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Communication

C−H Bond Amination from a Ferrous Dipyrromethene Complex

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In this Communication, we report an intramolecular C−H bond amination reaction of a dipyrromethene ferrous complex with organic azides. Monitoring of the spectral changes (variable-temperature NMR and UV−vis) of the Fe^{II} complex reveals no buildup of an intermediate during conversion of the starting material into the nitrene-inserted product. The rate-determining step appears to be azide addition to the 14-electron Fe^{II} complex, hinting at the potential that these and related platforms may have to effect atom- and group-transfer processes.

Introducing functionality into unactivated C−H bonds remains a significant challenge both in the realm of complex molecule synthesis and in the elaboration of simple hydrocarbon feedstocks into value-added commodity chemicals.[1] The current state-of-the-art C−H bond functionalization techniques mainly utilize late-transition-metal catalysts that facilitate C−H activation and functionalization. Several limitations exist in these methods: C−H bond activation typically requires forcing conditions where oxidation processes can become unselective under the conditions required for bond activation to occur[2] or C−H bond activation only occurs proximal to substrate-directing groups.[3] The development of new inorganic/organometallic catalysts to effect atom- or group-transfer processes will mitigate the reliance on directing groups to activate C−H bonds,[4] thereby minimizing waste generation during synthetic procedures.[5] One potential strategy for sequential C−H bond activation and functionalization is to utilize the transient formation of metal−ligand multiple bonds to effect atom- or group-transfer processes.[6] Herein we report an intramolecular C−H bond amination mediated by the reaction of a coordinatively and electronically unsaturated dipyrromethene iron(II) complex with organic azides.

A variety of ligand platforms have been employed that utilize strongly donating substituents (e.g., phosphines,[7] amines,[8] carbenes,[9] and β-diketiminates[10]), resulting in strongly nucleophilic metal complexes capable of supporting metal−ligand multiple bond formation. To target metal−ligand multiple bonds potentially more reactive toward bond-activating pathways, we sought an oxidatively resistant ligand system that sterically enforces minimal coordination at the metal center while maintaining an electrophilic metal envi-

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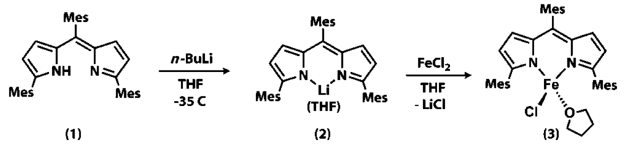
10.1021/ic900219b CCC: $40.75

Scheme 1



ronment, which may confer unique reactivity to the resulting metal complexes. Arylated dipyrromethene ligands are good candidates to satisfy both desired design criteria.[11] Using pyridinium *p*-toluenesulfonate as a catalyst (5%), 2-mesitylpyrrole was condensed with mesitaldehyde dimethyl acetal to form the dipyrromethane. Subsequent oxidation with dichlorodicyanoquinone in acetone affords the target 1,5,9-trimesityldipyrromethene [(pyac)H, **1**] in 68% overall yield. Dipyrromethene **1** precipitates from the acetone solution upon oxidation, obviating the need for chromatography as a purification step. Deprotonation of the ligand can be effected by the treatment of **1** with 1.2 equiv of *n*-BuLi in thawing tetrahydrofuran (THF) solutions to produce the solvated lithio complex [pyac][Li(THF)] (**2**), which was, in turn, suitable for installing the pyac moiety onto transition metals.

Reaction of the lithio complex **2** with a thawing slurry of FeCl$_2$ in THF furnished the four-coordinate, solvated species (pyac)FeCl(THF) (**3**) as a red solid (Scheme 1). The solid-state structure for **3** is provided in Figure 2, confirming the solvated state adopts a pseudotetrahedral environment at iron. THF in **3** is labile and can be exchanged for stronger binding ligands like pyridine to yield (pyac)FeCl(pyr) (**4**). Likewise, the Zn^{II} congener was synthesized by the reaction of **2** with ZnCl$_2$ in thawing THF, followed by treatment with pyridine to furnish (pyac)ZnCl(pyr) (**5**) as an isolable orange solid. Complexes **3**−**5** could be isolated as analytically pure solids in 75−84% yield. Complexes **4** and **5** adopt geometries similar to that of **3** in the solid state (see the Supporting Information).

Much like their porphyrin congeners, dipyrromethenes and their metal complexes exhibit intense ligand $\pi \rightarrow \pi^*$ transitions afforded by the conjugation and aromaticity of the dipyrromethene ligand system.[12] The dominant charge transfer occurs in the range of 460−500 nm for the parent ligand **1** and its metal complexes (Figure 1) [λ_{max} (ϵ) for **1** 467 nm (49 000 M^{-1} cm^{-1}); λ_{max} (ϵ) for **2** 499 nm (97 000 M^{-1} cm^{-1}); λ_{max} (ϵ) for **3** 503 nm (74 000 M^{-1} cm^{-1}); λ_{max} (ϵ) for **4** 506 nm (69 000 M^{-1} cm^{-1}); λ_{max} (ϵ) for **5** 501 nm (140 000 M^{-1} cm^{-1})]. The observed $\pi \rightarrow \pi^*$ transition for ligand **1** is not unlike other dipyrromethene ligand derivatives that are often employed as fluorescence tags or the parent porphyrin constructs.[12] While the zinc complex **5** is a diamagnetic species, the room temperature solution magnetic moments of complexes **3** and **4** are 5.21(5) and 5.29(1) μ_B, respectively, both consistent with high-spin ($S = 2$) iron centers (Evans method).[13] Cyclic voltammetry on **3** and **4** reveals fully reversible Fe$^{III/II}$ redox waves centered at −400 mV versus an internal ferrocene reference (Figure 1, inset; scan rate = 100 mV/s). Cyclic voltammetry on complex **5** reveals fully reversible, one-electron reduction (−2.0 V) and oxidation (+0.55 V) events originating from the ligand platform (see the Supporting Information). Reduction waves are observed for complexes **3** and **4** at similar potentials, whereas the onset to oxidation is shifted by ca. −300 mV and the processes are no longer reversible.

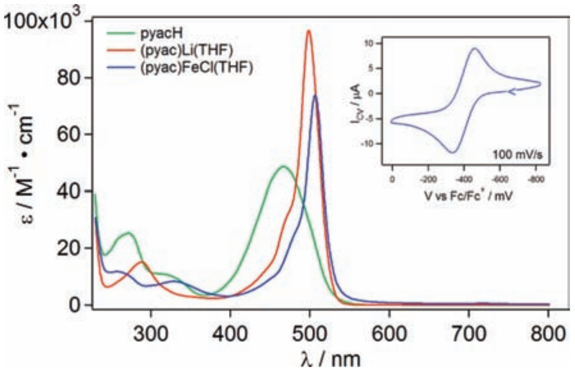


Figure 1. UV−vis spectra of **1**−**3** (THF). The inset shows the cyclic voltamagram of complex **3** in THF (0.1 M) with 0.3 M Bu$_4$NPF$_6$; scan rate = 100 mV/s on a glassy carbon electrode.

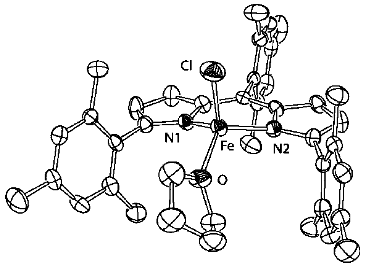


Figure 2. Solid-state structure for **3** with thermal ellipsoids set at the 50% probablility level (H atoms omitted for clarity). Bond lengths (Å) for **3**: Fe−N1, 2.017(3); Fe−N2, 2.034(4); Fe−Cl, 2.263(1); Fe−O, 2.029(3).

To test whether the dipyrromethene ligand could confer the same reactivity at the Fe^{II} center as their porphyrin counterparts, we canvassed the reactivity of **3** with a series of organic azides to examine whether nitrene transfer could be effected.[14] Reacting a thawing solution of **3** in dichloromethane with a stoichiometric amount of 1-azidoadamantane quantitatively produces a new paramagnetic, iron-containing complex, evidenced by the increase of observable proton resonances apparent in ^{1}H NMR, consistent with desymmetrization of the ligand environment (see the Supporting Information for ^{1}H NMR details). Solutions of **3** in thawing CH$_2$Cl$_2$ react quickly with organic azides (N$_3$Ph, N$_3$Mes, and N$_3$Ad) to expel dinitrogen, as evidenced by the disappearance of the azide stretch in the IR spectrum, and cleanly produce a new high-spin Fe^{II} product distinct from **3** by ^{1}H NMR, displaying a similar desymmetrization of the ligand proton resonances.

Characterization of crude reaction mixtures by electrospray ionization mass spectrometry revealed parent ions consistent with azide-derived nitrene insertion into a ligand C−H bond (Scheme 2). The masses obtained from the independent reactions of **3** with N$_3$R (R = ^{t}Bu, 1-Ad, Ph, Mes, Tos) suggest that multiple nitrene insertions into the ligand do not occur,

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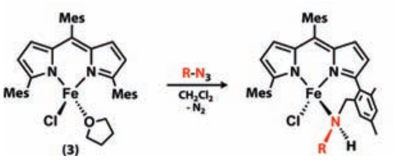
Scheme 2



R (N_3-*R*)	TOF/ESI *m*/*z*[a] [H(pyac) + NR + H]$^+$
Ad	648.4318 (648.4284)
CMe_3	570.3848 (570.3851)
Ph	590.3535 (590.3509)
Mes	632.4004 (632.3965)
Ts	668.3310 (668.3306)

[a] calculated (observed)

even when the azide reagent is used in excess (metal dissociation was consistently observed using this ionization method). Vapor diffusion of Et_2O into a THF solution of **3** + N_3Ad produced crystals suitable for X-ray diffraction analysis. The molecular structure of the product reveals insertion of the [NAd] fragment into a benzylic C−H bond from one of the ligand pyrrolic mesityl aryl groups (Scheme 2). The molecular structure of aminated product (pyac)FeCl(NHAd*) (**6**) is shown in Figure 3. The local geometry about the iron in **6** adopts a distorted trigonal-monopyramidal structure, where the azide-derived amine (N3) remains bound to the iron.

One mechanistic possibility for the observed insertion reaction involves azide addition to **3** (displacing the coordinated THF), followed by dinitrogen expulsion from the azide to yield a high-valent iron(IV) imido complex. Formation of the iron(IV) imido complex could then be quickly followed by H-atom abstraction and a radical-rebound mechanism to form the N−C bond found in the product in a hydroxylase-like fashion.[15] Variable-temperature (VT) ^{1}H NMR experiments did not reveal any discernible intermediate along the proposed pathway, only the starting material **3** and the emergence of the C−H bond-activated product **6** beginning at −30 °C. The emergence of the product peaks for **6** appear with a concomitant decrease in the observed peaks for **3** in a roughly 1:1 fashion. This latter observation was confirmed by following the reaction by the absorption spectral changes. The spectral changes for the reaction of **3** with 10 equiv of 1-adamantyl azide (Figure 4) only show the decay of **3** and growth of the product **6** [λ_{max} (ϵ): 518 nm (57 000 $M^{-1}cm^{-1}$)] with an isosbestic point at 516 nm, indicating that there is no buildup of an observable intermediate in the reaction. While in situ IR analysis of the reaction mixture did not reveal a shift in the azide stretch on the IR time scale, ^{1}H NMR analysis of the reaction of **3** with ^{t}BuN_3 did reveal a dynamic exchange of the azide ligand (from the shift of the ^{t}Bu resonance) bound to a (pyac)FeCl complex preceding formation of the nitrene-inserted product.

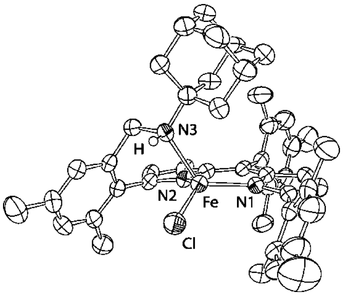


Figure 3. Solid-state structure for **6** with thermal ellipsoids set at the 50% probablility level (H atoms, solvent molecules and positional disorder omitted for clarity). Bond lengths (Å) for **6**: Fe−N1, 2.079(5); Fe−N2, 2.038(5); Fe−Cl, 2.245(2); Fe−N3, 2.190(5).

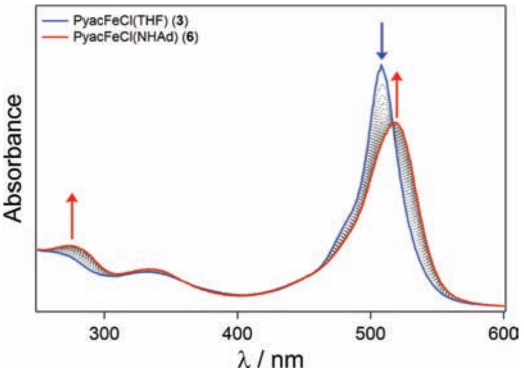


Figure 4. Changes in the electronic absorption spectrum during conversion of **3** → **6** in CH_2Cl_2 (3 mM in **3**, 23 °C, scans each 60 s). Arrows denote evolution of the absorption spectrum with time.

Several high-valent iron(IV) imido complexes have now been synthesized and characterized.[9c,16] Furthermore, reactions of phenyl-*N*-tosylimidoiodinane and organic azides with Fe^{II} complexes have been reported to produce iron amido or anilido products and have been proposed to go through iron(IV) imido intermediates.[17] Radical reactivity has also been observed from related iron(III) and cobalt(III) imido complexes and typically leads to H-atom abstraction products.[10c,18] While a nonredox-involved process cannot be ruled out in the conversion of **3** to **6**, reaction of the zinc complex **5** in place of the iron complex **3** does not afford any aminated product even after prolonged heating of **5** with excess organic azide (7 days, 50 °C). The iron pyridine analogue **4** does produce the same aminated product **6**, although the reaction proceeds much more slowly (50% completion after 7 days, 50 °C), presumably because of the presence of the less labile pyridine ligand.

In conclusion, we have reported a simple dipyrromethene-iron complex that is capable of mediating intramolecular C−H bond amination from an organic azide precursor. This reaction pathway diverges from typical radical H-atom abstraction reactions in that the entire amine is transferred to the C−H bond substrate. The presence of the electrophilic Fe^{II} in **6** serves to trap the aminated product, likely inhibiting further reaction. Work is currently underway to validate our mechanistic hypothesis and to target intermolecular versions of this reaction and related C−C and C−O bond-forming reactions via similar C−H activation pathways.

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Supporting Information Available: Experimental details, spectral data (VT ^{1}H NMR and UV−vis absorption spectra), and CIF files for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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