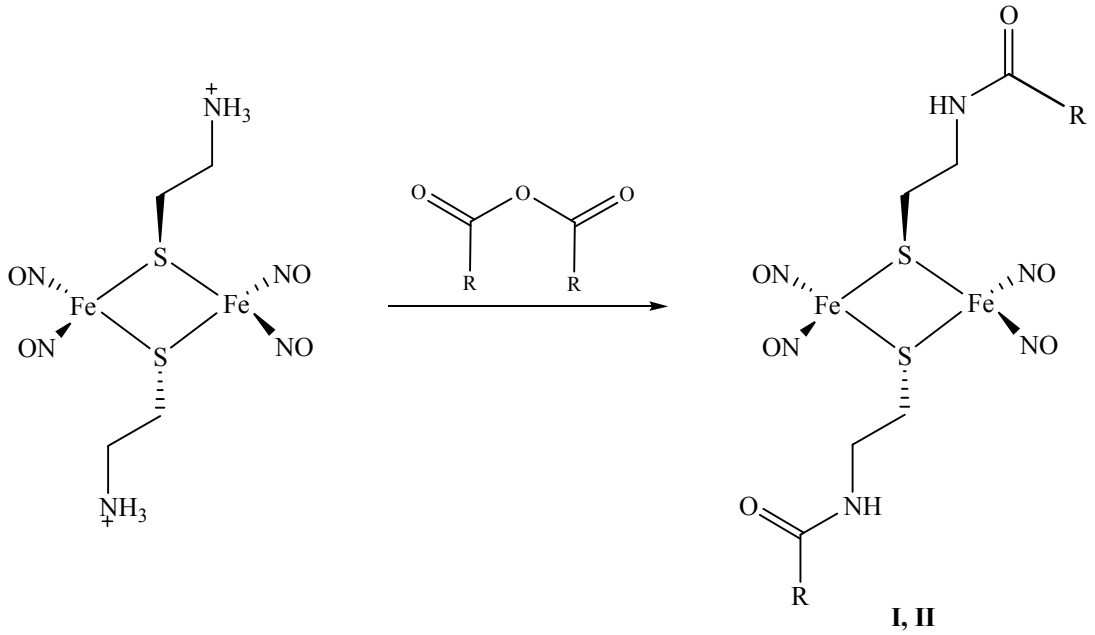
The molecular structure of the complex $[Fe_2(\mu\text{-}S(CH_2CH_2NHAc)_2(NO)_4]$ (**I**) is shown in the figure. The crystal structure of complex **I** is stabilized by four hydrogen bonds [10] between the donor amide groups NH and the carbonyl oxygen atoms [*d*(D···A) 2.883 Å] of three neighboring molecules along the crystallographic direction [100].

With the complex $[Fe_2(\mu\text{-}SCH_2CH_2NHBoc)_2(NO)_4]$ (**II**), we failed to obtain single crystals suibale for X-ray diffraction (XRD) analysis. Therefore, the geometry of the complex was established by quantum-chemical calculations with inclusion of aquation effects by the polarized continuum model [11]. The calculations showed that the substitution of Ac by Boc has no appreciable effect on the geometry of the



ORTEP drawing of the molecular structure of $[Fe_2(\mu\text{-}SCH_2CH_2NHAc)_2(NO)_4]$ (**I**). Non-hydrogen atoms are shown as 50% thermal ellipsoids, hydrogen atoms are not shown.

Scheme 1.



R=Ac (**I**), Boc (**II**).

common $[Fe_2(\mu\text{-}SCH_2CH_2NHC(O)R)_2(NO)_4]$ fragment, and the RMSD of internal coordinates for non-hydrogen atoms is 0.1 Å.

EXPERIMENTAL

Elemental analysis was performed on a LECO CHNS(O)-932 CHNS analyzer and a Perkin Elmer Optima 7300 DV ICP–OES spectrometer. The IR spectra in KBr were taken on a Shimadzu IR-Affinity-1 FTIR spectrometer. X-ray diffraction analysis was performed on a Bruker Smart APEX II CCD automated diffractometer. Quantum-chemical calculations were performed using Gaussian 09 software [12] by the DFT method with the PBEhVP86 exchange correlation in the cc-pVTZ basis set [13].

The crystal data for complex **I** were deposited in the Cambridge Structural Database (CCDC 990390) (http://www.ccdc.cam.ac.uk/deposit).

Acylation of the cysteamine complex $[Fe_2(\mu\text{-}SCH_2CH_2NH_3)_2(NO)_4]Cl_2$. The complex with the cysteamine bridging ligand ($\mu\text{-}SCH_2CH_2NH_3^+$) was prepared by the modified procedure [14]. The complex, 1 g (2.2 mmol) was dissolved in H_2O–EtOH, after which 1.23 g (2.2 mmol) of KOH and 0.55 g of $NaHCO_3$ (6.6 mmol) were added. Themixture was stirred for 15 min, and 0.21 mL (2.2 mmol) of Ac_2O was slowly added dropwise under stirring over the course of 10 min. After 1-h stirring the reaction product was extracted with ethyl acetate (2 × 20 mL). The extract was dried with anhydrous $NaSO_4$ and evaporated to dryness. The amorphous residue was crystallized from EtOH to obtain crystals of complex **I** suitable for XRD analysis.

Complex $[Fe_2(\mu\text{-}S(CH_2CH_2NHAc)_2(NO)_4]$ (I). Yield 55%. IR spectrum, ν, cm^{-1}: 1101, 1181, 1292, 1370, 1448, 1549, 1651, 1655, 1727, 1757, 3292. Crystall cell parameters: *a* 4.8462(3), *b* 8.0091(7), *c* 12.3753(8) Å; α 102.236(6)°, β 97.687(6)°, γ 106.263(7)°; *Z* 1, *V* 440.99(6) $Å^3$. Found, %: C 20.01; H 4.25; Fe 22.16; N 18.32; S 13.50. $C_8H_{16}Fe_2N_4O_6S_2$. Calculated, %: C 20.53; H 3.45; Fe 23.86; N 17.95; S 13.70.

Complex $[Fe_2(\mu\text{-}SCH_2CH_2NHBoc)_2(NO)_4]$ (II) was prepared in a similar way, using di-*tert*-butyl dicarbonate as the acylating agent. Yield 45%. IR spectrum, ν, cm^{-1}: 783, 865, 953, 1165, 1219, 1251, 1274, 1300, 1365, 1390, 1444, 1513, 1524, 1681, 1737, 1788, 1809, 2938, 2982, 3353, 3372, 3505. Found, %: C 28.26; H 4.66; Fe 20.01; N 19.58; S 10.47. $C_{14}H_{28}Fe_2N_6O_8S_2$. Calculated, %: C 28.78; H 4.84; Fe 19.12; N 14.39; S 10.98.

Thus we showed in the present work the dinitrosyl iron complex $[Fe_2(\mu\text{-}S(CH_2CH_2NH_3)_2(NO)_4]Cl_2$ can be used as a scaffold for synthesis of more complicated acylated complexes.

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