A cyclic tetra-nuclear dinitrosyl iron complex [Fe(NO)$_2$(imidazolate)]$_4$: synthesis, structure and stability†

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A novel cyclic tetra-nuclear dinitrosyl iron complex [Fe(NO)$_2$(Im-H)]$_4$ was isolated and characterized by X-ray crystallography, and in donor solvents this fragments into 17 e$^-$ monomeric units that give EPR spectra analogous to the g = 2.03 species seen in mammalian biology.

Dinitrosyl iron complexes are thought to play key roles in a number of diverse physiological processes.[1] For example, evidence suggests that they reserve and transport nitric oxide (NO) in vivo, and they have also been identified as products after the biosynthetic evolution of NO in vitro and intermediates of the iron-catalyzed degradation and formation of S-nitrosothiols.[2] EPR studies indicate that the immune system utilizes NO to combat intracellular pathogens and the process produces the dinitrosyl iron complex Cys$_2$Fe(NO)$_2$.[3] It has also been proposed that a dinitrosyl iron complex stabilizes NO in cells and provides both NO-transfer in tissues and its release to the active free state.[4] Moreover, Muller et al.,[5] and other groups[1,6,7] have reported that nitric oxide stores as non-heme iron-nitrosyl complexes. Such dinitrosyl iron complexes have been investigated extensively by EPR techniques in biological systems and exhibit a characteristic isotropic g-factor of "g = 2.03".[8–10] However, the difficulty of extracting and isolating these compounds has prevented their full characterization, so there is considerable interest in developing molecular models of biologically prevalent dinitrosyl iron complexes. These models help elucidate the dinitrosyl iron electronic structure, while serving as spectroscopic references and potential NO delivery systems.[11–14]

Our research focuses on the synthesis of iron dinitrosyl compounds containing histidine-based ligands and we have reported a tetrahedral structure of Fe(NO)$_2$(1-methylimidazole)$_2$.[15] Here we report the synthesis and X-ray crystal structure of a remarkable cyclic tetra-nuclear iron complex [Fe(NO)$_2$(Im-H)]$_4$ (1), with bridging imidazolate anions linking 17 e$^-$ iron dinitrosyl units.

The synthesis was carried out in a glove box under a nitrogen atmosphere. One equivalent of Fe(NO)$_2$(CO)$_2$ reacted with two equivalents of imidazole, C$_3$N$_2$H$_4$, in methylene chloride at room temperature. After stirring for twenty four hours, a dark reddish brown precipitate was obtained and collected by filtration with a 50% yield. Single crystals suitable for X-ray diffraction analysis

were isolated by the recrystallization of 1 from acetone at −38 °C under a nitrogen atmosphere.

The crystal structure of 1, determined by X-ray crystallography,[16] is shown in Fig. 1. It is monoclinic and crystallized in a C2/c space group, with four molecules per unit cell. Each iron center is coordinated to four nitrogen atoms, two from the nitrosyl ligands and two from the imidazolate ligands Im-H, with pseudo-tetrahedral center geometry. The four iron centers are linked together through four deprotonated imidazole bridging ligands forming a neutral 16-membered rhombic macrocycle with
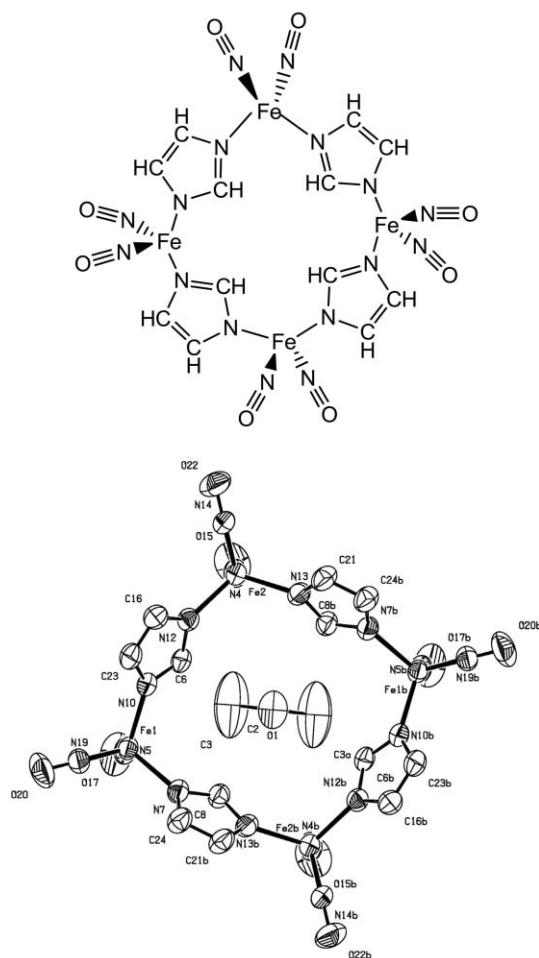

Fig. 1 Molecular drawing and X-ray crystal structure of [Fe(NO)$_2$(Im-H)]$_4$, showing the atomic numbering scheme. Anisotropic thermal displacement ellipsoids are shown at the 50% probability level.

alternating imidazolates and irons. The molecule has dimensions of 8.18 × 8.70 Å (Fe1···Fe1 × Fe2···Fe2). Additional electron density inside the ring has been assigned to one molecule of acetone.

There are substantial differences between the C–N bond lengths of the imidazolate ligands of **1** and the uncoordinated imidazole. The crystal structure of imidazole shows two different C–N bond lengths of 1.349(4) and 1.326(6) Å.[17] In the ligated imidazolates of **1**, however, the two C–N bond lengths are approximately equal with a mean value of 1.338(6) Å, between the two values of the free imidazole. This can be explained in terms of π-delocalization owing to deprotonation of the bridging ligand. To balance the negative charge on the imidazolate ligand, each iron center should carry one positive charge, since the whole molecule is neutral. This is reflected by the relatively short Fe–N (Im-H) bond distances (with an average value of 2.005(5) Å and a range from 1.997(5) to 2.009(5) Å) in comparison with the values reported for $Fe(NO)_2$-(1-MeIm)$_2$ (average value of 2.046(3) Å).[15]

The N–O bond lengths range from 1.162(7) to 1.172(7) Å with an average value (1.166 Å) shorter than the N–O distance of 1.189(3) Å of $Fe(NO)_2$(1-MeIm)$_2$. This is expected because the positive iron atom in the cyclic molecule would donate comparatively less electron density to the π* orbitals of the nitrosyl ligands than the neutral iron of $Fe(NO)_2$(1-MeIm)$_2$. The Fe–N (NO) bonds range from 1.688(5) to 1.698(5) Å with an average value of 1.694 Å and are longer than those in $Fe(NO)_2$-(1-MeIm)$_2$ due to the less extensive π back-bonding.

The FT-IR spectra of the product **1**, $Fe(NO)_2(CO)(Im)$ (**2**), and the starting material, $Fe(CO)_2(NO)_2$ (**3**) were recorded. For **1**, the nitrosyl stretching frequencies ν_{NO} occur at 1796 and 1726 cm^{-1}. The ν_{NO} values for **2** (1731 and 1687 cm^{-1}) appear at lower frequencies than those of **3** (1807 and 1758 cm^{-1}), consistent with replacing a CO with the more electron-donating imidazole ligand. Since in complex **1**, both carbonyls have been replaced by a donor ligand on each metal, one would expect the nitrosyl stretching frequencies to shift to even lower wavenumbers. This was not observed, and we conclude that the unexpected ν_{NO} shift to higher frequencies to the oxidation of the $Fe(NO)_2$ units to balance deprotonation of the bridging ligands. It has been established by Liaw *et al.*[18] that the NO stretching frequencies are related to the oxidation levels of DNIC and the observed ν_{NO} in **1** makes it $\{Fe(NO)_2\}^9$, according to the Enemark–Feltham notation.[19]

Taken separately, the $Fe(NO)_2L_2$ units of **1** are 17 e$^-$ complexes and should be paramagnetic. Since the four iron centers are closely connected, strong coupling between the four paramagnetic centers would be expected. However, a solid-state EPR spectrum recorded using an X-band Bruker EMX EPR spectrometer at room temperature showed a very broad peak at $g = 2.023$ with a peak-to-peak width of 250 G, indicating that the metal centers are weakly coupled to each other. In contrast, when the EPR spectrum was recorded at room temperature in THF solution, a signal at $g = 2.031$ with ΔHpp = 13.2 G was observed instead of the broad peak. The new signal observed in THF solution becomes a well-resolved 9-line spectrum at 170 K as shown in Fig. 2a. The computer simulation of this spectrum,[20] shown in Fig. 2b, indicates that the hyperfine structure is a result of the coupling of two equivalent ^{14}N ($I = 1$) nuclei from the nitrosyls and one ^{14}N from the imidazolate, with hyperfine coupling constants of 2.54 and 4.50 G, respectively. The characteristic g value close to 2.03 and the
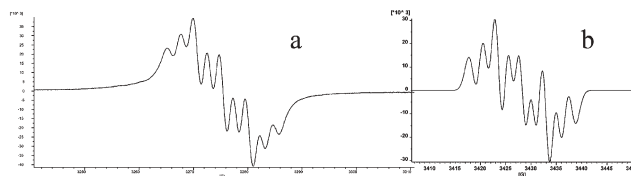

Fig. 2 (a) First derivative EPR spectrum of $[Fe(NO)_2(Im-H)]_4$ in THF at 170 K. (b) Computer simulation of the spectrum with $a_{N1}(2) = 2.54$ G and $a_{N2}(1) = 4.50$ G.

small hyperfine coupling constants (2–3 G) indicate that the unpaired electrons are localized on the Fe center, which is typical of dinitrosyl iron compounds found in biological systems.[8–10,21,22] However, if this signal was produced from the cyclic tetramer **1** with unpaired electrons localized on the iron center, one would expect to see couplings to two equivalent nitrogens from the bridging imidazolate ligands. The fact that coupling to only one imidazolate nitrogen was observed suggests that the tetrameric molecule may have fragmented and solvated to give the seventeen electron species $Fe(NO)_2(Im-H)(THF)$ or its protonated analog $[Fe(NO)_2(Im-H)(THF)]^+$, which has similar g and a values.[21,23]

The presence of the solvated species, $[Fe(NO)_2(Im-H)(THF)]$, was further investigated using FT-IR spectroscopy. Complex **1** was dissolved in the non-coordinating solvent CH_2Cl_2 and the coordinating solvents CH_3CN, THF, and DMF. In CH_2Cl_2, the two nitrosyl peaks appear at 1801 and 1735 cm^{-1}. In the coordinating solvents, additional nitrosyl peaks showed up in the range of 1630–1641 cm^{-1}. These additional peaks were attributed to the solvated species. The relative ν_{NO} absorbances from the nitrosyls of the two species were used to estimate the percentage of solvated species in each solvent, which were 5%, 43%, and 55% in THF, CH_3CN, and DMF, respectively. Although the solvated species is only a minor component in THF, a strong EPR signal was still observed because of the high selectivity and sensitivity of the EPR technique.

The TGA curve[24] of the complex **1** under a N_2 atmosphere in the dark showed that there were four steps of weight loss. Between 100 and 140 °C, there is about 14.3% weight loss, which is attributed to the loss of one imidazole and one NO (calcd. 13.4%). The second weight loss of 10.2% at temperatures ranging from 180 to 220 °C is ascribed to the loss of one imidazole. Further decomposition was observed when heated at higher temperatures.

In conclusion, a novel cyclic tetra-nuclear dinitrosyl iron complex, $[Fe(NO)_2(Im-H)]_4$, has been synthesized. Each Fe center can be described as a 17-electron complex based on X-ray, IR and EPR spectroscopic results. This complex showed NO release when heated under N_2.

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16 Crystal data (MoKα chemical formula $C_{12}H_{12}Fe_4N_{16}O_8$, C_3H_6O; formula weight 789.85; $a = 21.30(3)$, $b = 6.709(9)$, $c = 22.73(3)$ (Å); $\alpha = 90$, $\beta = 103.93(4)$, $\gamma = 90°$; volume 3151(7); space group $C2/c$; $Z = 4$; absorption coefficient 1.871 mm^{-1}; independent reflections $[I > 2\sigma(I)]$ 3085; R_{int} 0.086; GOF 1.196; final R indices $[I > 2\sigma(I)]$ $R_1 = 0.0597$, $wR_2 = 0.1475$; R indices (all data) $R_1 = 0.0706$, $wR_2 = 0.1535$.‡
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