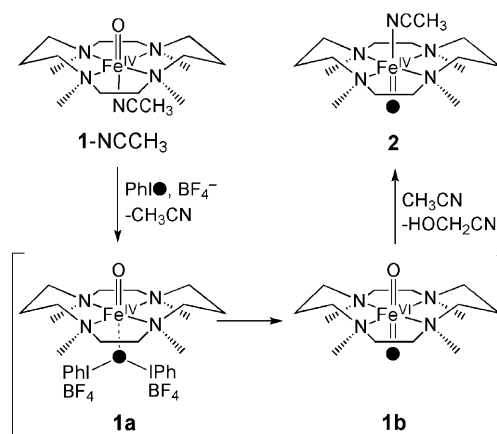


An Inverted and More Oxidizing Isomer of $[\text{Fe}^{\text{IV}}(\text{O})(\text{tmc})-(\text{NCCH}_3)]^{2+}$ **

Kallol Ray, Jason England, Adam T. Fiedler, Marlène Martinho, Eckard Münck,* and Lawrence Que, Jr.*

High-valent oxoiron species are often invoked as the oxidants in the catalytic cycles of dioxygen-activating mononuclear nonheme iron enzymes.^[1] To date, such iron(IV) intermediates have been characterized for four enzymes, lending strong support for this notion.^[2] Within the same time frame, synthetic nonheme complexes containing oxoiron(IV) units have also been described that serve as models for such reactive intermediates.^[3] The first crystallographically characterized and most extensively studied member of this family of synthetic oxoiron(IV) complexes is $[\text{Fe}^{\text{IV}}(\text{O})(\text{tmc})-(\text{NCCH}_3)](\text{OTf})_2$ (**1-NCCH₃**; tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane).^[4] Its structure features a short Fe=O bond (1.646 Å) with an acetonitrile bound *trans* to the oxo atom.^[4] The macrocyclic tmc ligand adopts a *trans*-I (*R,S,R,S*) configuration,^[5] such that all four methyl groups are oriented in the same direction with respect to the FeN₄ plane, and *anti* to the oxo atom. On the other hand, monoanionic X ligands coordinate *syn* to the methyl groups in crystal structures of five-coordinate $[\text{Fe}^{\text{II}}(\text{tmc})(\text{X})]^+$ complexes.^[6] Herein, we report the unexpected preparation of an inverted isomer of **1-NCCH₃** in which the oxo group binds to the site *syn* to the four methyl groups (Scheme 1). The conversion of **1-NCCH₃** to its inverted isomer is effected by treatment with PhIO in the presence of tetrafluoroborate, an otherwise inert anion. The switch in binding site of the oxo group engenders changes in the spectroscopic properties of the oxoiron(IV) complex and, more importantly, a significantly enhanced reactivity in hydrogen-atom abstraction and oxo-transfer reactions.

The reaction of $[\text{Fe}^{\text{II}}(\text{tmc})(\text{OTf})](\text{OTf})$ with solid iodosylbenzene (PhIO) (ca. 5 equiv) in CH₃CN at 25 °C affords in quantitative yield pale green **1-NCCH₃** with λ_{max} at 820 nm ($\epsilon = 400 \text{ M}^{-1} \text{ cm}^{-1}$; Figure 1), as described previously.^[4] The near-IR band has been assigned to d–d transitions that arise



Scheme 1. Mechanism of the conversion of **1-NCCH₃** to **2**.

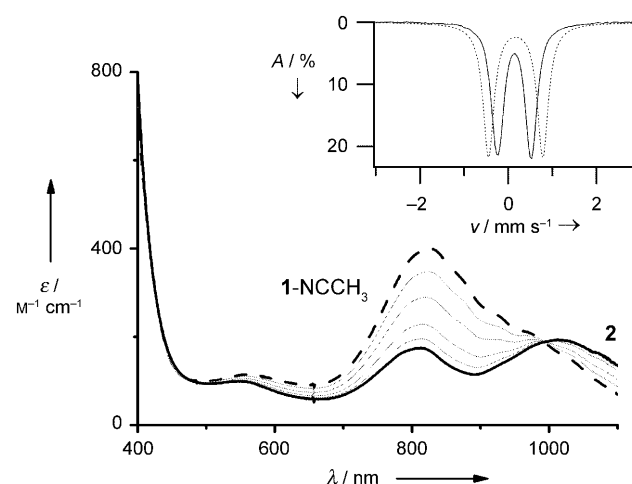


Figure 1. Vis/NIR spectra of **1-NCCH₃** (dashed line) and **2** (dark solid line). Intermediate spectra show the conversion of **1-NCCH₃** to **2** upon successive addition of 1 equiv PhI(OAc)₂ in the presence of NBu₄BF₄. The inset shows the Mössbauer spectra of **1-NCCH₃** (dashed line) and **2** (solid line) recorded in zero magnetic field at 4.2 K.

from the *S* = 1 oxoiron(IV) center.^[7] However, in the presence of NBu₄BF₄, the reaction produces a different species, yellowish green **2**, with bands at 806 ($\epsilon = 170 \text{ M}^{-1} \text{ cm}^{-1}$) and 1026 nm ($\epsilon = 190 \text{ M}^{-1} \text{ cm}^{-1}$; Figure 1), absorption features significantly different from those of **1-NCCH₃**. Mössbauer analysis of **2** further underscores its distinct nature from **1-NCCH₃**. As shown in Figure 1 inset, the 4.2 K Mössbauer spectrum of **2** ($\Delta E_Q = 0.78 \text{ mm s}^{-1}$, $\delta = 0.14 \text{ mm s}^{-1}$) is quite distinct from that obtained for **1-NCCH₃** ($\Delta E_Q = 1.24 \text{ mm s}^{-1}$

[*] Dr. M. Martinho, Prof. Dr. E. Münck
Department of Chemistry, Carnegie Mellon University
Pittsburgh, PA 15213 (USA)
E-mail: emunck@cmu.edu

Dr. K. Ray, Dr. J. England, Dr. A. T. Fiedler, Prof. Dr. L. Que, Jr.
Department of Chemistry and Center for Metals in Biocatalysis
University of Minnesota, Minneapolis, MN 55455 (USA)
Fax: (+1) 612-624-7029
E-mail: larryque@umn.edu

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and $\delta = 0.17 \text{ mm s}^{-1}$). However, the zero-field splittings and magnetic hyperfine tensors of **1**-NCCH₃ and **2**, determined from studies in strong applied magnetic fields, are practically the same (see Figure S1 and Table S1).

Additional measurements provide further insight into the nature of **2**. Conductivity experiments on **2** in CH₃CN yield an Onsager plot^[8] with a slope comparable to those of known 1:2 electrolytes (cation:anion ratio), such as **1**-NCCH₃ and [Fe^{IV}(O)(N4Py)](ClO₄)₂ (**3**, N4Py = bis(2-pyridylmethyl)-bis(2-pyridyl)methylamine), and much larger than those for known 1:1 electrolytes (e.g. NBu₄PF₆ and NBu₄BF₄; Figure S2). Therefore **2**, like **1**-NCCH₃, is a 1:2 electrolyte. Secondly, electrospray ionization mass spectrometry (ESI-MS) of solutions of isolated **1**-NCCH₃ and **2** gives rise to identical spectra, with prominent peaks corresponding to [Fe(O)(tmc)(NCCH₃)₂]²⁺ (m/z 184.4) and {[Fe(O)(tmc)](OTf)}⁺ (m/z 476.9) ions (Figure S3). Lastly, EXAFS analysis of **2** reveals Fe–ligand distances ($r_{\text{Fe–O}} = 1.64 \text{ \AA}$; $r_{\text{Fe–N(ave)}} = 2.08 \text{ \AA}$) identical to those found for **1**-NCCH₃ (Figure S4 and Table S2). Thus, **1**-NCCH₃ and **2** appear to be isomers with the same composition.

How then does **2** differ structurally from **1**-NCCH₃? ¹H NMR data (Figure 2) limit the possibilities. Since the tmc

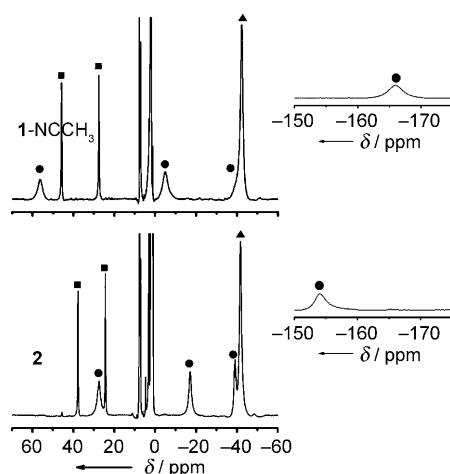


Figure 2. ¹H NMR spectra of **1**-NCCH₃ and **2** in CD₃CN at 25 °C in the range from 70 to –60 ppm. The insets show the NMR spectra in the range from –150 to –175 ppm. The peaks are assigned to the tmc ligand as follows: ■: NCH₂CH₂CH₂N (2 × 2H); ●: NCH₂ (4 × 4H); ▲: NCH₃ (12H).

ligand in **1**-NCCH₃ is known to adopt a *trans*-I configuration,^[4] the four methyl groups are equivalent and give rise to a single methyl resonance that is readily assigned by integration. Although distinct from that of **1**-NCCH₃, the ¹H NMR spectrum of **2** exhibits the high symmetry found in **1**-NCCH₃, indicating that the tmc ligand retains a *trans*-I configuration. These results led us inexorably to the conclusion that **2** is simply the inverted isomer of **1**-NCCH₃ in which the positions of the oxo and acetonitrile ligands are interchanged (see Scheme 1).

Additional support for the inverted-isomer hypothesis comes from ligand exchange reactions of **1**-NCCH₃ and **2** with

NBu₄SCN. As reported previously,^[6a] the reaction between **1**-NCCH₃ and NBu₄SCN forms **1**-NCS with a molecular composition of [Fe(O)(tmc)(NCS)]⁺ as deduced from ESI-MS (m/z 386.1). The analogous reaction with **2** leads to the formation of **2**-NCS with an identical molecular composition by ESI-MS. Although **1**-NCS and **2**-NCS have very similar Mössbauer spectra both in zero and applied magnetic fields (Tables 1 and S1; Figures S5 and S6), their electronic spectra

Table 1: Spectroscopic properties of the complexes.

Complex	λ_{max} [nm] (ϵ [M ^{–1} cm ^{–1}])	ΔE_Q [mm s ^{–1}]	δ [mm s ^{–1}]
1 -NCCH ₃	820(400)	1.24(1)	0.17(1)
2	806(170) 1026 (190)	0.78(2)	0.14(1)
1 -NCS	386 (4200) 850 (200) 1010 (160)	0.60(2)	0.16(2)
2 -NCS	415 (5400) 812 (120) 1015 (140)	0.61(2)	0.14(1)

are clearly distinct, with characteristic absorptions at 386, 850, and 1010 nm for **1**-NCS, and 415, 812, and 1015 nm for **2**-NCS (Figure 3). Additionally, their ¹H NMR spectra exhibit different paramagnetic shift patterns (Figure S7). Thus, based on the accumulated data, **1**-NCS and **2**-NCS are best described as position isomers with the positions of the axial oxo and NCS ligands switched.

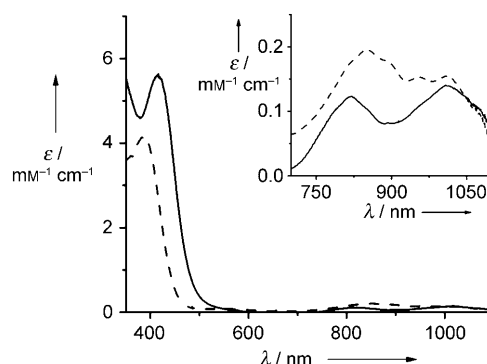


Figure 3. UV/Vis/NIR spectra of **1**-NCS (dashed line) and **2**-NCS (solid line) formed by the reaction of **1**-NCCH₃ and **2** with 1 and 5 equiv NBu₄SCN, respectively, in CH₃CN at –30 °C. The inset shows the vertical expansion of the NIR region. The extinction coefficients are estimated based on the iron(IV) fractions determined by Mössbauer spectroscopy (85% for **1**-NCS and 70% for **2**-NCS).

The conversion of [Fe^{II}(tmc)(OTf)](OTf) to **2** in the presence of NBu₄BF₄ can be conveniently monitored by UV/Vis/NIR spectroscopy with PhI(OAc)₂ as the oxidant, which unlike PhIO is a well-defined material and readily soluble in MeCN. Addition of only 1 equiv PhI(OAc)₂ to [Fe^{II}(tmc)(OTf)](OTf) affords **1**-NCCH₃ quantitatively in the absence or in the presence of NBu₄BF₄. Addition of a second equivalent PhI(OAc)₂ to the thus formed solution of **1**-

NCCH₃ does not effect any change in the absence of NBu₄BF₄, but converts **1**-NCCH₃ to **2** in the presence of NBu₄BF₄ (Figure 1). These results show that a minimum of 2 equiv PhI(OAc)₂ is required for the complete conversion of [Fe^{II}(tmc)(OTf)](OTf) to **2**. The first equivalent generates **1**-NCCH₃, and the second transforms **1**-NCCH₃ to **2** in the presence of NBu₄BF₄.

What is the role of NBu₄BF₄? Experiments varying the amount of added NBu₄BF₄ show that a minimum of 0.2 equiv is required for the conversion of **1**-NCCH₃ to **2**. Furthermore, when excess PhI(OAc)₂ is present, **1**-NCCH₃ converts to **2** in a pseudo-first-order fashion over the course of minutes at room temperature (Figure 4); this rate of conversion increases

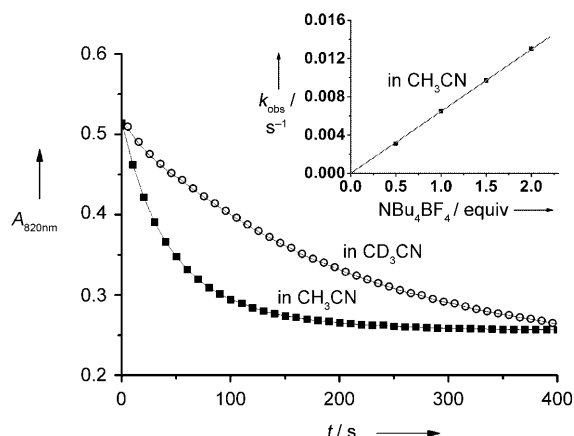


Figure 4. The time traces for the formation of **2** from **1**-NCCH₃ under pseudo-first-order conditions (10 equiv PhI(OAc)₂ and 0.5 equiv NBu₄BF₄) in CD₃CN ($k_{\text{obs}} = 0.0006 \text{ s}^{-1}$) and CH₃CN ($k_{\text{obs}} = 0.003 \text{ s}^{-1}$) at 25 °C. Lines drawn through the experimental data represent the pseudo-first-order fits. The inset shows the dependence of the pseudo-first-order rate constant on the amount of NBu₄BF₄.

linearly with NBu₄BF₄ concentration (Figure 4 inset). We propose that the addition of BF₄[−] converts PhIO to PhIOPh(BF₄)₂, which is known to be a more powerful oxidant than PhIO,^[9] and this in situ generated oxidant reacts with **1**-NCCH₃ to generate **2**. In support of this proposal, **1**-NCCH₃ converts to **2** nearly quantitatively upon addition of 1 equiv isolated PhIOPh(BF₄)₂.^[9] Furthermore, when ¹⁸O-labeled **1**-NCCH₃ is treated with 1 equiv PhI¹⁸OPh(BF₄)₂, the resultant **2** is found to be ¹⁶O-labeled. Conversely, when ¹⁶O-labeled **1**-NCCH₃ is treated with PhI¹⁸OPh(BF₄)₂, **2** is found to be ¹⁸O-labeled. Thus the oxo atom of **2** derives not from the oxo atom of **1**-NCCH₃ but from the added oxidant. Based on these observations, a mechanism for the conversion of **1**-NCCH₃ to **2** is proposed in Scheme 1 that postulates formation of adduct **1a**, analogous to metal–oxo–oxidant adducts previously proposed to be more powerful oxidants than their parent metal–oxo species.^[10] Formation of **1a** activates the Fe=O unit to oxidize the CH₃CN solvent and form **2** either directly or via a transient dioxoiron(VI) species **1b**. In support, we observed a deuterium kinetic isotope effect of 5 for the conversion of **1**-NCCH₃ to **2**, when CD₃CN was used as the solvent (Figure 4), so solvent C–H bond cleavage is rate-determining. Since both **1**-NCCH₃ and **2** have long half-lives in CH₃CN ($t_{1/2} = 10$ and

7 h, respectively), a more powerful oxidant must be generated that is capable of cleaving the C–H bond of CH₃CN; we propose this oxidant to be either **1a** or **1b**. Thus, in the course of the conversion, the oxo group of **1**-NCCH₃ is effectively displaced by backside attack of PhIOPh(BF₄)₂ to form its inverted isomer **2**.

Ruthenium analogues of the various species postulated in the mechanism shown in Scheme 1 have been reported by Che et al.^[11] For example, [Ru^{IV}(O)(tmc)(NCCH₃)]²⁺ is the ruthenium analogue of **1**-NCCH₃, with the oxo atom *anti* to all four N-methyl groups, while [Ru^{IV}(O)(tmc)(NCO)]⁺ has a structure similar to that proposed for **2**, with the oxo atom *syn* to all four N-methyl groups. More importantly, [Ru^{VI}(O)₂(tmc)]²⁺, the ruthenium analogue to the putative dioxoiron(VI) species **1b**, has also been characterized, lending credence to our dioxoiron(VI) hypothesis.

The most striking difference between **1**-NCCH₃ and **2** is in their reactivities. For example, **2** oxidizes PPh₃ and dihydroanthracene 35- and 170-fold faster, respectively, than **1**-NCCH₃ (Table S3). The greater reactivity of **2** is also reflected in the relative intermetal oxo-transfer abilities of the two isomers. Nam and co-workers^[12] previously established an oxo-transfer hierarchy of **4** > **3** > **1**-NCCH₃ (**3** = [Fe^{IV}(O)(N4Py)]²⁺; **4** = [Fe^{IV}(O)(Bn-tpen)]²⁺; Bn-tpen = *N*-benzyl-*N*,*N'*,*N'*-tris(2-pyridylmethyl)-1,2-diaminoethane), with facile oxo transfer from **3** or **4** to [Fe^{II}(tmc)(NCCH₃)]²⁺ to yield **1**-NCCH₃, but not from **1**-NCCH₃ to [Fe^{II}(N4Py)(NCCH₃)]²⁺ and [Fe^{II}(Bn-tpen)(NCCH₃)]²⁺. According to Nam's work,^[12] this descending series reflects the progressive decrease in the Fe^{IV}/Fe^{III} redox potential of the Fe^{IV}=O unit. In stark contrast to **1**-NCCH₃, **2** readily oxidizes [Fe^{II}(N4Py)(NCCH₃)]²⁺ (Figure 5), [Fe^{II}(Bn-tpen)(NCCH₃)]²⁺ (Figure S8), and [Fe^{II}(tmc)(NCCH₃)]²⁺ (Figure S9) to corresponding oxo complexes **3**, **4**, and **1**-NCCH₃, respectively. Thus, **2** leapfrogs over the other three complexes, that is, **2** > **4** > **3** > **1**-NCCH₃, and is the most powerful oxidant in this series.

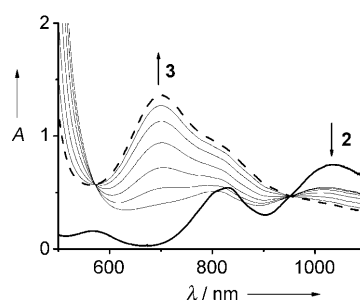


Figure 5. Changes in the absorption spectrum associated with the reaction of a 4 mM solution of **2**, generated by addition of 2 equiv PhI(OAc)₂ and 0.2 equiv NBu₄BF₄ to [Fe^{II}(tmc)(OTf)](OTf), with 1 equiv [Fe^{II}(N4Py)(CH₃CN)]²⁺ in CH₃CN at 25 °C.

The higher reactivity of **2** may arise from kinetic and/or thermodynamic factors.^[7b] The axial iron site *syn* to the N-methyl groups may in fact be sterically less hindered, as suggested by the fact that anions bind only at this position in the structures of [Fe^{II}(tmc)(X)]⁺ complexes,^[6] so as to make **2** kinetically the more effective oxidant. On the other hand, the

intermetal oxo-transfer hierarchy established above, following Nam's arguments,^[12] suggests that the higher oxidizing ability of **2** may reflect a higher Fe^{IV}/Fe^{III} potential. DFT calculations on the two isomers (Figure S10, Tables S4 and S5) in fact support this thermodynamic argument, as **2** is calculated to be higher in energy than **1**-NCCH₃ by about 4 kcal mol⁻¹. A comparison of the two geometry-optimized structures suggests that the energy difference may arise from the 0.1 Å lengthening of the Fe–NCCH₃ bond in **2** accompanied by a 0.01 Å shortening of the Fe=O and Fe–N_{tmc} bonds.^[13] Establishing which factors determine the greater reactivity of **2** requires additional spectroscopic, electrochemical, and computational studies, which are in progress.

In summary, we reported herein spectroscopic evidence for the unexpected conversion of previously characterized **1**-NCCH₃ to its inverted isomer **2** by reaction with PhIOIPh-(BF₄)₂. Strikingly, the simple interchange of the positions of the axial oxo and CH₃CN ligands between **1**-NCCH₃ and **2** significantly enhances the oxidative reactivity of the latter relative to the former, making these two complexes the first example of an isomer pair in which a particular face of a macrocyclic ligand affects reactivity so dramatically. Whatever the rationale, these results illustrate the subtle power of the coordination environment to tune the redox properties of the oxoiron(IV) unit.

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