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Unexpected Assembly of a Novel Triply Bridged Diiron(II) Core by a Bidentate Schiff Base Ligand

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Abstract

The unusual dinucleating properties of a simple bidentate Schiff base (LH, **1**) in the presence of weakly coordinating methanol solvent lead to the self-assembly of $[\text{Fe}^{\text{II}}_2(\text{L}_b)_2(\text{L}_t)_2(\mu\text{-MeOH})]$ (**2**) (*b* and *t* refer to *bridging* and *terminally* bound ligands, respectively). Complex **2** is the first diiron (II) species in which the two metal centers are triply bridged by single atoms in an asymmetric fashion, involving both $\mu\text{-O}^{\text{Ph}}$ and $\mu\text{-OH}^{\text{Me}}$ bridges. This binding mode produces an $\text{Fe}\cdots\text{Fe}$ distance of 3.139 (1) Å. Dinucleation appears to be driven by a combination of ligand deficiency and solvent-mediated chemistry reminiscent of host–guest interactions. The presence of a $\mu\text{-MeOH}$ ligand is unprecedented in iron chemistry. Parallel-mode EPR spectra of complex **2** recorded at 4 K show an intense negative signal at $g_{\parallel} \approx 16$, suggesting the dimeric form exists in solution.

Keywords

Schiff base; Diiron(II) complex; Ferromagnetic coupling; Crystal structure; EPR spectroscopy

1. Introduction

Salicylaldimine-type (sal) Schiff bases have found wide application as ligands in coordination chemistry. Bioinorganic model chemistry has made extensive use of tetradentate salen [*N,N'*-ethylenebis(salicylideneaminato)] and related ligands to mimic the active sites in metalloproteins and metalloenzymes [1–4]. Salen complexes also show great utility in small-molecule activation. Metal–salens are widely used in catalysis [5] because they can expand their coordination numbers and stabilize metals in various oxidation states. In addition, Schiff-base complexes have been described that mediate oxidative DNA cleavage [6] or act as superoxide dismutase (SOD) mimics [7], suggesting potential biochemical and clinical applications. We have synthesized the novel sal derivative, *N*-(2-(4-methoxybenzylsulfanyl)ethyl)salicylaldimine (LH, **1**, Scheme 1), to act as a bioactive tridentate N,O,S iron(II) chelator. We report here the unexpected self-assembly of a novel diiron(II) core from **1**, which, contrary to its design, acts as a bidentate N,O-donor (Scheme 1). Dinucleation appears to be driven by a combination of ligand deficiency and host–guest chemistry.

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2. Experimental

2.1. Preparation of compounds

2-(4-methoxybenzylsulfanyl)ethylamine—A solution of 4-methoxybenzyl chloride (1.23 ml, 9.0 mmol) in 50 ml of dry CH_2Cl_2 was added dropwise within 1.5 h at 0 °C to a mixture of 2-aminoethanethiol hydrochloride (1.03 g, 9.0 mmol) and 9 ml of trifluoroacetic acid in 50 ml of CH_2Cl_2 . When addition was complete, the solution was allowed to warm to room temperature while stirring was continued (approximately 1 h). The reaction mixture was extracted with 150 ml of a MeOH/water (1:3) mixture and another 60 ml of water. The combined aqueous layers were washed with 100 ml of CH_2Cl_2 and concentrated to a volume of 30–40 ml by rotary evaporation. The pH of the strongly acidic aqueous solution was adjusted to 7.3 by adding saturated aqueous NaHCO_3 in small portions. After storing the solution at 4 °C for 12 h, the precursor precipitated as a flaky white solid, which was filtered, washed exhaustively with cold water, and finally dried in vacuum. Yield: 1.31 g (74%). ^1H NMR (300 MHz, $\text{MeOH}-d_4$): δ 2.52 (t, 2H, ethylene- CH_2), 2.72 (t, 2H, ethylene- CH_2), 3.68 (s, 2H, benzyl- CH_2), 3.77 (s, 3H, O- CH_3), 6.86 (d, 2H, phenyl-H), 7.24 (d, 2H, phenyl-H).

N-(2-(4-methoxybenzylsulfanyl)ethyl)salicylaldehyde (LH, 1)—A mixture of 0.80 g (4.0 mmol) of 2-(4-methoxybenzylsulfanyl)ethylamine and 0.54 g (4.4 mmol) of salicylaldehyde was heated at reflux in 20 ml of CH_2Cl_2 for 4 h in the presence of anhydrous MgSO_4 . The drying agent was removed by filtration, and the solvent removed in vacuum. To the oily residue were added 3 ml of absolute EtOH, and the solution stored at 4 °C for 24 h. Schiff base **1** crystallized as bright yellow crystals which were recovered by filtration and dried in vacuum at room temperature. Yield: 0.85 g (70%). mp: 51 °C. ^1H NMR (300 MHz, $\text{MeOH}-d_4$): δ 2.74 (t, 2H, ethylene- CH_2), 3.71 (s, 2H, benzyl- CH_2), 3.73 (t, 2H, ethylene- CH_2), 3.77 (s, 3H, O- CH_3), 6.85 (d, 2H, phenyl-H), 6.82–6.87 (m, 2H, sal-H), 7.24 (d, 2H, phenyl-H), 7.21–7.30 (m, 2H, sal-H), 8.37 (s, 1H, aldimine-H). Analysis for **1**: $\text{C}_{17}\text{H}_{19}\text{NO}_2\text{S}$. Calc.: C, 67.74; H, 6.35; N, 4.65; S, 10.64. Found: C, 67.10; H, 6.49; N, 4.50; S, 10.25.

$[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})] \cdot \text{MeOH}$ ($2 \cdot \text{MeOH}$)—All manipulations were performed under argon atmosphere in a glove box in dry and O_2 -free solvents. Sodium methoxide was generated by dissolving 19 mg (0.83 mmol) of sodium metal in 25 ml of MeOH. To this solution were added 250 mg (0.83 mmol) of Schiff base **1**. A clear yellow solution resulted (approximately 15 min), to which 53 mg (0.42 mmol) of anhydrous FeCl_2 were added with stirring. The solution immediately turned red, and a fluffy red precipitate formed. Stirring was continued for another 30 min, and the solvent was removed in vacuum. The solid residue was redissolved in 20 ml of CH_2Cl_2 to afford a deep burgundy-red solution, which was passed through a medium-pore size filter to remove insoluble NaCl. The filtrate was concentrated to a thick oily residue, which turned into a microcrystalline solid after adding 20 ml of MeOH and stirring of the mixture for 48 h. The red precipitate was filtered off and dried in vacuum at room temperature for 12 h. Yield: 183 mg (64%) of the mono-MeOH solvate, $2 \cdot \text{MeOH}$. Analysis for **2**: $\text{C}_{70}\text{H}_{80}\text{Fe}_2\text{N}_4\text{O}_{10}\text{S}_4$. Calc.: C, 61.04; H, 5.85; N, 4.07. Found: C, 61.18; H, 5.34; N, 4.17. UV-vis (75% CH_2Cl_2 /25% MeOH): 353 nm (8600), 496 (1100). See Fig. 3 for NMR spectroscopic data.

2.2. Physical measurements

The X-ray intensity data for complex $2 \cdot 1.5\text{MeOH}$ were measured on a Bruker SMART APEX CCD area detector system. The structure was solved and refined using the Bruker SHELXTL software package (version 6.12). Crystallographic data for $2 \cdot 1.5\text{MeOH}$ are summarized in Table 1. The disorder of one of the 4-methoxyphenyl rings was modeled. The disorder of one MeOH molecule was modeled with half occupancy. All non-hydrogen atoms were refined

anisotropically, except for the disordered 4-methoxyphenyl ring and the half-occupancy MeOH. Details of the structure determination have been deposited in CIF format.

UV-visible spectra of $[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})] \cdot 1.5\text{MeOH}$ (**2** · 1.5MeOH) in 75% CH_2Cl_2 /25% MeOH were recorded at 298 K on a Hewlett Packard 8453 diode array spectrophotometer equipped with a Peltier temperature-controlled cell-holder unit. Solutions were prepared in a glove box under Ar atmosphere. ^1H NMR spectra of $[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})] \cdot 1.5\text{MeOH}$ (**2** · 1.5MeOH) (500 MHz, 298 K, 75% CD_2Cl_2 /25% MeOH- d_4) were recorded on a Bruker DRX-500 spectrometer equipped with an inverse 3-channel Z-gradient TBI probe and a variable-temperature unit. Data were acquired with a spectral width of 380000 Hz, a relaxation delay of 30 ms, and a total of 512 transients. The FIDs were multiplied with an exponential apodization function using a line broadening of 30 Hz before Fourier transformation. Data processing was done with Felix 2000 (Accelrys, San Diego). Solutions were prepared in a glove box under argon atmosphere in deuterated solvents purged with purified argon. Chemical shifts (δ) are reported vs. internal TMS standard. Assignments were assisted by T_1 measurements (inversion recovery experiments), and integral signal intensities. X-band EPR spectra of a 2 mM frozen solution of $[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})] \cdot 1.5\text{MeOH}$ (**2** · 1.5MeOH) in 35% MeOH/65% CH_2Cl_2 were recorded on a Bruker E-500 spectrometer equipped with an Oxford ESR-10 liquid-helium cryostat. Spectra were recorded in parallel mode.

3. Results and discussion

Compound **1** was obtained in good yields in a two-step reaction involving benzylation of the mercapto sulfur in 2-aminoethanethiol [8] and subsequent condensation of the primary amino group with salicyl aldehyde. The title complex, $[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})]$ (**2**), forms under anaerobic conditions by reaction of anhydrous FeCl_2 with two equivalents of deprotonated Schiff base **1** in MeOH. Complex **2** was isolated in 64% yield as a MeOH solvate in the form of thin red needles and fully characterized by single-crystal X-ray crystallography, NMR, EPR, and UV-visible spectroscopy, and elemental analyses.

Single crystals of the methanol solvate, **2** · 1.5MeOH, suitable for X-ray diffraction were grown by slow evaporation of a MeOH/ CH_2Cl_2 solution. The structure of complex **2** and an expanded view of the diiron core along with selected geometric parameters are presented in Figs. 1 and 2. The asymmetric unit contains a discrete, neutral dinuclear complex, $[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})]$ (**2**), and 1.5 molecules of methanol solvent. The two Fe^{II} ions are bridged by the phenoxo groups of two of the four bidentate Schiff bases and the oxygen atom of a MeOH molecule. The resulting dinuclear geometry is best described as face-sharing distorted octahedral with iron in a N_2O_4 mixed-donor environment. Fe–O and Fe–N distances for the terminally bound sal ligands are consistent with those observed in similarly substituted diiron complexes [9,10]. The sal ligands in **2** adopt a propeller-like arrangement. While the planar six-membered chelate rings attached to the same Fe^{II} center show a nearly perpendicular orientation, the mean planes through the N,O-chelates of adjacent Fe^{II} centers intersect at 41.5° (mean). This arrangement leads to short distances between the aromatic groups of the mutually *cis*-oriented bridging and terminal sal ligands, which produces stacking of the edge of one of the phenyl rings into the π -cloud of the neighboring ring. The steric hindrance produced by this interaction appears to be the source of the Fe_2O_2 unit's unequal Fe–O distances, which are significantly longer for the phenoxo-mediated bonds between the $[\text{FeL}_2]$ moieties [2.230(3) Å, mean] compared to the bonds within each moiety [2.017(3) Å, mean]. Likewise, an asymmetric binding mode is observed for the $\mu\text{-MeOH}$ (C18) ligand with Fe–O distances of 2.353(5) and 2.501(5) Å. The latter value indicates a weak interaction with one of the metal centers. The $\mu\text{-MeOH}$ ligand is involved in a hydrogen bond network mediated by another non-coordinated solvent molecule (O4/C19), which most likely causes the asymmetry. The triply bridged geometry produces a short Fe–Fe separation of 3.139(1) Å. Short van der Waals contacts of 3.743 and 3.753 Å are

observed between C18 and S1B, and between C19 and S1, respectively. This feature corroborates the notion that the ligand peripheries contribute to the stabilization of the weak MeOH coordination.

Electronic absorption spectra (not shown) recorded of solutions of complex **2**, which are deep red in color, show a broad feature at $\lambda_{\text{max.}} = 496 \text{ nm}$ ($\epsilon = 1100$), which can be assigned to a charge-transfer transition [10]. The ^1H NMR spectrum of **2** in $\text{CD}_2\text{Cl}_2/\text{MeOH-}d_4$ (Fig. 3) shows the well-resolved signals of the Schiff base protons, which are isotropically shifted due to the strong paramagnetism of the iron centers. The magnitude and signs of the isotropic shifts and the line widths of the resonances of the ethylsalicylaldimine portion of the ligand are consistent with spin delocalization onto the N,O-bound ligand from the high-spin Fe^{II} centers [11]. The most dramatic isotropic shift is observed for the imine proton ($\text{CH}=\text{N}$), which resonates at 446.2 ppm. Only one set of NMR signals is observed, suggesting that the terminal and bridging sal ligands in **2** exchange rapidly on the NMR time scale, perhaps by a monomer–dimer equilibrium. While the NMR data cannot rule out the coexistence of mononuclear and dinuclear species, X-band EPR spectra recorded in parallel mode of a frozen solution of complex **2** at 4 K in the same solvent mixture suggest that a dinuclear entity is the dominant species in solution: An intense low-field signal is observed at $g \approx 16$, characteristic of the $S = 4$ integer spin state of ferromagnetically coupled diiron(II) centers (Fig. 4) [12].

The structure of **2** suggests that the driving force for the self-assembly of the dinuclear entity is a combination of ligand deficiency and ligand–receptor interactions. The ligand deficiency is the result of the inability of the Schiff base L to accommodate mononuclear tridentate coordination involving thioether sulfur, $[\text{Fe}(\text{L-N,O,S})_2]$, as implicated by the dangling 4-methoxybenzylsulfanyl groups in complex **2**. To ameliorate this situation, the system dimerizes through formation of a $\text{Fe}_2\text{O}^{\text{Ph}}_2$ core and recruitment of an exogenous solvent molecule into the hydrophobic scaffold produced by the ligand peripheries.

The presence of a bridging MeOH ligand *per se* is unprecedented in iron(II) chemistry. We postulate that this binding mode in **2** is feasible because of favorable interactions between the MeOH ligand and the walls of the binding pocket defined by the methoxybenzylsulfanyl groups (Fig. 1). It is important to note that the reaction of ferrous ion with the Schiff base *N*-isopropylsalicylaldimine (LH') in MeOH results in a distorted corroborating tetrahedral complex, $[\text{FeL}'_2]$, both in the solid state and in solution [13], that the presence of MeOH alone is not sufficient to induce dinucleation.

A search of the Cambridge Structural Database confirms the uniqueness of the structure reported in this note. Complex **2** is the first example of a diiron(II) species containing three single-atom bridges, in which one bridge is formed by a weakly bound solvent molecule. Only a few examples of similarly coordinated diiron complexes are known, which either lack a neutral bridging ligand, such as dimeric bis(acetylacetonato)iron(II) [14], and/or contain iron (III). Two examples of the latter type of complex are the tris(μ -hydroxo)-bridged mixed-valent species, $[\text{Fe}_2(\text{OH})_3(\text{tmtacn})_2]^{2+}$ ($\text{tmtacn} = N,N',N''$ -trimethyltriazacyclononane) [15], and ferric citrate [16].

4. Conclusions

The structure reported in this paper can be considered a self-assembled, *pseudo-coordinatively unsaturated* diiron(II)-based small-molecule receptor. The question arises, if the Fe^{II}_2 center is accessible to other exogenous molecules, such as dioxygen. The structure and several of the spectroscopic properties of complex **2** are reminiscent of those observed for the reduced forms of non-heme dioxygen-activating enzymes. Synthetic functional models of these enzymes are of interest for their use as catalysts in C–H bond activation (*e.g.*, as hydroxylation catalysts).

An important aspect of complex **2** (and related compounds) is therefore its reactivity with dioxygen. Substitution of the neutral (and presumably labile) MeOH ligand in **2** by an O₂ molecule in a controllable manner could potentially lead to catalytically and/or biochemically useful (high-valent) iron oxygenation chemistry [17]. With respect to potential biological applications, it is also important to assess if the chemistry reported in this communication extends to aqueous solutions. Studies addressing these issues are currently underway. In conclusion, we have demonstrated that ferrous ion self-assembles into a triply bridged dimer in the presence of a simple Schiff-base derivative. The core structure and scaffold produced by ligand **1** will serve as a prototype for the design of related polydentate ligands for probing and exploiting high-valent iron chemistry.

Appendix A. Supporting Information Available

Details of the structure determination have been deposited in CIF format with The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K., deposition code CCDC-278005.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.
Thermal ellipsoid presentation of [Fe₂L₄(μ-MeOH)] (**2**) in the solid state with selected atoms labeled. Hydrogen atoms have been omitted for clarity.

Fig. 2.

Expanded view of the diiron(II) core in complex **2** giving atom numbering. The 4-OMe-benzyl groups are not shown for clarity. Selected bond lengths (Å) and angles (°) with standard deviations: Fe(1)–O(1A) 1.950(4), Fe(1)–O(1) 2.027(3), Fe(1)–N(1A) 2.106(5), Fe(1)–N(1) 2.122(5), Fe(1)–O(1B) 2.259(3), Fe(1)–O(3) 2.353(5), Fe(2)–O(1C) 2.005(3), Fe(2)–O(1B) 2.008(3), Fe(2)–N(1B) 2.100(4), Fe(2)–N(1C) 2.111(4), Fe(2)–O(1) 2.200(3), Fe(2) ... O(3) 2.501(5), Fe(1)–Fe(2) 3.139(1); Fe(1)–O(1)–Fe(2) 95.82(14), Fe(2)–O(1B)–Fe(1) 94.56(14), Fe(1)–O(3)–Fe(2) 80.52(15).

Fig. 3.

^1H NMR spectrum of $[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})] \cdot 1.5\text{MeOH}$ ($2 \cdot 1.5\text{MeOH}$) (500 MHz, 298 K, 75% $\text{CD}_2\text{Cl}_2/25\%$ $\text{MeOH-}d_4$). Chemical shift assignments (δ , vs. internal TMS standard): 446.2 ($\text{C}_{\alpha'}\text{H}$), 84.1 ($\text{C}_{\alpha}\text{H}_2$), 49.9 (H_6), 43.4 (H_4), 30.3 ($\text{C}_{\delta}\text{H}_2$), 7.32 (H_3'/H_5'), 5.80 (H_2'/H_6'), 3.92 (OCH_3), -5.1 (H_5), -13.0 ($\text{C}_{\beta}\text{H}_2$), -14.4 (H_3). Assignments were assisted by T_1 measurements (inversion recovery experiments) and integral signal intensities. Peaks labeled with an asterisk or a cross, are assigned to residual solvent protons.

Fig. 4. X-band EPR spectrum of a 2 mM frozen solution of $[\text{Fe}_2\text{L}_4(\mu\text{-MeOH})] \cdot 1.5\text{MeOH}$ (**2** · 1.5MeOH) in 35% MeOH/65% CH_2Cl_2 recorded in parallel mode.

Scheme 1.

Table 1

Crystal data for **2** · 1.5MeOH

Empirical formula	$C_{70.5}H_{82}Fe_2N_4O_{10.5}S_4$
Formula weight	1393.34
Temperature (K)	193(2)
Wavelength Mo K α (Å)	0.71073
Crystal system	triclinic
Space group	<i>P</i> $\bar{1}$
<i>Unit cell dimensions</i>	
<i>a</i> (Å)	10.851(2)
<i>b</i> (Å)	17.916(4)
<i>c</i> (Å)	19.710(4)
α (°)	67.684(4)
β (°)	78.240(4)
γ (°)	83.065(4)
Volume (Å ³)	3466.4(12)
<i>Z</i>	2
ρ_{calcd} (Mg/m ³)	1.335
Absorption coeff. (mm ⁻¹)	0.599
Crystal size (mm ³)	0.44 × 0.06 × 0.02
θ Range for data collection (°)	3.82–24.5
Data/restraints/parameters	11465/78/880
Final <i>R</i> indices [<i>I</i> > 2 σ (<i>I</i>)]	<i>R</i> 1 = 0.0666, <i>wR</i> 2 = 0.1108
<i>R</i> indices, all data	<i>R</i> 1 = 0.1704, <i>wR</i> 2 = 0.1337
Largest difference in peak and hole (e Å ⁻³)	0.584, −0.606