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Bar, Arun Kumar, Ojea, Maria Jose Heras, Tang, Jinkui and Layfield, Richard A (2020) Coupling of nitric oxide and release of nitrous oxide from rare-earth-dinitrosyliron complexes. Journal of the American Chemical Society, 142 (9). pp. 4104-4107. ISSN 0002-7863

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Coupling of Nitric Oxide and Release of Nitrous Oxide from Rare-Earth-Dinitrosyliron Complexes

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Supporting Information Placeholder

**ABSTRACT:** Addition of Lewis acidic [Cp*2M]+ (M = Y, Gd) to the dinitrosyliron complexes [DNICs] [(NacNac⁰)Fe(NO)]⁻ (Ar = mesityl, 2,6-diisoproplyphenyl) results in formation of the isonitrosyl-bridged DNICs [(Cp*)₂M(μ-ON):Fe(NacNac⁰)]. When Ar = 2,6-diisoproplyphenyl, coupling of the NO ligands and release of NO occurs. Two factors contribute to this previously unobserved DNIC reactivity mode. Firstly, the oxophilic rare-earth elements drive the formation of isonitrosyl bonds, forcing the DNIC nitrogen atoms into proximity. Secondly, the bulky substituents further squeeze the DNIC, which ultimately overcomes the barrier to NO coupling and demonstrating that NO elimination can occur from a single iron centre.

Nitric oxide plays a key role in signalling functions in the cardiovascular system of higher mammals.¹ It is involved in the degradation and re-assembly of iron-sulphur clusters,² and it is a reactive nitrogen species involved in nitrosative stress – a process that can lead to cell damage and disease.³ Removal of intracellular nitric oxide is achieved through the action of flavo-diiron nitric oxide reductase (FNOR), resulting in the formation of nitrous oxide during bacterial denitrification.⁴ The mechanism through which two molecules of NO are coupled by FNOR to produce N₂O is the subject of intense discussion.⁵,⁶ The NO coupling step is thought to produce metal-bound hyponitrite, [N₂O₃]²⁻, a process that may involve the ligand forming either in the cis- or the trans-geometries.⁷ Evidence for each pathway has been obtained from studies of enzymes and of biomimetic compounds,⁸,⁹ including structural and functional studies in which the metals are bridged by a hyponitrite ligand.¹⁰

Dinitrosyliron complexes (DNICs) are important intracellular NO-containing species, small-molecule models of which abound.¹¹-¹⁴ The coupling of the two NO ligands in a monometallic model DNIC to produce NO has, however, never been observed. The apparent reluctance of a DNIC to couple two NO ligands is a consequence of the distance between the two nitrogen atoms and the covalent nature of the Fe–NO linkage, which results in a parallel alignment of the unpaired spins, hence the coupling is spin-forbidden.¹⁵,¹⁶ Having previously studied the isocarbonyl-bridged rare-earth-iron compounds [Cp*₂M(μ-O:FeCp)]₂ (M = Y, Dy)¹⁷ which contain oxophilic [Cp*₂M]+ units (Cp* = pentamethylyclopentadienyl), we reasoned that it should be possible to synthesize isonitrosyl-bridged rare-earth-iron compounds in which the DNIC structure is distorted by an oxophilic rare-earth, forcing the NO ligands closer together. The structure-directing influence of the rare-earth could therefore provide a means of overcoming the barrier to NO coupling, leading potentially, to release of NO from the DNIC, thus demonstrating that NO release from a monometallic DNIC is indeed possible.

As building blocks for the isonitrosyl bridges, we selected the DNICs [(NacNac⁰)Fe(NO)]⁻ in which the iron centre is additionally complexed by the bulky β-diketiminate ligands [(ArNMe)₂CH]: (Ar = mesityl, 1a; 2,6-diisopropolpheny, 1b).¹² The reactions of [Bu₄N][1a] and [Bu₄N][1b] with [Cp*₂M][BPh₄] (M = Y, Gd) delivered the target isonitrosyl-bridged compounds 2a and 3a according to Scheme 1.

![Scheme 1. Synthesis of 2a-4a (M = Y, Gd).](image)

Compounds 2a and 3a (M = Y, Gd) were isolated in yields of 91%, 93%, 75% and 73%, respectively, and characterized by NMR, IR and UV-visible spectroscopies, in addition to EPR characterization of gadolinium compounds (Figures S1-S21). The molecular structures of the heterobimetallic DNICs were also determined by single-crystal X-ray diffraction (Figures 1, S32, S33, Tables S1-S4), with the core of each consisting of a distorted tetrahedral iron center based on the two nitrogen atoms of the β-diketiminate ligand and the [Fe(NO)]₂¹⁸ DNIC unit (according to Enemark-Feltham notation¹⁹).
Figure 1. Molecular structures of 2a (left), molecule 1 of 3a (centre) and 4a (right). Hydrogen atoms not shown. Selected bond lengths (Å) and angles (°) for 2a: Fe(1)–N(1), 1.648(6); Fe(1)–N(2), 1.661(6); N(1)–O(1), 1.239(7); N(2)–O(2), 1.248(7); (1)–O(1), 1.239(5); Gd(1)–O(2), 2.372(5); Y(1)–Cp, 2.352, 2.380; N(1)–Fe(1)–N(2), 152.5(3); Fe(1)–N(1)–O(1), 119.3(4); N(1)–O(1)–Gd(1), 109.2(2)°.

Bending at the nitrosyl nitrogen atoms allows the oxygen atoms to establish isonitrosyl linkages to the rare-earth, which is also bound to two $\eta^1$-Cp$^*$ ligands.

Whilst 27 and 3a are paramagnetic with $\chi_T$ values of 7.86 and 7.71 cm$^3$ mol$^{-1}$, respectively, at 300 K ($\chi_T$ is the molar magnetic susceptibility), the slight variation in this quantity with temperature being characteristic of Gd$^3+$ (Figures S36, S38). The field dependence of the magnetization, $M(H)$, for 2a and 3a is also characteristic of Gd$^3+$, reaching values of 7.11 and 6.73 $\mu$ at 1.9 K and 7 T (Figures S37, S39). Based on $\chi$ vs $1/T$ data, solutions of diamagnetic 2a are stable indefinitely at room temperature and show no sign of decomposition when heated to 100°C in toluene (Figure S22). In contrast, green solutions of 3a in toluene turn brown/yellow after stirring for five days at room temperature. The sharp resonances observed in the $^1$H NMR spectrum of diamagnetic 3a (Figure S16) broaden and become distributed over chemical shifts ranging from +119.5 ppm to −151.2 ppm, indicating paramagnetism (Figures S23, S24). GC-MS analysis of the headspace gas after stirring confirmed that N$_2$O is produced during this process (Figure S25). For 3a, filtration of the solutions obtained after stirring, subsequent concentration and cooling to 0°C resulted in the formation of yellow crystals of the oxo-bridged compounds $\text{[CP}^*\text{M(O-O)Fe(NaNac)}_{2199}]_n$ (4a) ($M = Y$, Gd), which were isolated in yields of 72% and 78%, respectively (Scheme 1).

Analysis by X-ray diffraction revealed that complexes 4M are isomorphous and consist of a three-coordinate iron center in a distorted trigonal-planar environment (Figures 1, S35). The $\mu$-oxo link to the rare-earth metal coincides with a crystallographic two-fold rotation axis and, hence, the Fe-O-M angle is 180.0° in both complexes. The $\text{[CP}^*\text{M}]_n$ units in 4M adopt bent metalloocene structures similar to those in 2a and 3a. The magnetic susceptibility of 4a shows a $\chi_T$ value of 5.63 cm$^3$ mol$^{-1}$ at 300 K and a magnetization of 2.89 $\mu_B$ at 1.9 K and 7 T, which suggest a high-spin $S = 2$ iron(II) with an appreciable orbital contribution to the magnetic moment (Figures S40, S41). A satisfactory fit of the susceptibility data could not be achieved using a standard spin Hamiltonian, which may indicate that the large orbital contribution originates from mixing of a low-lying electronic excited state into the ground state, a phenomenon that has previously been observed in closely related three-coordinate iron(II) complexes. An approximate fit of the $\chi_T(T)$ data yielded a large, negative axial zero-field splitting parameter of $D = –28(1)$ cm$^{-1}$.
The chemistry of model DNICs and related systems is well-established, with many examples providing insight into the mechanisms through which NO is transported and delivered

\(^{1}\) and \(g = 2.6(1)\) (Figure S40), similar to the values determined for other three-coordinate iron(II) compounds.\(^{24}\) The \(g\) value for \(4a\) at 300 K is 12.54 cm\(^{-1}\) K mol\(^{-1}\), which gradually decreases down to 20 K before increasing to 14.84 cm\(^{-1}\) K mol\(^{-1}\) at 2 K, indicating ferromagnetic coupling between \(g\) and \(Fe^{2+}\) (Figures S42, S43). A fit of the data was achieved using an exchange coupling constant of \(J = +0.25\) cm\(^{-1}\) (J2-296mactical formalism), along with \(g_{ex} = 2.00, g_{ex} = 2.49\) and \(D_{ex} = -18.3\) cm\(^{-1}\).\(^{25}\)

The removal of NO from biological systems as N\(_2\)O has been observed. The reluctance of DNICs to couple the two NO molecules is significant since the reactivity shows that NO can occur at a single iron center.\(^{27}\) In the case of \(3a\), the steric bulk imposed on the isonitrosyl (M[ON]:Fe) cores by the diisopropylphenyl substituents helps to overcome this barrier by forcing the nitrogen atoms much closer together than in mesityl-substituted \(2a\) and the ensuing nitrosyl coupling and elimination of nitrous oxide proceeds under milder conditions. The systems described here are clearly different to naturally occurring iron-nitrosyl complexes, yet when the biological N\(_2\)O elimination reaction in its most elementary form, i.e. \(2NO + 2e^- + 2H^+ \rightarrow N_2O + H_2O\), is compared to the synthetic analogue \([Fe(NO)]_2^{2+} + [Cp^*]^{2+} \rightarrow N_2O + \text{Cp}^*[MFe]^{2+}\), similarities are apparent. Since the DNIC unit can provide the required number of electrons to couple the NO ligands. The instability of \(3m\) with respect to the formation of \(4a\) and \(N_2O\) is significant since the reactivity shows that conversion of NO to N\(_2\)O can occur at a single iron center, the first time that such reactivity has been demonstrated. Furthermore, the formation and subsequent reactivity of \(3m\) showcases the structural flexibility of the DNIC unit in the presence of a strongly Lewis acidic rare-earth organometallic fragment, which forces the nitrogen atoms into the correct conformation to allow NO coupling and N\(_2\)O release. These observations provide a potential blueprint for the design and synthesis of other heterobimetallic DNICs capable of releasing N\(_2\)O.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available on the ACS Publications website. Synthesis, spectroscopic characterization, crystallography details, magnetic property measurements.

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Notes
The authors declare no competing financial interests.

ACKNOWLEDGEMENT

The authors thank the Royal Society for a Newton International Fellowship to ABK (NF1605853) and a Newton Advanced Fellowship to JT (NA160075). For financial support, RAL thanks the European Research Council (CoG RadMag, grant 646740) and the EPSRC (EP/M022064/1), and JT thanks the National Natural Science Foundation of China (grants 21525103 and 21871247). The authors are grateful to Mr. D. Fehr and Prof. K. Meyer (Friedrich-Alexander University Erlangen-Nuremberg) for measuring the EPR spectra of compounds 3\(_{4a}\) and 4\(_{a}\).

REFERENCES


$\text{N}_2\text{O elimination from a DNIC}$

$\text{Ar} = \text{mesityl, disopropylphenyl}$

$\text{Ar} = \text{Mes, Dipp}$

$\text{Ar} = \text{Dipp only}$