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Uncoupled Redox-Inactive Lewis Acids in the Secondary Coordination Sphere Entice Ligand-Based Nitrite Reduction

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Abstract

Metal complexes composed of redox-active pyridinediimine (PDI) ligands are capable of forming ligand-centered radicals. In this Forum article, we demonstrate that integration of these types of redox-active sites with bioinspired secondary coordination sphere motifs produce direduced complexes, where the reduction potential of the ligand-based redox sites is uncoupled from the secondary coordination sphere. The utility of such ligand design was explored by encapsulating redox-inactive Lewis acidic cations via installation of a pendant benzo-15-crown-5 in the secondary coordination sphere of a series of Fe(PDI) complexes. Fe(^{15bz5}PDI)(CO)₂ was shown to encapsulate the redox-inactive alkali ion, Na⁺, causing only modest (31 mV) anodic shifts in the ligand-based redox-active sites. By uncoupling the Lewis acidic sites from the ligand-based redox sites, the pendant redox-inactive ion, Na⁺, can entice the corresponding counterion, NO₂[−], for reduction to NO. The subsequent initial rate analysis reveals an acceleration in anion reduction, confirming this hypothesis.

Graphical Abstract

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Notes

The authors declare no competing financial interest

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CCDC 1582611–1582614 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:10.1021/acs.inorgchem.8b00032. X-ray crystallographic data, spectroscopic data, NMR titration data, kinetic data, cyclic voltammetry data, yield determination data, and NO trapping data (PDF)

INTRODUCTION

Among the common structural features used to regulate the reduction potential of metalloenzyme active sites are redox-active amino acids (or modified amino acids). These amino acids produce ligand-based radicals¹ that tune the reduction potential of the active site. One of the best understood examples of this is galactose oxidase, which is the metalloenzyme responsible for the two-electron oxidation of alcohols to aldehydes.^{2,3} In this active site (Figure 1, left), a Cu(II) metal center and a stable modified tyrosyl radical function as a two-electron redox unit during catalytic turnover. The metalloprotein active site combines two distinct one electron acceptors to perform the two electron redox reaction(s). The oxygen evolving complex (OEC) in photosystem II also utilizes a tyrosyl radical (Y_Z) in the four electron oxidation of H_2O to O_2 . Y_Z is located between the Mn_4CaO_5 cluster and the photosystem II reaction center (Figure 1, right), and functions to mediate electron transfer between the two.^{4,5} Biological examples such as these have inspired numerous studies focused on redox-active ligands^{6–10} and also secondary coordination regulation.^{11–21} This Forum article explores the area of integrating uncoupled redox-active sites with bioinspired secondary coordination sphere motifs,^{22,23} and the utilization of these ligands for the reduction of nitrite.^{24–26}

Redox Potential Tuning via Redox-Inactive Lewis Acid Cations

Extensive precedent exists for the role of redox-inactive Lewis acid cations to modulate redox activity in both the biological and synthetic realm(s). Some of the most important chemical reactions in both Nature and Industry utilize redox-inactive metals in combination with redox-active transition metals to invoke reactivity.^{27,28} For example, in the oxygen-evolving complex (OEC) of photosystem II,^{29–32} the redox-inactive Ca^{2+} plays a critical role in water oxidation³³ and K-promoted Fe surfaces are vital in the Haber–Bosch process.³⁴ Redox-inactive Lewis acids can be employed to facilitate O–O,^{35,36} N–N,³⁷ and H–H³⁸ bond cleavage in synthetic systems, as well as enable –O and –H atom transfer.^{39–41} Recently, the concept of cation-induced hemilability⁴² and allosteric control of substrate access has seen a resurgence.^{43,44}

However, one of the most common reasons for installing redox-inactive metals proximal to a redox-active center is for redox-tuning, including the enhancement of electron transfer rates and the anodic shifting of reduction potentials.^{45–48} One of the early examples⁴⁹ was that of a benzo-15-c-5 ether appended ferrocene (see Chart 1A), which, upon alkali-metal encapsulation, caused an anodic shift in the Fe(III/II) reduction potential up to 70 mV. More significant anodic shifts (130–300 mV) are observed in systems where the Lewis acid and the redox-active site are more tightly coupled, such as the Co(II)(salen) system (Chart 1B).⁴⁷ Bimetallic metalloligand systems (Chart 1C) incorporating dative bonds between a redox-

inactive Lewis acid and the redox-active Ni(0) have redox potentials that span 600 mV,^{50,51} and oxobridged multimetallic manganese clusters (Chart 1D) incorporating Lewis acid cations into a “cubane” structure result in anodic shifts over 1.2 V.^{52–54} The compounds exhibited in Chart 1 display a wide range in redox potentials, illustrating the intimate coupling between the proximal Lewis acid and the redox-active metal.

The Pyridinediimine (PDI) Ligand Platform

Inspired partly by the observations that redox-active amino acids are able to tune reduction potentials in metalloenzyme active sites, there has been a recent renaissance into the rich chemistry of redox-active or “non-innocent” ligands.^{55–57} These redox-active ligands have energetically accessible levels that can facilitate redox reactions to change their charge state, similar to the modified tyrosyl radical in Figure 1. The pyridinediimine (PDI) family of ligands has received particular attention, since their development by Brookhart⁵⁸ and Gibson.⁵⁹ These ligands (Figure 2) are stable in four different oxidation states, forming neutral complexes, as well as monoanions, dianions, and trianions.^{60–62} Given the utility of incorporating redox-activity into ligand scaffolds, the reactivity scope of numerous important processes has been expanded dramatically.^{63,64} One consequence of this is that the ligand can be used to access redox states not available to the metal, and open new avenues of observed reactivity.

Previous work^{65–67} has shown that the dicarbonyl derivatives of direduced FePDI complexes are viable probes for the oxidation/reduction behavior of the redox-active PDI. It is worth mentioning here that the ground state of the neutral Fe(*iPr*PDI)(CO)₂ complex is best described (through computational and spectroscopic studies)⁶⁰ as a hybrid of the two limiting resonance forms of (a) low-spin Fe(II) with a singlet, dianionic PDI₂[−] (S_{PDI} = 0), and (b) the *d*⁸ Fe(0), with a neutral PDI ligand (see Figure 3). This hybrid form is derived from the DFT computed highest occupied molecular orbital (HOMO), which is 68% in PDI character and possesses significant contributions from the Fe center. For the purpose of this Forum article, we are representing the direduced PDI scaffold as the dianionic, delocalized ligand system⁶⁸ (see Figure 3, left). Furthermore, as shown in eq 1, Fe(PDI)(CO)₂ complexes are capable of undergoing a reversible (or quasi-reversible) “ligand-based” one electron oxidation to form [Fe(PDI)(CO)₂]⁺, and a reversible (or quasi-reversible) one electron “metal-based” reduction to form [Fe(PDI)(CO)₂][−].⁶⁹

Uncoupling Ligand-Based Redox-Activity with Secondary Coordination Sphere

As illustrated above, the transition-metal-based redox sites of many bioinspired complexes are *highly coupled* with the protonation state and/or the presence of nonredox active Lewis acids. We have been utilizing the PDI scaffold, which contains ligand-based redox sites to demonstrate a different paradigm, that of *uncoupling* the redox-activity from the effective “charge state” of the secondary coordination sphere.⁷⁰ This is achieved because of the

redox-activity of PDI ligand scaffold, which allows the generation of highly reduced complexes, where the protonation state of the pendant base is very weakly coupled to the ligand-based reduction potential ($E_{1/2} = 105$ mV; see Figure 4, left). These integrated (yet uncoupled) complexes are capable of storing both protons and electrons for transfer to substrate.^{71,72}

We extended this concept to nonredox active, pendant Lewis acids, where the ligand-based redox-sites are uncoupled even further.⁷³ We have previously shown that the direduced FePDI complex, $\text{Fe}^{(15c5\text{PDI})}(\text{CO})_2$, which contains the pendant 15-c-5 ether in the secondary coordination sphere, is capable of binding the Lewis acidic alkali ions Na^+ or Li^+ . Remarkably, upon alkali ion encapsulation, the ligand-based redox sites undergo virtually no shift in the reduction potential (~ 50 mV). Given this extraordinary uncoupling of the Lewis acidic sites and the ligand-based redox sites, we reasoned that we could utilize the encapsulated alkali ions in the secondary coordination sphere in a novel fashion to “lure in” anions for reduction. Here, we report the results of those studies and show that, for the Na^+ encapsulated system, the unattenuated ligand-based redox sites are active for the rate enhancement of oxyanion reduction of nitrite (NO_2^-) to nitric oxide (NO), which is an extremely important reaction both physiologically and in the biosphere.^{74,75}

RESULTS AND DISCUSSION

The direduced $\text{Fe}^{(15bz5\text{PDI})}(\text{CO})_2$ complex, which contains the pendant crown ether, benzo-15-crown-5, was first synthesized from the $\text{Fe}^{(15bz5\text{PDI})}\text{Br}_2$ (**1**) precursor. **1** was produced in high yields ($\sim 90\%$) via the Schiff base condensation⁷⁶ of the asymmetric ketone-imine, $[(2,6\text{-}^i\text{Pr-C}_6\text{H}_3\text{N}=\text{CMe})(\text{O}=\text{CMe})\text{C}_5\text{H}_3\text{N}]$, and 4'-aminobenz-15-crown-5 in the presence of FeBr_2 (Scheme 1). The room-temperature (RT), zero-field Mössbauer parameters ($\delta = 0.821(5)$, $E_Q = 1.644(7)$ mm/s) confirm a five-coordinate high-spin ($S = 2$) Fe(II) center.^{58,60,61,77}

1 was then reduced under a CO atmosphere with NaHg in CH_2Cl_2 to form $\text{Fe}^{(15bz5\text{PDI})}(\text{CO})_2$ (**2**). Slow evaporation of a saturated diethyl ether solution of **2** yielded a green, diamagnetic crystalline solid in 71% yield. The ATR-FTIR spectrum of **2** displays two ν_{CO} stretches at 1948 and 1886 cm^{-1} in the range of a more electron-rich PDI ligand.⁶⁷ An ORTEP view of **2** is shown in Figure 5. The Fe center is five-coordinate with a square pyramidal geometry ($\tau = 0.1$).⁷⁸ The $\text{C}_{\text{imine}}\text{--N}_{\text{imine}}$ bond lengths in **2** are 1.324(5) and 1.325(5) Å and the $\text{C}_{\text{imine}}\text{--C}_{\text{ipso}}$ bond lengths are 1.436(7) and 1.427(6) Å. These data, taken in conjunction with the RT zero-field Mössbauer parameters ($\delta = -0.088(3)$, $E_Q = 1.126(4)$ mm/s) suggest that the complex is best described as a $S = 0$ Fe(II) center with a doubly reduced $^{15bz5\text{PDI}}$ ligand.

Compound **2** is able to chelate the alkali ion Na^+ , as illustrated by the solid-state structure of $[\text{Fe}^{(15bz5\text{PDI})}(\text{CO})_2\text{Na}][\text{BPh}_4]$ (**3**; see Figure 6). Compound **3** was prepared by stirring a solution of **2** in CH_3CN with a slight excess of NaBPh_4 . After workup, green, diamagnetic X-ray-quality crystals were obtained. **3** crystallizes as a centrosymmetric dimer (see Figure S50 in the Supporting Information (SI)) with the encapsulated Na^+ interacting with the equatorial CO ligand on the opposite molecule. As in **2**, the Fe center in **3** ($\tau = 0.05$) is five-

coordinate with a square pyramidal geometry. The oxidation state of the ligand is not changed upon alkali-metal encapsulation, as indicated by the $C_{\text{imine}}-N_{\text{imine}}$ (1.324(2), 1.323(2) Å) and the $C_{\text{imine}}-C_{\text{ipso}}$ (1.430(3), 1.425(3) Å) bond lengths. The Mössbauer parameters for **3** confirm a doubly reduced $^{15}\text{bz}^5\text{PDI}$ ligand. The ν_{CO} of **3** are shifted to lower wavenumbers (1929 and 1857 cm^{-1}) in the solid state, because of the interaction with the Na^+ in the crystal. This interaction is not present in solution, as the liquid cell Fourier transform infrared (FTIR) ν_{CO} of **3** are identical to **2** (1956 and 1892 cm^{-1}) and the resonance associated with the CO ligands in the ^{13}C NMR is located at 215 ppm in both **2** and **3**.

The pendant Na^+ in **3** lies to one side of the benzo-15-crown-5 ring at 0.7715(11) Å above the x,y,z coordinates of a plane formed by the O atoms of the benzo-15-crown-5. The Na^+ is six-coordinated in the centrosymmetric dimer, with five Na–O contacts from the benzo-15-crown-5 and one Na–O contact from the equatorial CO ligand on the second $[\text{Fe}(^{15}\text{bz}^5\text{PDI})(\text{CO})_2\text{Na}]^+$. As shown in Table 1, four of the Na–O contacts to the benzo-15-crown-5 are shorter—Na(1)–O(6) (2.348(2) Å), Na(1)–O(5) (2.332(2) Å), Na(1)–O(4) (2.377(2) Å), and Na(1)–O(3) (2.374(2) Å)—and one is longer (Na(1)–O(7), 2.408(2) Å), with the Na(1)–O(2) of the Na–CO ligand interaction being 2.372 Å. These values fall into the range of common Na^+ and benzo-15-crown-5 interactions from the CSD.⁷⁹

In order to further determine the solution behavior and stoichiometry of the pendant benzo-15-c-5 in **2** with Na^+ , the C–H resonances of the benzo-15-c-5 were monitored via a series of ^1H NMR titrations of varying amounts of Na^+ in acetonitrile- d_3 . As can be seen in Figure 7, the addition of increasing amounts of NaBPh_4 to a solution of **2** causes a downfield shift in the resonances associated with the pendant benzo-15-c-5 up to 1 equiv of NaBPh_4 , suggesting the formation of the 1:1 Na^+ complex (**3**) in solution. Each spectrum was internally referenced to TMS, and the shift in the benzo-15-c-5 resonances was significantly larger than that for any other resonance in the spectrum. The shifts in the nonbenzo-15-c-5 resonances (~ 0.05 ppm) indicate that the changes in the solvent dielectric are small.

From the binding isotherms in Figure 7, the association constants of the different C–H regions ($K_{\text{Na}^+} > 10^5 \text{ L mol}^{-1}$) were extracted by utilizing an iterative fitting program.⁸⁰ These values, which are beyond the upper limit of determination via NMR,^{81,82} are indicative of tight binding of the Na^+ with the pendant benzo-15-c-5, and are orders of magnitude larger than those recently reported for Na^+ encapsulation by pincer crown complexes in CH_3CN .⁸³

Cyclic voltammetry (CV) of **2** and **3** was utilized to determine the extent of anodic shift upon encapsulation of Na^+ . As stated above, $\text{Fe}(\text{PDI})(\text{CO})_2$ complexes are well-known to display a one-electron oxidation (E_{OX}) to form $[\text{Fe}(\text{PDI})(\text{CO})_2]^+$ and a reversible (or quasi-reversible) one-electron reduction (E_{RED}) to form $[\text{Fe}(\text{PDI})(\text{CO})_2]^-$ (eq 1). Because of the documented solvent dependence on the different events,⁷³ the E_{OX} values were obtained in DCM and the E_{RED} values were obtained in CH_3CN . In DCM (vs $\text{Fc}^{+/0}$), upon Na^+ encapsulation,⁸⁴ the E_{OX} event shifts 31 mV (from -0.523 V in **2** to -0.492 V in **3**; see Figure 8). In CH_3CN , a similar anodic shift (31 mV) in the E_{RED} event is observed upon Na^+ encapsulation (see Figure S29 in the SI). It is clear from these results that Na^+

encapsulation does not attenuate the reduction potential of the ligand-based redox sites. Furthermore, these shifts are much smaller than the ~100 mV shift recently reported for a similar cyclam-PDI hybrid.⁸⁵

Given the unattenuated ligand-based redox sites in **3**, we reasoned that the alkali metal in the secondary coordination sphere could entice the corresponding anion for reduction. We chose to test this hypothesis by examining the reduction of the anion NO₂[−] to NO, which is a ligand-based reduction reaction that we have shown is amenable to study using Fe(PDI)(CO)₂ complexes.^{71,72} The 1:1 binding of Na⁺ in NaNO₂ to form **3**[NO₂] was verified by a series of ¹H NMR titrations in CH₃CN (*K*_{Na⁺} = 2.26 × 10³ L mol^{−1} (see Figures S23–S25 in the SI), and the unattenuated redox-sites (*E*_{OX} = −0.513 V and *E*_{RED} = −2.23 V) were established by CV experiments (see Figure 8, as well as Figure S29 in the SI).⁸⁶ Reaction of **2** with 2 equiv of NaNO₂ and 4 equiv of [HNEt₃][X] (where X = Cl[−], PF₆[−], or BPh₄[−]) results in the clean formation of [Fe(¹⁵bz⁵PDI)−(NO)₂Na][X]₂ (**4**).⁸⁷ (See the SI.)

We were able to obtain a crystal of **4** suitable for X-ray analysis in the PF₆[−] system, with the solid-state structure shown in Figure 9. The Fe center is five-coordinate and has a distorted square pyramidal structure (*τ* = 0.20). Confirming the ligand-based reduction, the PDI backbone is in the neutral form, as evidenced by the contracted C_{imine}–N_{imine} bonds (1.29(1) and 1.29(1) Å), and the elongated C_{imine}–C_{ipso} bonds (1.49(1) and 1.47(1) Å). The average Fe–N(O) bond lengths in **4** are 1.688 Å and the average N–O bond lengths are 1.164 Å. The Fe–N–O units are slightly bent in an “attracto” confirmation⁸⁸ with an average angle of 159.6°. According to the Enemark–Feltham notation,⁸⁹ **4** can be characterized as a {Fe(NO)₂}⁹ complex. Other dinitrosyl iron complexes (DNICs) reported on the PDI ligand scaffold^{71,72,90} are also characterized as {Fe(NO)₂}⁹ complexes, and the reported bond lengths and angles are similar to those observed in **4**. The IR spectrum of **4** (Figure S16 in the SI) exhibits ν_{NO} at 1785 and 1712 cm^{−1}, which shift to 1754 and 1664 cm^{−1}, respectively, upon isotopic substitution with ¹⁵NO (via substitution of Na¹⁵NO₂ in the reaction mixture; see the SI). The measured μ_{eff} of 2.07 μ_B in solution is consistent with *S* = 1/2 and the zero-field Mössbauer parameters [*δ* = 0.25(1); *E*_Q = 1.16(2) mm/s] (Figure S15 in the SI) are in the range of other reported *S* = 1/2, cationic {Fe(NO)₂}⁹ DNICs.⁹¹

Similar to **3**, **4** retains the Na⁺ ion in the secondary coordination sphere. The pendant Na⁺ in **4** lies to one side of the benzo-15-crown-5 ring at 0.733(5) Å above the *x,y,z* coordinates of a plane formed by the O atoms of the benzo-15-crown-5. The Na⁺ is seven-coordinate with five Na–O contacts from the benzo-15-crown-5 and two Na–F contact from a PF₆[−] counterion (see Table 1). Three of the Na–O contacts to the benzo-15-crown-5 are shorter—Na(1)–O(4), 2.364(6) Å; Na(1)–O(6), 2.366(8) Å; and Na(1)–O(7), 2.381(6) Å—and two are longer—Na(1)–O(3), 2.471(7) Å and Na(1)–O(5), 2.400(8) Å, with Na(1)–F(1) = 2.59(1) Å and Na(2)–F(2) = 2.503(9) Å.

With the formation of **4** from **2**, NO_2^- , and $[\text{HNEt}_3]^+$ established, we probed the role of the encapsulated Na^+ in NO_2^- reduction by performing a series of kinetic experiments and comparing the initial rates.⁹² In order to rule out any effects due to simply solubilizing the NO_2^- , all nitrite reductions were run in CH_3CN with TBANO_2 as the source of soluble NO_2^- . The control compound that was chosen for comparison of the initial rates was $\text{Fe}^{\text{MeOPDI}}(\text{CO})_2$ (**5**) (where $\text{MeOPDI} = [(2,6\text{-}^i\text{PrC}_6\text{H}_3)\text{N}=\text{CMe})(2\text{-MeO-}6\text{-MeC}_6\text{H}_3)\text{N}=\text{CMe})\text{-C}_5\text{H}_3\text{N}]$).⁹³ **5** contains a single methoxy group in the secondary coordination sphere (Figure 10) and is active in the nitrite reduction reaction, illustrated by the formation of the DNIC $[\text{Fe}^{\text{MeOPDI}}(\text{NO})_2]^+$ (**6**; see Figure 10, as well as Figure S51 in the SI) from the reaction of **5**, NO_2^- , and $[\text{HNEt}_3]^+$. As shown in Figure 11 and Table 2, the initial rate for the reduction of NO_2^- by both **2** and **5** are virtually identical, establishing that simple solubilization of the NO_2^- does not have any significant effect on the rate of reduction.

In order to probe the role of the pendant redox-inactive Lewis acid, we performed a set of experiments in which Na^+ (in the form of NaBPh_4) was added to the solution of **2**, TBANO_2 , and $[\text{HNEt}_3]^+$. The observed initial rate increases from $1.79 \times 10^{-8} \text{ M s}^{-1}$ to $6.16 \times 10^{-8} \text{ M s}^{-1}$, by a factor of ~ 3.5 . This increase in rate is likely due to the pendant Na^+ , through an electrostatic interaction with the NO_2^- , providing a route for accelerated NO_2^- reduction. Support for this argument comes from the observed binding constants (described above) for Na^+ with **2** in the presence of the different anions. The K_{Na^+} for the $\text{NaNO}_2 = 2.26 \times 10^3 \text{ L mol}^{-1}$, as opposed to $K_{\text{Na}^+} > 10^5 \text{ L mol}^{-1}$ in the case of NaBPh_4 , illustrating a weaker Na^+ -crown interaction in the presence of NO_2^- , resulting in a stronger Na^+ - NO_2^- interaction. By tethering the Na^+ to the secondary coordination sphere, the Na^+ is able to effectively “lure in” the associated NO_2^- for reduction. The control experiment of **5**, TBANO_2 , $[\text{HNEt}_3]^+$, NaBPh_4 , and exogenous benzo-15-crown-5 ether was also run, lending further support for this argument. A decrease in the initial rate, by a factor of 2, is observed ($0.866 \times 10^{-8} \text{ M s}^{-1}$). Without the pendant Na^+ , the NO_2^- likely has difficulty reaching the metal center, because of its interaction with the encapsulated Na^+ . This 7-fold difference in initial rate clearly demonstrates that tethering the pendant Na^+ in the secondary coordination sphere has an accelerating effect on the reduction of the NO_2^- anion. The reactivity mirrors allosteric docking in nature, whereby distal binding of an effector changes the activity at the active site.

Lastly, we examined whether an intermolecular process may be involved, given the propensity for **3** to form dimers in the solid state. As stated above, the binding curves of **2** and Na^+ in Figure 7 yield 1:1 binding, suggesting that **3** is monomeric in solution. However, by replacing Na^+ with K^+ , dimeric structures^{94,95} are formed in solution. The binding curves⁹⁶ (Figure S27 in the SI) clearly indicate 2:1 binding of **2**: K^+ in CH_3CN ($K_{\text{K}^+}^{1:1} = 1.95 \times 10^3 \text{ L mol}^{-1}$ and $K_{\text{K}^+}^{2:1} = 1.04 \times 10^3 \text{ L mol}^{-1}$) and the unattenuated redox-sites ($E_{\text{OX}} = -0.499 \text{ V}$ and $E_{\text{RED}} = -2.22 \text{ V}$) were established by CV experiments (see Figures S30 and S31 in the SI). Inspection of the initial rate with 0.5 equiv K^+ ($1.84 \times 10^{-8} \text{ M s}^{-1}$; see Figure S48 in the SI) and 1.0 equiv K^+ ($2.03 \times 10^{-8} \text{ M s}^{-1}$; see Figure 11) reveals virtually no increase, compared to **2** alone, indicating that an intermolecular process is likely

not occurring in the case of **2** + NaBPh₄.⁹⁷ (Data corresponding to that depicted in Figure 11 are given in Table 2.)

CONCLUSION

In conclusion, by uncoupling the Lewis acidic sites from the ligand-based redox sites in a series of Fe(PDI) complexes, we have demonstrated that the pendant redox-inactive ion, Na⁺, can entice the corresponding counterion, NO₂[−], for reduction to NO. Through the synthesis of [Fe(¹⁵bz⁵PDI)(CO)₂Na]⁺ and subsequent initial rate analysis of NO₂[−] reduction, we have presented a potentially useful method of accelerating substrate reduction, emulating allosteric docking in nature. We are currently exploring the mechanism for NO₂[−] reduction and expanding this concept to more inert anions.

EXPERIMENTAL SECTION

All reagents were purchased from commercial sources and used as received. The asymmetric ligand [(ArN=C(CH₃))C₂H₃N((CH₃)-C=O)]⁹⁸ (Ar= 2,6-ⁱPr-C₆H₃) and Fe(MeOPDI)(CO)₂ (**5**)⁹³ were synthesized according to literature procedures. Solvents were dried and deoxygenated with a PureSolv solvent purification system. Unless otherwise noted, air-sensitive materials were handled and stored on a Schlenk line or in a glovebox under N₂ atmosphere. Infrared spectra were recorded on a Thermo Scientific Nicolet iS10 FT-IR spectrometer equipped with an ATR accessory. ¹H and ¹³C NMR spectra were recorded on a Bruker 500 MHz FT-NMR spectrometer. Data are reported in units of parts per million (ppm) from the solvent resonance as the internal standard, unless otherwise noted. UV-vis absorbance data were acquired using a Jasco UV-vis/NIR spectrometer that was equipped with a Peltier controlled six-cell linear autosampler. All data were obtained at 298 K in 1 cm quartz cuvettes (Starna Cells). Elemental analyses were performed by ALS Environmental (Tuscon, AZ, USA). Solution magnetic susceptibilities were calculated from NMR measurements using Evan's method.⁹⁹ Solid-phase magnetic susceptibilities were recorded on a Johnson Matthey MSB-1 magnetic susceptibility balance that was calibrated with HgCo(SCN)₄. Diamagnetic correction factors were calculated from Pascal's constants.¹⁰⁰

Fe(¹⁵bz⁵PDI)(CO)₂ (**2**)

The synthesis of **2** was achieved via a two-step synthesis. In the first step, Fe(¹⁵bz⁵PDI)Br₂ (**1**) was synthesized by dissolving the asymmetric PDI ligand [(ArN=C(CH₃))C₂H₃N-((CH₃)C=O)] (0.500 g, 1.551 mmol) and FeBr₂ (0.3344 g, 1.551 mmol) in ~40 mL of ethanol into a 100-mL round-bottom Schlenk flask with a stir bar. The solution was heated to 50 °C for 20 min under N₂ gas and stirred. A solution of 4'-aminobenzo-15-crown-5 ether (0.4394 g, 1.551 mmol) in 5 mL of acetonitrile was slowly deposited into the flask using a syringe, and the solution was subjected to heating at 78 °C for 12 h under N₂ gas. The solvent was removed in vacuo, and a dark blue solid was obtained. Inside the glovebox, the solid was redissolved in 40 mL of CH₂Cl₂ and filtered through Celite. The solution was layered with 50 mL of pentane and set aside to precipitate the product. The resulting dark blue solid was used in the next step without further purification.

In a nitrogen-filled glovebox, compound **1** (0.300 g, 0.420 mmol), NaHg (0.4054 g, 5% Na), ~10 mL of CH₂Cl₂, and a stir bar were added to a Fisher Porter tube. The tube was closed with a pressure valve, removed from the box, and charged with 35 psi of CO, and the solution was stirred vigorously overnight. The solvent was removed by vacuum and brought into the glovebox. The green solid was redissolved in 40 mL of diethyl ether and filtered through a Celite plug. Slow evaporation of diethyl ether yielded dark green crystals identified as **2** in 71% yield (0.1858 g, 0.265 mmol). FT-IR (ATR): 1948, 1886 cm⁻¹ (C=O). ¹H NMR (500 MHz, CD₂Cl₂) δ 8.16 (dd, 2H), 7.58 (t, 1H), 7.23 (m, 3H), 6.86 (d, 1H), 6.68 (d, 1H), 6.64 (dd, 1H), 4.14–3.70 (m, 16H), 2.51 (sept, 2H), 2.46 (s, 3H), 2.38 (s, 3H), 1.21 (d, 6H), 1.01 (d, 6H). ¹³C NMR (125 MHz, CD₂Cl₂) δ 15.52, 16.45, 24.39, 27.25, 68.46, 69.00, 69.38, 70.17, 70.78, 109.21, 112.70, 114.71, 117.44, 120.85, 121.21, 123.45, 126.13, 140.15, 144.50, 146.72, 148.41, 149.58, 155.19, 156.32, 198.33, 214.03. Anal. Calcd for C₃₇H₄₅FeN₃O₇: C, 63.52; H, 6.48; N, 6.01. Found: C, 62.93; H, 6.28; N, 5.87.

[Fe(¹⁵bz⁵PDI)(CO)₂Na][BPh₄] (**3**)

A 20 mL scintillation vial was charged with compound **2** (0.250 g, 0.357 mmol), NaBPh₄ (0.1222 g, 0.357 mmol), a stir bar, and ~5 mL of CH₃CN. The solution was stirred overnight. The solvent was removed via vacuum and redissolved in 5 mL of CH₂Cl₂. The dark green solution was filtered through Celite. The solution was then carefully layered with pentane and set aside for crystallization. The resulting dark green crystals were identified as **3** in 68% yield (0.2529 g, 0.243 mmol). FT-IR (ATR): 1929, 1857 cm⁻¹ (C=O); 734, 707 cm⁻¹ (BPh₄⁻). ¹H NMR (500 MHz, CD₂Cl₂) δ 8.22 (t, 2H), 7.64 (s, 1H), 7.34–6.83 (br, 26H), 4.15–3.68 (br, 16H), 2.51–2.44 (br, 8H), 1.24 (s, 3H), 1.05 (s, 3H). ¹³C NMR (125 MHz, CD₂Cl₂) δ 214.28, 164.55, 164.16, 163.77, 163.38, 157.28, 154.99, 149.48, 145.79, 145.40, 144.23, 140.18, 135.93, 126.29, 125.61, 123.55, 121.16, 116.45, 112.45, 109.15, 68.90, 68.52, 68.10, 67.99, 67.30, 67.05, 27.30, 24.41, 16.58, 15.69. Anal. Calcd for C₆₁H₆₅BFeN₃NaO₇: C, 70.32; H, 6.29; N, 4.03. Found: C, 71.15; H, 6.98; N, 3.68. This sample likely contains excess pentane (see the Xray section). Calcd for C₆₁H₆₅BFeN₃NaO₇·C₅H₁₂: C, 71.16; H, 6.97; N, 3.77.

[Fe(¹⁵bz⁵PDI)(CO)₂Na][NO₂] (**3**[NO₂])

A 20 mL scintillation vial was charged with compound **2** (0.250 g, 0.357 mmol), NaNO₂ (0.0246 g, 0.357 mmol), a stir bar, 5 mL of CH₃CN, and 2 mL of CH₃OH. The solution was stirred for 2 h. The solvent was removed via vacuum and redissolved in 5 mL of CH₂Cl₂. The dark green solution was filtered through Celite. Multiple attempts to crystallize this compound were unsuccessful. FT-IR (ATR): 1949, 1884 cm⁻¹ (C=O).

[Fe(¹⁵bz⁵PDI)(NO)₂Na][X]₂ (**4**) (X = Cl⁻, PF₆⁻, BPh₄⁻)

A 20 mL scintillation vial was charged with compound **2** (0.250 g, 0.357 mmol), NaNO₂ (0.050 g, 0.714 mmol), [NEt₃H][X] (1.428 mmol), a stir bar, and ~10 mL of CH₃CN. The solution was stirred for 18 h. The resulting dark orange solution was filtered through Celite and dried under vacuum. Crystals were only obtained with PF₆⁻. The solid was redissolved in 5 mL of tetrahydrofuran and then carefully layered with 10 mL of toluene and set aside for crystallization. The resulting orange crystals were identified as **4**(PF₆)₂.

(4[PF₆]₂)

FT-IR (ATR): 1784, 1712 cm⁻¹ (N=O), 828 cm⁻¹ (PF₆⁻). ¹H NMR (500 MHz, CD₂Cl₂)
Anal. Calcd for C₃₅H₄₅F₁₂FeN₅O₇P₂: C, 41.35; H, 4.46; N, 6.89. Found: C, 41.26; H, 4.26;
N, 6.69. μ_{eff} : 2.07 μ_{B} (solution).

(4[BPh₄]₂)

FT-IR (ATR): 1790, 1721 cm⁻¹ (N=O); 703, 732 cm⁻¹ (BPh₄⁻). Multiple attempts at
crystallization resulted in oiling out of the product.

[Fe(^{MeO}PDI)(NO)₂][PF₆] (6)

A 20 mL scintillation vial was charged with **5** (0.250 g, 0.452 mmol), NaNO₂ (0.0624 g,
0.904 mmol), and [NEt₃H][PF₆] (0.447 g, 1.808 mmol), a stir bar, and 10 mL of CH₃CN.
The solution was stirred for 18 h. The resulting dark orange solution was filtered through
Celite and dried under vacuum. The solid was redissolved in tetrahydrofuran (THF), and X-
ray-quality crystals were obtained by slow vapor diffusion of pentane into this solution. The
compound was identified as **6**. FT-IR (ATR): 1797, 1729 cm⁻¹ (N=O), 830 cm⁻¹ (PF₆⁻).
 μ_{eff} : 1.67 μ_{B} (solution).

¹H NMR Titrations

In a typical experiment, a sample of Fe(^{15b_z5}PDI)(CO)₂ (20 mmol) in CD₃CN (500 μ L) was
added to a J. Young NMR tube. Twenty microliter (20 μ L) aliquots (60 mM, 0.15 equiv) of
either NaBPh₄ in CD₃CN, NaNO₂ in CD₃OD, or KPF₆ in CD₃CN were added to the tube
inside the glovebox. The resulting mixture was vigorously shaken for 15 s and inserted into
the NMR probe, where it was allowed to equilibrate at 298 K for 10 min before a spectrum
was obtained. The tube was brought back into the glovebox to add the next aliquot, and the
process was repeated until the titration was complete.

Mössbauer Spectra

Mössbauer spectra were recorded at room temperature with a constant acceleration
spectrometer (Wissel GMBH, Germany) in a horizontal transmission mode using a 50 mCi
⁵⁷Co source. Approximately 0.200 g of sample was crushed in a Mössbauer sample holder
and a drop of Paratone-N was used to cover the sample, to prevent oxidation. Data
acquisition varied from 2 days to 7 days to get a statistically reasonable spectrum for each
sample to analyze. The velocity scale was normalized with respect to metallic iron at room
temperature; hence, all isomer shifts were recorded relative to metallic iron. The Mössbauer
spectra were fitted by assuming Lorentzian line shapes using the NORMOS (Wissel GMBH)
least-squares fitting program. The isomer shifts and quadrupole splitting parameters were
determined from the fitted spectra.

X-ray Crystallography

Diffraction intensities for **2**, **3**, **4**, and **6** were collected at 173 and 218 K (**3**) on a Bruker
Apex2 CCD diffractometer using a Incoatec Cu I μ S source (Cu K α radiation, 1.54178 Å).
Space groups were determined based on systematic absences and intensity statistics (**3**).
Absorption corrections were applied by SADABS.¹⁰¹ Structures were solved by direct

methods and Fourier techniques and refined on F^2 using full-matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. All H atoms in the investigated structures were refined in calculated positions in a rigid group model. Crystals of **2** and **4** are very thin plates or needles, and X-ray diffraction (XRD) signals from them at high angles was very weak. Even by using a strong Incoatec Cu $I\mu S$ source, it was possible to collect diffraction data only up to $2\theta_{\max} = 101.08^\circ$ and 98.34° , respectively, for **2** and **4**. The structure of **3** has highly disordered solvent molecules filling empty space in the packing (C_5H_{12} in **3**), which has been treated by SQUEEZE.¹⁰² Corrections of the X-ray data by SQUEEZE are 241 electrons per the unit cell, respectively, for **3**; the required number of electrons are 168 for four solvent molecules in the structure. The difference between evaluated and required values in **3** seems to be related to the fact that pentane molecules fill out a large space between molecules and are disordered over several positions around an inversion center. Even using a strong Incoatec Cu $I\mu S$ source for data collection, diffraction signals from these crystals were not strong, especially at the high angles. However, the obtained X-ray structures clearly confirm the structure and compositions of the investigated compounds. All calculations were performed by the Bruker SHELXL-2014/7 package.¹⁰³

Electrochemistry

Cyclic voltammetry was carried out using a Pine WaveNow potentiostat employing a standard three-electrode electrochemical cell consisting of a glassy carbon working electrode, a platinum wire auxiliary electrode, and a freshly prepared Ag/AgNO₃ reference electrode with a Vycor tip filled with acetonitrile. All potentials were internally referenced to the ferrocene redox couple. Unless otherwise noted, experiments were carried out under a dinitrogen atmosphere at room temperature using either acetonitrile or methylene chloride. Solutions of the analyte at 0.001 M and 0.100 M tetra(*n*-butyl)ammonium hexafluorophosphate (TBAPF₆) as the supporting electrolyte were prepared.

UV-vis Kinetics

All samples were prepared under an N₂ atmosphere inside the glovebox. A typical kinetics experiment was performed by preparing an acetonitrile solution consisting of 225 μM of **2** or **5**, 225 μM of appropriate additives (NaBPh₄, KBPh₄, benzo-15-crown-5 ether), and 550 μM tetrabutylammonium nitrite. A quantity of 3.0 mL of this solution was added to a quartz cuvette that was equipped with a stir bar and sealed with a pierceable septa. An excess of a 9 mM [NEt₃H][BPh₄] solution was drawn into a syringe that was equipped with a needle, and the needle was pierced into a scintillation vial that was equipped with a septa to keep the solution under an N₂ atmosphere. The cuvette and syringe were brought outside the box, where the cuvette was placed into the spectrometer to equilibrate at 25 °C for 10 min before injection of 0.3 mL of the acid solution into the cuvette while starting the spectrometer. Initial rates were obtained by fitting 6 min of measurements, starting after 120 s to ensure thorough mixing after the injection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Active site of galactose oxidase (left) and the Mn₄CaO₅ cluster composing the oxygen-evolving complex of Photosystem II (right). Some residues have been omitted for the sake of clarity.

Figure 2.

Redox-activity of ⁱPrPDI ligand scaffold illustrating three (of four) oxidation states. Ar = 2,6-diisopropylaniline.

Figure 3. Resonance forms of the direduced $\text{Fe}^{\text{iPr}}\text{PDI}(\text{CO})_2$, illustrating the dianionic (left) and neutral (right) forms of the PDI ligand.

Figure 4. $[\text{Fe}(\text{Hdidpa})(\text{CO})_2]^+$ (left) and $[\text{Fe}({}^{15}\text{c}5\text{PDI})-(\text{CO})_2(\text{M}^{n+})]^{n+}$ (right). The $E_{1/2}$ values represent the ligand-based reduction potential upon deprotonation of the Bronsted base (left) or encapsulation of the alkali-metal ion, Na^+ (right).

Figure 5.

Solid-state structure (30% probability) of $\text{Fe}(\text{15bz5PDI})-(\text{CO})_2$ (**2**). The H atoms have been omitted for the sake of clarity. Selected bond lengths: Fe(1)–C(36), 1.784(5) Å; Fe(1)–C(37), 1.783(5) Å; Fe(1)–N(1), 1.943(4) Å; Fe(1)–N(2), 1.840(3) Å; Fe(1)–N(3), 1.936(4) Å; C(2)–N(1), 1.324(5) Å; and C(8)–N(3), 1.325(5) Å. Selected bond angles: C(36)Fe(1)C(37), 97.7(2)°; N(2)Fe(1)C(36), 148.4(2)°; and N(1)Fe(1)N(3), 156.3(2)°.

Figure 6.

Chemdraw (left) and solid-state structure of the asymmetric unit (right, 30% probability) of $[\text{Fe}(\text{}^{15}\text{bz}^5\text{PDI})(\text{CO})_2\text{Na}]^+$ (**3**). The H atoms have been omitted for the sake of clarity.

Selected bond lengths: Fe(1)–C(36), 1.776(3) Å; Fe(1)–C(37), 1.770(2) Å; Fe(1)–N(1), 1.966(2) Å; Fe(1)–N(2), 1.847(2) Å; Fe(1)–N(3), 1.945(2) Å; C(2)–N(1), 1.323(2) Å; C(8)–N(3), and 1.324(2) Å. Selected bond angles: C(36)Fe(1)C(37), 97.1(1)°; N(2)Fe(1)C(37), 152.35(9)°; and N(1)Fe(1)N(3), 155.42(7)°.

Figure 7. Plot of chemical shift of representative C-H resonances (6.64 ppm = blue; 4.10 ppm = red; 3.78 ppm = black) in **2** vs added equivalents NaBPh₄ and corresponding stacked ¹H NMR spectra. The spectra plotted correspond to 0 equiv (bottom spectrum) up to 3.5 equiv NaBPh₄ (top spectrum).

Figure 8.

E_{OX} cyclic voltammograms of 1 mM **2** (solid green, $E_{1/2} = -0.523$ V), $[\mathbf{3}][\text{BPh}_4]$ (dashed red line, $E_{1/2} = -0.492$ V) and $[\mathbf{3}][\text{NO}_2]$ (dashed blue line, $E_{1/2} = -0.513$ V) in CH_2Cl_2 ; glassy carbon WE, Pt wire CE and Ag/AgNO_3 in CH_3CN RE, 100 mM TBAPF_6 electrolyte.

Figure 9.

Chemdraw (left) and solid-state structure (right, 30% probability) of $[\text{Fe}(\text{15bz5PDI})(\text{NO})_2\text{Na}][\text{PF}_6]^+$ (**4**). The H atoms and one PF_6^- counterion have been omitted for the sake of clarity. Selected bond lengths: Fe(1)–N(1), 2.113(8) Å; Fe(1)–N(2), 2.071(7) Å; Fe(1)–N(3), 2.202(8) Å; Fe(1)–N(4), 1.692(9) Å; Fe(1)–N(5), 1.684(9) Å; N(1)–C(2), 1.29(1) Å; and N(3)–C(8), 1.29(1). Selected bond angles: N(4)–Fe(1)–N(5), 109.3(4)°, N(2)–Fe(1)–N(4), 135.6(4)°, and N(1)–Fe(1)–N(3), 147.6(3)°.

Figure 10.
Chemdraw of $\text{Fe}(\text{MeOPDI})(\text{CO})_2$ (**5**, left) and $[\text{Fe}(\text{MeOPDI})(\text{NO})_2]^+$ (**6**, right).

Figure 11.

Initial rate plots for the reduction of TBANO₂ by selected Fe(PDI)(CO)₂ species and 4 equiv H⁺. Orange line (top) represents **5** + 1 equiv NaBPh₄ and 1 equiv Bz-15-c-5; green line represents **2**; blue line represents **2** + 1 equiv KBPh₄; black line represents **5**; and red line (bottom) represents **2** + 1 equiv NaBPh₄.

Scheme 1.
Synthesis of $\text{Fe}(\text{15bz5PDI})(\text{CO})_2$ (2)

Chart 1. (A) Crown Ether Appended Ferrocene, (B) Crown Ether Incorporated Co(salen), (C) Bimetallic Metalloligand System, and (D) Manganese Cubane Core Structure^a

^aThe $E_{1/2}$ values represent the metal-based reduction potential upon redox-inactive Lewis acid cation encapsulation.

Table 1Selected Bond Lengths of Fe(¹⁵bz⁵PDI) Complexes

	Bond Length (Å)		
	2	3	4
C(2)–N(1)	1.324(5)	1.323(2)	1.29(1)
C(8)–N(3)	1.325(5)	1.324(2)	1.29(1)
C(2)–C(3)	1.436(7)	1.430(3)	1.49(1)
C(7)–C(8)	1.427(6)	1.425(3)	1.47(1)
Na(1)–O(7)		2.408(2)	2.381(6)
Na(1)–O(6)		2.348(2)	2.366(8)
Na(1)–O(5)		2.332(2)	2.400(8)
Na(1)–O(4)		2.377(2)	2.364(6)
Na(1)–O(3)		2.374(2)	2.471(7)
Na(1)–O(2)		2.372(2)	
Na(1)–F(1)			2.59(1)
Na(2)–F(2)			2.503(9)

Table 2Selected Initial Rates of TBANO₂ Reduction^a

Compound	Rate ^b ($\times 10^{-8}$ Ms ⁻¹)	Std.Dev. ($\times 10^{-8}$ Ms ⁻¹)	Rate Relative to 2
5	2.11	2.1	1.18

^a Color coding in this table matches that used in Figure 11.Conditions: 25 °C, 2 equiv. TBANO₂, 4 equiv. [HNEt₃]⁺, CH₃CN.^b Average initial rate.^c 1 equiv. NaBPh₄.^d 1 equiv. KBPh₄.^e 1 equiv.Bz15c5 + 1 equiv. NaBPh₄.