Oxidative Addition of Aryl and Alkyl Halides to a Reduced Iron Pincer Complex

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ABSTRACT: The two-electron oxidative addition of aryl and alkyl halides to a reduced iron dinitrogen complex with a strong-field tridentate pincer ligand has been demonstrated. Addition of iodobenzene or bromobenzene to $(3,5-Me_2^{Mes}CNC)Fe(N_2)_2$ $(3,5-Me_2^{Mes}CNC = 2,6-(2,4,6-Me-C_6H_2-imidazol-2-ylidene)_2-3,5-Me_2-pyridine)$ resulted in rapid oxidative addition and formation of the diamagnetic, octahedral Fe(II) products $(3,5-Me_2^{Mes}CNC)Fe(Ph)(N_2)(X)$, where X = I or Br. Competition experiments established the relative rate of oxidative addition of aryl halides as I > Br > Cl. A linear free energy of relative



reaction rates of electronically differentiated aryl bromides ($\rho = 1.5$) was consistent with a concerted-type pathway. The oxidative addition of alkyl halides such as methyl-, isobutyl-, or neopentyl halides was also rapid at room temperature, but substrates with more accessible β -hydrogen positions (e.g., 1-bromobutane) underwent subsequent β -hydride elimination. Cyclization of an alkyl halide containing a radical clock and epimerization of neohexyl iodide- d_2 upon oxidative addition to $(3,5-Me_2^{Mes}CNC)Fe(N_2)_2$ are consistent with radical intermediates during $C(sp^3)-X$ bond cleavage. Importantly, while $C(sp^2)-X$ and $C(sp^3)-X$ oxidative addition produces net two-electron chemistry, the preferred pathway for obtaining the products is concerted and stepwise, respectively.

INTRODUCTION

The oxidative addition of both polar and nonpolar bonds by reduced transition metal complexes is a fundamental organometallic transformation and key substrate activation step in many catalytic cycles.^{1–4} Among the most prominent is the net two-electron oxidative addition of carbon–halogen bonds invoked in palladium-⁵ and nickel-catalyzed cross-coupling reactions.^{6–8} The impact of these reactions cannot be overstated, as transition-metal catalyzed cross-coupling reactions are among the most widely utilized carbon–carbon bond forming reactions in synthetic chemistry. Not only are more than half of all carbon–carbon bonds in medicinal chemistry formed using these methods,^{9,10} but they are also widely employed in large-scale reactions and in commercial contexts.¹¹

Due to the high terrestrial abundance, comparatively low cost and toxicity of iron, there has been a growing interest in developing iron-catalyzed cross coupling reactions in both academia and industry.^{12–14} Building on early examples,^{15,16} several successful protocols for iron-catalyzed cross-coupling have been developed in the past two decades.^{17,18} These methods are mechanistically distinct from traditional palladium- and nickel-catalyzed cross-coupling reactions and do not proceed through the same types of intermediates. While iron-catalyzed cross-coupling reactions are mechanistically diverse and much remains to be learned, a general feature is that transmetalation with typically strongly nucleophilic organometallic reagents takes place prior to carbon–halide bond

activation.¹⁹ As a consequence, the activation of the electrophile occurs with a more oxidized iron intermediate and likely does not occur in a discrete two-electron fashion in analogy to palladium or nickel examples. In addition, it remains an open question whether a molecular iron intermediate forms that contains iron–carbon bonds from both the nucleophilic and electrophilic partners.

One of the seminal and most prominent iron-catalyzed cross-coupling procedures was reported by Nakamura and coworkers and involves combination of alkyl halides with aryl boronates activated with Grignard reagents or alkyl lithium reagents in the presence of an iron(II) precursor with a bis(phosphine) ligand.^{20,21} Subsequent, in-depth spectroscopic and mechanistic studies by Neidig and co-workers^{22,23} support a pathway involving halide-atom abstraction from the electrophile by a bis(phosphine)-ligated Fe(II)–aryl complex followed by C–C bond formation by capture of the alkyl radical by the resulting Fe(III) aryl complex (Scheme 1a).

Similar catalytic²⁴⁻²⁷ and stoichiometric^{28,29} chemistry has also been reported with *N*-heterocyclic carbene (NHC)

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Scheme 1. Overview of Aryl and Alkyl Halide Oxidative Addition to Iron Complexes

A. Oxidative Addition/Reductive Elimination Proposed During Iron Catalyzed Cross Coupling



stabilized iron complexes. While reactions with bis(phosphine) or NHC-supported iron precatalysts are typically limited to alkyl halide electrophiles, Bedford and co-workers recently disclosed that aryl halides with an *N*-pyrrole amide directing group *ortho* to the C–X bond engaged in iron-catalyzed cross-coupling.³⁰ Details on the nature of the C–X activation step operative during catalysis were not reported.

While early examples of polar oxidative additions featured anionic supernucleophilic organometallic iron complexes such as $[(\eta^{5}-C_{5}H_{5})Fe(CO)_{2}]^{-}$ and $[Fe(CO)_{4}]^{2-}$ (Scheme 1b),³¹ direct observation of the oxidative addition of alkyl- and arylhalides to reduced iron complexes has remained rare and the mechanisms are poorly understood. In the course of investigations of an iron-catalyzed cross-coupling reaction between alkyl- or electron poor aryl-halides and Grignard reagents, $^{32-34}$ Fürstner and co-workers proposed that reaction of an iron salt with the Grignard reagent forms the active iron alkyl or aryl intermediate which then undergoes reaction with the carbon-halogen bond.35-38 It was also reported that negatively charged iron ate-complexes underwent net twoelectron reactions with aryl halides in a nucleophilic displacement-type reaction (Scheme 1b).³⁸ Related studies with alkyl halides supported a radical pathway en route to the observed products. 39,40

While iron and cobalt complexes bearing redox-active pyridine(diimine) ligands have exhibited a rich catalytic chemistry,^{2,41,42} observation of well-defined oxidative addition reactions is rare. Addition of biphenylene to the iron dinitrogen complex, $(^{iPr}PDI)Fe(N_2)_2$, resulted in oxidative

addition of the C–C bond, forming a metallacycle.⁴³ The addition of aryl or alkyl halides to reduced iron or cobalt complexes often leads to halogen abstraction yielding the corresponding one-electron oxidized metal complex and an organic radical (Scheme 1c).^{20,44–48} An alternative possibility is that the two-electron oxidative addition product forms initially but is unstable toward comproportionation.⁴⁹ While there is some precedent that certain strong field ligands such as CO enable the formal two electron oxidative addition of alkyl iodides to iron,^{50–52} the only successful isolations of an iron aryl halide complex rely on the stabilizing effect of directing groups in the position *ortho* to the halide.^{53,54}

The design of reduced iron complexes capable of twoelectron oxidative addition of aryl and alkyl halides has been a long-standing challenge but, if successful, will likely open new opportunities for iron-catalyzed reactions. As a general strategy, two-electron oxidative addition to first-row transition metals may be favored by introduction of a strong ligand field around the metal center to increase d-orbital splitting and minimize one-electron processes.^{2,3} Pincer ligands with strongly σ -donating phosphines or *N*-heterocyclic carbenes are a privileged ligand class for this task, enabling several ironand cobalt-catalyzed processes that involve two-electron oxidative addition of nonpolar bonds.²

Reduced iron complexes supported by bis(imidazol-2ylidene)pyridine (CNC) ligands, originally synthesized by Danopoulos and co-workers,⁵⁵ have been reported to promote the oxidative addition of C–H,⁵⁶ H–H,⁵⁷ and Si–H⁵⁸ bonds and are among the most active first row transition metal catalysts for the hydrogenation of sterically hindered olefins⁵⁹ and hydrogen isotope exchange reactions with arenes involving C-H activation.^{60,61} The resulting oxidative addition products as well as [(CNC)Fe] dialkyl compounds⁶² are isolable, octahedral, low-spin, S = 0 complexes. Additionally, (CNC)- $Fe(N_2)_2$ derivatives have two labile ligands, potentially enabling facile generation of 14-electron complexes, which are a prerequisite for Pd(0) complexes to engage in concerted oxidative addition of aryl halides.^{63–66} These characteristics make $(CNC)Fe(N_2)_2$ complexes attractive candidates for the study of the oxidative addition of aryl and alkyl halides. Here we describe successful demonstration of the net two-electron oxidative addition of aryl and alkyl halides to a bis-(arylimidazol-2-ylidene)pyridine iron dinitrogen complex and study the mechanism through a combination of competition experiments, radical clock reactions, and stereochemical probes (Scheme 1c).

RESULTS AND DISCUSSION

Our initial studies focused on the oxidative addition of essentially unfunctionalized aryl halides to $(3,5-Me_2^{Mes}CNC)$ -Fe $(N_2)_2$ $(1-(N_2)_2, 3,5-Me_2^{Mes}CNC = 2,6-(2,4,6-Me_3-C_6H_2-imidazolin-2-ylidene)_2-3,5-Me_2-pyridine), a readily synthesized variant of <math>(CNC)$ Fe $(N_2)_2$ complexes⁶² where the 3,5-methyl groups on the central pyridine increase the electron donation of the pincer. Addition of 1 equiv of bromobenzene to a toluene solution of $1-(N_2)_2$ resulted in the precipitation of a diamagnetic red-brown solid, isolated by filtration in 79% yield, identified as the two-electron oxidative addition product $(3,5-Me_2^{Mes}CNC)$ FePh (N_2) Br $(1-Ph(N_2)Br)$ (Scheme 2). In a similar manner, $(3,5-Me_2^{Mes}CNC)$ FePh (N_2) I $(1-Ph(N_2)I)$ was isolated as a brown-red and diamagnetic solid in 59% yield following addition of iodobenzene to $1-(N_2)_2$ was sluggish, and

Scheme 2. Oxidative Addition of Phenyl Halides to $1-(N_2)_2$



although $(3,5-Me_2^{Mes}CNC)FePh(N_2)Cl$ was generated, other unidentified products were detected.

The benzene- d_6 ¹H NMR spectrum of 1-Ph(N₂)Br exhibits four signals for the methyl groups of the CNC-chelate between 1.4 and 2.9 ppm, establishing inequivalent methyl groups on the aryl rings of the pincer and an overall C_s-symmetric iron compound. The signals corresponding to the phenyl group were located between 6.4 and 6.7 ppm while the carbon of the phenyl group directly attached to the iron center appears at 165.5 ppm in the ¹³C NMR spectrum. The carbene carbons of the CNC chelate were located at 219.4 ppm, comparable to other (CNC)Fe complexes.⁶² The ¹H and ¹³C NMR spectra of $1-Ph(N_2)I$ exhibit similar features. The benzene solution IR spectra of $1-Ph(N_2)Br$ and $1-Ph(N_2)I$ display bands at 2139 and 2134 cm⁻¹ respectively, corroborating dinitrogen coordination. While attempts to obtain single crystals of $1-Ph(N_2)Br$ produced poorly diffracting samples, slow diffusion of pentane into a concentrated toluene solution of $1-Ph(N_2)I$ at -35 °C yielded single crystals suitable for X-ray diffraction. The solidstate structure exhibits an idealized octahedral geometry around the iron center with the iodide (Fe–I = 2.7195(5)Å) and phenyl ligand (Fe-C32 = 1.993(4) Å) in a trans arrangement (C32–Fe–I = $179.08(4)^\circ$, Figure 1a). The sixth coordination site trans to the pyridine of the CNC-chelate is occupied by the dinitrogen ligand. The same spatial arrangement of two trans X-type and one L-type ligand has been previously observed with (CNC)Fe dialkyl and dihydride complexes.⁶² The plane of the phenyl ligand is parallel to mesityl substituents on the CNC-ligand, likely minimizing steric interactions.

Zero-field ⁵⁷Fe Mößbauer spectra of 1-Ph(N₂)Br and 1-Ph(N₂)I recorded at 80 K exhibits doublets with isomer shifts of $\delta = 0.16$ mm/s and $\delta = 0.15$ mm/s respectively with quadrupole splittings of $|\Delta E_Q| = 1.77$ mm/s and $|\Delta E_Q| = 1.72$ mm/s, consistent with the observed diamagnetism and lowspin iron(II) complexes (Figure 1b, c).⁶⁷ The weaker ligand field imparted by the halide results only in a slightly higher isomer shift than the value reported for (3,5-Me₂^{Mes}CNC)Fe-(CH₂SiMe₃)₂(N₂) ($\delta = 0.11$ mm/s)⁶² but does not change the overall spin state of the complex. The absence of detectable quantities of (CNC)FeX₂ (X = Br or I)⁶⁸ in the Mößbauer spectra is noteworthy, as these products are typically formed from halogen atom abstraction pathways common with iron.⁴⁸

Given the importance of heteroarenes in cross-coupling reactions,⁹ 2-bromo-6-methylpyridine was added to a toluene solution of $1-(N_2)_2$ and a green solid identified as $(3,5-Me_2^{Mes}CNC)Fe(6-Me pyridin-2-yl)Br (1-(MePy)Br)$ was isolated in 79% yield (Scheme 3). The benzene- $d_6^{-1}H$ NMR spectrum of 1-(MePy)Br is consistent with a C_s symmetric iron compound exhibiting similar features to $1-Ph(N_2)Br$. The



Figure 1. (a) Solid-state molecular structure of $(3,5-Me_2^{Mes}CNC)$ -FePh (N_2) I at 30% probability ellipsoids. Hydrogen atoms and one mesityl group of the CNC-chelate are omitted for clarity. (b and c) Solid-state, zero-field ⁵⁷Fe Mößbauer spectra of $(3,5-Me_2^{Mes}CNC)$ -FePh (N_2) I and $(3,5-Me_2^{Mes}CNC)$ FePh (N_2) Br, respectively at 80 K. Simulated parameters (blue lines) are (b) δ = 0.15 mm/s, $|\Delta E_Q|$ = 1.72 mm/s; (c) δ = 0.16 mm/s, $|\Delta E_Q|$ = 1.77 mm/s.

Scheme 3. Oxidative Addition of 2-Halo-6-methylpyridines to $(3,5-Me_2^{Mes}CNC)Fe(N_2)_2$



signals corresponding to the pyridyl group were assigned to the two doublets at 6.04 and 5.55 ppm (the third resonance is overlapping), with the 6-methyl group located at 1.60 ppm. In contrast to 1-Ph(N₂)Br, no N=N band was observed in the benzene- d_6 infrared spectrum. The zero-field ⁵⁷Fe Mößbauer spectrum of 1-(MePy)Br exhibits a doublet at $\delta = 0.16$ mm/s with a quadrupole splitting of $|\Delta E_Q| = 2.26$ mm/s. Although the quadrupole splitting is slightly higher compared to 1-Ph(N₂)Br and 1-Ph(N₂)I, it remains consistent with an idealized, low-spin iron(II) center, as a potential 5-coordinate compound is expected to have a much higher $|\Delta E_Q|$ value.⁶⁷ The structure of 1-(MePy)Br is therefore assigned in analogy to 1-Ph(N₂)I with the coordination site *trans* to the pyridine of the CNC-chelate occupied by the N atom of the 6-methylpyridin-2-yl ligand. Addition of 2-chloro- and 2-iodo-

6-methylpyridine to benzene- d_6 solutions of $1-(N_2)_2$ generated the corresponding two-electron oxidative addition products $(3,5-Me_2^{Mes}CNC)Fe(6-Me pyridin-2-yl)Cl (1-(MePy)Cl)$ and $(3,5-Me_2^{Mes}CNC)Fe(6-Me pyridin-2-yl)I (1-(MePy)I)$.

To establish the relative reactivity of different aryl halides, competition experiments were conducted: 1 equiv of both bromo- and iodobenzene were added to $1-(N_2)_2$ at ambient temperature. Because the two products, $1-Ph(N_2)Br$ and 1- $Ph(N_2)I$, have different and relatively low solubility in benzene- d_6 and peaks in the respective ¹H NMR spectra are overlapping, NMR spectroscopy was not used for analysis. The relative conversion was determined by GC analysis of the supernatant solution following precipitation of the iron complexes by the addition of pentane. In this manner, a reactivity ratio of $conversion_{PhI}/conversion_{PhBr} = 4/1$ was determined. This reactivity trend of oxidative addition on the dependence of the identity of the halide is the same observed with similar experiments using palladium^{69,70} although oneelectron pathways often show the same trend.¹

Electronic effects were also evaluated for the oxidative addition of C–X bonds with $1-(N_2)_2$. Relatively electron-poor 1-bromo-4-(trifluoromethyl)benzene underwent clean reaction with $1-(N_2)_2$ to yield the two-electron oxidative addition product, $(3,5-Me_2^{Mes}CNC)Fe(C_6H_4CF_3)(N_2)Br$ ($1-(C_6H_4CF_3)(N_2)Br$), as a diamagnetic brown-red solid in 73% yield (Scheme 4). Likewise, $(3,5-Me_2^{Mes}CNC)Fe$ -

Scheme 4. Oxidative Addition of 4-Substituted Aryl Halides to $(3,5-Me,^{Mes}CNC)Fe(N_2)$,



 $(C_6H_4OMe)(N_2)Br$ $(1-(C_6H_4OMe)(N_2)Br)$ was isolated in 67% yield from addition of the more electron-rich 1-bromo-4methoxybenzene to $1-(N_2)_2$. Both complexes exhibit features in the ¹H and ¹³C NMR spectra similar to parent 1-Ph(N₂)Br and were therefore assigned to have the same geometry around the iron center and spin state as $1-Ph(N_2)Br$. Accordingly, the benzene solution infrared spectrum of 1-(C6H4CF3)(N2)Br exhibited a strong N≡N band at 2141 cm⁻¹. The analogous spectrum of $1-(C_6H_4OMe)(N_2)Br$ surprisingly exhibited two $N \equiv N$ bands at 2117 and 2136 cm⁻¹. Because only one iron product was observed by NMR spectroscopy, it is likely that two different conformers or isomers rapidly interconvert on the time scale of the experiment but are resolved by infrared spectroscopy. Given the variance in the stretching frequencies, the two isomers are likely differentiated by the ligand trans to the N₂ ligand.

Having established the tolerance of the iron-promoted oxidative addition with bromobenzene with electron-donating and -withdrawing groups, the relative rates of reaction of electronically differentiated aryl bromides were determined by competition experiments (Figure 2). Treatment of 1 equiv of $1-(N_2)_2$ with 1 equiv of each of the two aryl bromides in



Figure 2. (a) Competition experiments between electronically differentiated aryl halides, (b) relative conversions and rate constants, and (c) Hammett plot showing the effect of aryl halide substitution on rate, modeled with COPASI.

benzene at ambient temperature yielded a mixture of two $(3,5-Me_2^{Mes}CNC)Fe(aryl)(N_2)Br$ complexes that were precipitated by the addition of pentane. The relative conversions of the aryl bromides established by quantitative GC-analysis of the supernatant are reported in Figure 2b. In general, electronpoor aryl bromides reacted faster than the electron-rich, consistent with a buildup of negative charge on the aromatic ring during the transition state for C–X oxidative addition, a trend generally observed for the oxidative addition of aryl halides to group 10 transition metals.^{64,69–74}

Taking the relative conversions as an approximation for the relative rate of reaction, a Hammett plot was generated by correlating log(conversion_R/conversion_H) with the sigma values⁷⁵ of the substituents in the 4-position of the aryl bromide. The linear regression generated from this data produced a slope of $\rho = 1.0$. For a more accurate value for ρ , which is not subject to varying concentrations of the aryl halides during the reaction, the relative conversions were fit against $k_{\rm rel} = k_{\rm R1}/k_{\rm R2}$ using a reaction model assuming two competing second-order reactions which are both first-order dependent on iron and the aryl halide (Figure 2b; see Supporting Information (SI) for details). By employing the so obtained numbers for $k_{\rm rel}$, a ρ value of $\rho = 1.5$ was obtained (Figure 2c), slightly higher than $\rho = 1.0$ derived from the relative conversions.

Relative reaction rates of electronically differentiated aryl halides and the corresponding Hammett plots have been previously used to inform on the mechanism of oxidative addition with palladium and nickel.^{64,72–74} While oxidative addition reactions with small positive ρ values of ρ = ca. 2 are generally considered to proceed through a concerted transition state,^{64,73} more charge buildup on the arene and therefore higher ρ values of ρ = ca. 4 are observed for reactions proceeding by SnAr^{70,74} or SET⁷² mechanisms. While certainly not conclusive, the comparatively small positive ρ value of ρ = 1.5 for the presented oxidative addition to iron indicates a small charge buildup on the aryl ring during the transition state and a more concerted reaction.

Oxidative Addition of Alkyl Halides. The oxidative addition of alkyl halides to $1-(N_2)_2$ was also explored to

establish the generality of the iron-promoted reaction. Treatment of a toluene solution of $1-(N_2)_2$ with methyl iodide resulted in an immediate color change from brown to bright green, and following filtration, a diamagnetic, green solid identified as the corresponding two-electron oxidative addition product $(3,5-Me_2^{Mes}CNC)Fe(Me)(N_2)(I)$ $(1-Me(N_2)I)$ was isolated in 84% yield (Scheme 5). The ¹H NMR spectrum

Scheme 5. Oxidative Addition of Alkyl Iodides to $(3,5-Me_2^{Mes}CNC)Fe(N_2)_2$



exhibits features similar to the aryl halide oxidative addition products, again consistent with a C_s symmetric iron compound. A diagnostic feature in the spectrum was the signal at -1.28 ppm, assigned as the methyl group bound to the iron.

The solid-state structure of $1-Me(N_2)I$ was determined by X-ray diffraction on single crystals obtained from a concentrated toluene solution of $1-Me(N_2)I$ stored at -35 °C (Figure 3a). An idealized octahedral coordination geometry was observed about iron and is analogous to $1-Ph(N_2)I$ with a



Figure 3. (a) Solid-state molecular structure of $(3,5-Me_2^{Mes}CNC)$ -FeMe (N_2) I at 30% probability ellipsoids. Hydrogen atoms and a mesityl group of the CNC-chelate are omitted for clarity. (b and c) Solid-state, zero-field ⁵⁷Fe Mößbauer spectra of $(3,5-Me_2^{Mes}CNC)$ -Fe $(Me)(N_2)$ I and $(3,5-Me_2^{Mes}CNC)$ Fe $(isobutyl)(N_2)$ I respectively at 80 K. Simulated parameters (blue lines) are (b) $\delta = 0.19$ mm/s, $|\Delta E_Q|$ = 1.90 mm/s; (c) $\delta = 0.20$ mm/s, $|\Delta E_Q|$ = 1.96 mm/s.

slightly longer iron–carbon bond to the methyl group (Fe– C32 = 2.237(10) Å). The iodine and methyl ligands are both slightly bent toward the CNC chelate producing a C32–Fe–I angle of 170.0(2)°. IR spectroscopy confirmed N₂ coordination in solution (ν_{N2} (benzene- d_6) = 2127 cm⁻¹), and zero-field ⁵⁷Fe Mößbauer parameters (δ = 0.19 mm/s, $|\Delta E_Q|$ = 1.90 mm/ s, Figure 3b) are consistent with a low-spin, octahedral iron(II) complex.⁶⁷

Analogous reactivity was observed with isobutyl iodide (Scheme 5), resulting in the isolation of a green, diamagnetic solid in 69% yield identified as $(3,5-Me_2^{Mes}CNC)$ Fe(isobutyl)- $(N_2)(I)$ (1-iBu $(N_2)I$) using a combination of NMR, IR (ν_{N2} (benzene- d_6) = 2130 cm⁻¹), and zero-field ⁵⁷Fe Mößbauer ($\delta = 0.20 \text{ mm/s}$, $|\Delta E_Q| = 1.96 \text{ mm/s}$, Figure 3c) spectroscopies. An iron compound with nearly identical features in the ¹H NMR spectrum was detected as the sole organometallic product when isobutyl bromide was used, which was assigned accordingly as $(3,5-Me_2^{Mes}CNC)$ Fe(isobutyl)(N_2)(Br) (1-iBu (N_2) Br). The stability of isolable 1-iBu (N_2) I is noteworthy as the alkyl ligand contains β -hydrogens potentially accessible for elimination. Heating a sample of the compound in benzene- d_6 to 60 °C resulted in generation of isobutylene and a new, diamagnetic iron product (Scheme 6a). A C_s

Scheme 6. β -Hydride Elimination from (3,5-Me₂^{Mes}CNC)Fe(alkyl)(N₂)I Complexes



symmetric iron product was observed by ¹H NMR spectroscopy with a high field signal at -19.54 ppm diagnostic of an iron hydride.³⁹ The iron product, assigned as $(3,5-Me_2^{Mes}CNC)Fe(H)(N_2)(I)$ (1-H(N₂)I), was also generated by exposure of a benzene- d_6 solution of 1-iBu(N₂)I to 1 atm of H₂ with attendant formation of isobutane, and subsequently isolated in 68% yield as a red solid.

Iron alkyl complexes with more sterically accessible hydrogens in the β -position of the alkyl ligand proved kinetically unstable. For example, addition of 1-bromobutane to a benzene- d_6 solution of $1-(N_2)_2$ resulted in a 78:22 ratio of *trans* to *cis*-2-butene, along with a C_s symmetric iron compound with a ¹H NMR signal at -21.71 ppm assigned as $(3,5-Me_2^{Mes}CNC)Fe(H)(N_2)(Br)$ $(1-H(N_2)Br)$ (Scheme 6b). It is likely that this iron product arises from oxidative addition of the alkyl halide to $1-(N_2)_2$ to form the unobserved *n*-butyl iron complex that undergoes rapid β -hydride elimination to produce 1-butene and $(1-H(N_2)Br)$. Subsequent isomerization generates the observed internal olefins. To determine if $(1-H(N_2)Br)$ was competent for the isomerization of 1-butene to *trans*- and *cis*-2-butene, $(1-H(N_2)Br)$ was independently prepared and 5 equiv of 1-butene were added. The same ratio of *trans*- and *cis*-2-butene was observed as judged by ¹H NMR spectroscopy. Addition of 2-bromobutane to a benzene- d_6 solution of $1-(N_2)_2$ also produced $1-H(N_2)Br$ and the same equilibrium mixture of *trans*- and *cis*-2-butene, as judged by analysis of the volatile components by ¹H NMR spectroscopy. This type of reactivity was consistent among secondary alkyl halides as addition of bromocycloxane to a benzene- d_6 solution of $1-(N_2)_2$ yielded $1-H(N_2)Br$ in 86% yield along with cyclohexene, as judged by ¹H NMR spectroscopy.

Treatment of a benzene- d_6 solution of $1-(N_2)_2$ with *tert*butyl bromide resulted in the exclusive formation of $1-iBu(N_2)Br$ by ¹H NMR spectroscopy, through rearrangement of the alkyl ligand (Scheme 7). Similar reactivity was observed previously with iron⁴⁶ and cobalt⁴⁴ complexes arising from a chain walking mechanism by β -hydride elimination and reinsertion⁴⁴ or radical pathways.⁴⁶

Scheme 7. Oxidative Addition of *tert*-Butyl Bromide to $(3,5-Me_2^{Mes}CNC)Fe(N_2)_2$



The observed alkyl rearrangement from the oxidative addition of tert-butyl bromide prompted a more thorough investigation into the nature of the oxidative addition of alkyl halides to $1-(N_2)_2$ and more specifically the presence of alkyl radical intermediates. Accordingly, oxidative addition of an alkyl halide bearing a radical clock was conducted (Scheme 8).⁷⁶ 6-Iodo-1-hexene was selected, as this substrate has been used previously in iron-catalyzed cross-coupling reactions to support the intermediacy of alkyl radicals.^{22,27} Ăddition of 6iodo-1-hexene to a benzene- d_6 solution of $1-(N_2)_2$ resulted in a color change from brown to green, and a green solid identified as the cyclized product (3,5-Me2^{Mes}CNC)Fe(cyclopentylmethyl) $(N_2)(I)$ (1-cylcopentylmethyl $(N_2)I$) was isolated in 78% yield (Scheme 8a). The benzene- d_6 ¹H NMR spectrum of 1-cylcopentylmethyl (N_2) I exhibited analogous features to the product arising from the oxidative addition of iodomethylcyclopentane with $1-(N_2)_2$ under the same conditions. As an additional mechanistic probe, treatment of $1-(N_2)_2$ with (bromomethyl)cyclopropane as a radical clock resulted in formation of a mixture of iron-containing products as judged by ¹H NMR spectroscopy that upon treatment with H₂ and vacuum transfer of volatiles resulted in isolation of *n*-butane as the sole detected organic product. This observation is consistent with intermediate formation of the ring-opened cyclopropyl product.

The observed iron product following reaction of $1-(N_2)_2$ with 6-iodo-1-hexene is consistent with the initial generation of

Scheme 8. Oxidative Addition of an Alkyl Halide Containing a Radical Clock to $(3,5-Me_2^{Mes}CNC)Fe(N_2)_2$



a radical followed by rapid cyclization and capture by the iron complex. An alternative pathway, however, is two-electron oxidative addition followed by insertion to form the C-C bond. To assess the feasibility of this latter pathway, $1-H(N_2)I$ was treated with 1,5-hexadiene in benzene- d_6 at room temperature, resulting in a color change from brown to green. The ¹H NMR spectrum of the iron product following addition is consistent with formation of an olefin insertion product in equilibrium with $1-H(N_2)I$ (Scheme 8b; see SI for details). Formation of 1-cyclopentylmethyl(N_2)I was not observed under these conditions as judged by ¹H NMR spectroscopy. Exposure of this mixture to 1 atm of H₂ resulted in formation of $1-H(N_2)I$ and *n*-hexane as the major organic product without any evidence for methylcyclopentane formation. Therefore, a two-electron oxidative addition of 6iodo-1-hexene to $1-(N_2)_2$ followed by migratory insertion is unlikely to account for the observed cyclized product, and the available data are more consistent with the intermediacy of alkyl radicals.

The stereochemistry of alkyl halide oxidative addition to 1- $(N_2)_2$ was also explored to provide additional mechanistic insights. Deuterated neohexyl halide isotopologues have been applied to determine the stereochemistry of oxidative addition, as the H-H coupling constants are diagnostic for the presence of the two possible diastereomers.⁷⁷ Diastereomerically pure threo-ICHDCHDC(CH₃)₃ was prepared by a modified literature procedure using the hydrozirconation of neohexene- d_2 and subsequent treatment with iodine. The addition of three-ICHDCHDC(CH₃)₃ to a benzene- d_6 solution of 1- $(N_2)_2$ produced an immediate color change to green, and subsequent analysis by ¹H NMR spectroscopy established formation of $(3,5-Me_2^{Mes}CNC)Fe(CHDCHDC(CH_3)_3)(N_2)$ -(I) (1-neohexyl(N₂)I) (Scheme 9). However, the ${}^{3}J_{H-H}$ coupling of the neohexyl group was poorly resolved, likely due to dynamic reversible N2 coordination. To eliminate the dynamic process substitution of the labile N2 ligand with a more substitutionally inert carbonyl group was carried out by addition of 0.1 atm of CO to 1-neohexyl $(N_2)I$. The resulting iron carbonyl complex, $(3,5-Me_2^{Mes}CNC)Fe(CHDCHDC-(CH_3)_3)(CO)(I)$ (**1-neohexyl(CO)I**), exhibited well-resolved Scheme 9. Synthesis of Dideuterated *threo*-Neohexyl Iodide and Oxidative Addition to $(3,5-Me_2^{Mes}CNC)Fe(N_2)_2$



 ${}^{3}J_{\rm HH}$ coupling in the neohexyl group and established formation of a near-equimolar mixture of the *threo* and *erythro* diastereomers. The observed scrambling of stereochemistry supports a radical pathway for oxidative addition and is inconsistent with $S_{\rm N}2$ or concerted pathways.

To further understand reactivity trends, the relative rates of oxidative addition of various alkyl halides with $1-(N_2)_2$ were investigated. We note that measurement of absolute rate constants and determination of overall reaction order have been unsuccessful due to the fast rates of oxidative addition even at cryogenic temperatures. Competition experiments between 1.5 equiv each of isobutyl iodide and neopentyl iodide to $1-(N_2)_2$ resulted in a 4:1 ratio of the corresponding oxidative addition products, $1-iBu(N_2)I$ and (3,5- $Me_2^{Mes}CNC$)Fe(neopentyl)(N₂)(I) (1-Np(N₂)I), supporting a possible steric effect on the rate of oxidative addition. The relative rates of alkyl halide oxidative addition were also sensitive to the identity of the halide. The series of neosilyl halides, $(CH_3)_3SiCH_2X$ (X = I, Br, Cl), all underwent oxidative addition to $1-(N_2)_2$ in benzene- d_6 as judged by ¹H NMR spectroscopy. Related alkyl chlorides, including neopentyl chloride, isobutyl chloride, and hexyl chloride, exhibited no reaction even at elevated temperatures of 60 °C with $1-(N_2)_2$. When $1-(N_2)_2$ was added to an equimolar mixture of neosilyl chloride and neosilyl bromide, only the product arising from oxidative addition of the latter, (3,5-Me2^{Mes}CNC)Fe(neosilyl)- $(N_2)(Br)$, was observed by ¹H NMR spectroscopy. Similarly, when $1-(N_2)_2$ was added to an equimolar mixture of neosilyl bromide and neosilyl iodide, only the product from neosilyl iodide oxidative addition, $(3,5-Me_2^{Mes}CNC)Fe(neosilyl)(N_2)$ -(I), was observed. These results establish the relative rates of alkyl halide oxidative addition as I > Br > Cl.

CONCLUDING REMARKS

In summary, the two-electron oxidative addition of a variety of aryl and alkyl halides to a reduced iron complex, $1-(N_2)_2$, has been demonstrated. Key to this reactivity is introduction of an electron-donating pincer to generate a strong ligand field around the iron favoring two-electron chemistry rather than the atom abstraction pathways typically observed with iron. Aryl iodides and bromides containing electron-donating and -withdrawing functional groups were tolerated in these reactions and generated two-electron oxidized, diamagnetic Fe(II) aryl halide complexes. Linear free energy relationships established minimal charge buildup on the arene in the transition state, supporting a concerted pathway for $C(sp^2)-X$ bond cleavage. Alkyl halides were also activated, again giving rise to the two-electron oxidative addition iron products. If the alkyl ligand contained β -hydrogens, elimination to the corresponding Fe(II) hydride halide complexes was observed.

Despite the similarity in the iron products, radical clocks and deuterium labeling experiments support a radical pathway for $C(sp^3)$ -H oxidative addition and demonstrates that even when alkyl radicals are intermediates, net two-electron chemistry can result. Gaining a detailed understanding of iron-mediated carbon-halogen bond activation adds important fundamental insights for the development of iron catalysts for cross-coupling by more traditional palladium-like pathways.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.1c01486.

General considerations; preparation of transition metal complexes; general procedures; spectroscopic and crystallographic data (PDF)

Accession Codes

CCDC 2061553–2061554 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, UK; fax: +44 1223 336033.

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