

Roles of Iron Complexes in Catalytic Radical Alkene Cross-Coupling: A Computational and Mechanistic Study

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Supporting Information

ABSTRACT: A growing and useful class of alkene coupling reactions involve hydrogen atom transfer (HAT) from a metal-hydride species to an alkene to form a free radical, which is responsible for subsequent bond formation. Here, we use a combination of experimental and computational investigations to map out the mechanistic details of ironcatalyzed reductive alkene cross-coupling, an important representative of the HAT alkene reactions. We are able to explain several observations that were previously mysterious. First, the rate-limiting step in the catalytic cycle is the formation of the reactive Fe-H intermediate, elucidating the



importance of the choice of reductant. Second, the success of the catalytic system is attributable to the exceptionally weak (17 kcal/mol) Fe-H bond, which performs irreversible HAT to alkenes in contrast to previous studies on isolable hydride complexes where this addition was reversible. Third, the organic radical intermediates can reversibly form organometallic species, which helps to protect the free radicals from side reactions. Fourth, the previously accepted quenching of the postcoupling radical through stepwise electron transfer/proton transfer is not as favorable as alternative mechanisms. We find that there are two feasible pathways. One uses concerted proton-coupled electron transfer (PCET) from an iron(II) ethanol complex, which is facilitated because the O-H bond dissociation free energy is lowered by 30 kcal/mol upon metal binding. In an alternative pathway, an O-bound enolate-iron(III) complex undergoes proton shuttling from an iron-bound alcohol. These kinetic, spectroscopic, and computational studies identify key organometallic species and PCET steps that control selectivity and reactivity in metal-catalyzed HAT alkene coupling, and create a firm basis for elucidation of mechanisms in the growing class of HAT alkene cross-coupling reactions.

INTRODUCTION

The alkene functional group is an inexpensive and versatile building block for biologically active molecular structures. However, the chemoselective functionalization of unactivated alkenes to generate highly substituted carbon centers is challenging, because traditional routes based on carbocations often suffer from side reactions.¹ As a milder alternative, chemists have developed a class of transition-metal-catalyzed Markovnikov-selective hydrofunctionalization reactions for forming C-C, C-O, and C-N bonds from unactivated alkenes.^{1b,2} These reactions have excellent functional-group tolerance, predictable regioselectivity, and experimental simplicity.³ The precatalysts are typically simple Mn, Fe, or Co salts of halide, acac, or oxalate, and the reducing equivalents come from borohydrides or silanes.^{2,4}

A general mechanism has been proposed for these reactions (Scheme 1), which features hydrogen atom transfer (HAT) to the alkene from a putative metal-hydride complex, which is generated in situ from a metal salt and a hydride source.^{1b} HAT would generate a reduced metal species and the alkyl radical at the more substituted side of the original alkene.

Scheme 1. General Mechanism Proposed for Catalytic HAT **Alkene Coupling Reactions**



When this radical reacts with a trapping agent, the product is the Markovnikov product with a new C-C, C-N, or C-O bond. In many HAT alkene reactions, such as Co-catalyzed hydrohydrazination, Fe-catalyzed hydroamination, hydromethylation, and alkene coupling, the product of trapping is

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another radical.^{1b} According to the proposed mechanism, this coupled radical undergoes an electron transfer reaction with the metal byproduct, which oxidizes the metal to a form that reacts with borohydride or silane to regenerate the active metal-hydride.

In this report, we focus on one specific HAT alkene reaction, the intermolecular cross-coupling of two alkenes. The catalytic cycle is proposed to follow the general pathway of Scheme 1, with an electron-poor alkene serving as the trap. This reaction was reported by Baran in 2014,⁵ and later publications demonstrated the reaction scope and utility in C–C bond constructions of synthetic relevance for natural products.⁶ This reaction uses $Fe(acac)_3$ as a precatalyst and PhSiH₃ as a reductant, and HAT catalysis was proposed to proceed through the iron(III)/iron(II) cycle shown in Scheme 2. It

Scheme 2. Previously Proposed Mechanism for Iron-Catalyzed Intermolecular Cross-Coupling of Alkenes



was presumed that the hypothetical iron(III) hydride selectively attacks the electron-rich "donor" alkene (blue in Scheme 2), giving an iron(II) species and a nucleophilic alkyl radical. This radical then is trapped by the electron-poor "acceptor" alkene (green in Scheme 2), and the formation of the new C-C bond generates a product with a radical adjacent to the electron-withdrawing group. In the final steps, this radical accepts an electron and a proton to generate product. Lo et al. concluded that this is a stepwise process proceeding through a carbanion for two reasons: (a) The use of EtOD solvent gives deuteration α to the electron-withdrawing group (shown in purple in Scheme 2), even though the ethanol O-H bond $(104 \text{ kcal/mol})^7$ is stronger than the C–H bond that is formed. (b) It was possible to perform a three-component coupling that adds an aldehyde α to the electron-withdrawing group.⁶⁵ Below, we systematically evaluate a number of alternative mechanisms for this proton-coupled electron transfer (PCET) pathway.

So far, this proposed mechanism lacks key tests of its veracity. In the alkene cross-coupling, as in all the catalytic HAT alkene reactions, no organometallic species or radicals have been observed. Detection of the metal-containing species in HAT alkene reactions in general is complicated by the lack of chelating supporting ligands to stabilize the intermediate metal complexes, and by the weak-field nature of halides, acac, and oxalate that render the metal sites high-spin and difficult to observe by ¹H NMR spectroscopy. Broad peaks in ¹H NMR spectra of a cobalt-catalyzed silylperoxidation reaction were tentatively assigned to a metal-bound hydride, but the interpretation of the data is ambiguous.⁸ In the iron-catalyzed HAT alkene cross-coupling, we took first steps toward identifying relevant metal species, by discovering that during catalysis both iron(II) and iron(III) acac complexes gave ¹H NMR resonances that could be assigned by comparison with independently synthesized complexes.^{6b} These measurements were complemented by ⁵⁷Fe Mössbauer spectroscopy studies⁹ that showed that Fe(acac)₂ is the reduced iron species and that [Fe(acac)₂(μ -OEt)]₂ is catalytically competent.^{6b} However, there have been no systematic computational studies showing that the catalytic cycle as proposed in Scheme 2 is energetically feasible or would give the observed selectivity.

Another issue that has been proposed in the context of HAT alkene reactions^{1b,3} is the persistent radical effect (PRE).¹⁰ In the PRE, the life of a reactive radical (normally susceptible to bimolecular self-termination) is extended by its engagement in an equilibrium with a high-concentration trapping species, usually having radical character (the "persistent radical"), thus lowering its concentration and hence the rate of bimolecular termination (Scheme 3). The PRE often leads to cross-

Scheme 3. Persistent	Radical	Effect	in	Organometallic-
Mediated Processes				



selectivity of radical addition reactions,¹¹ and similarly leads to the controlled polymerization of alkenes.^{10b} The PRE can influence metal-catalyzed reactions through reversible trapping of a radical by a reduced metal (M^*) to form a metal–alkyl complex (M^{x+1} –R). If subsequent reactions take place only through the free radical, then the formation of the M–C bond "protects" most of the radical, lowering the concentration of the free radical. This effect has been used for controlling freeradical polymerization reactions by the approach termed organometallic-mediated radical polymerization (OMRP), in which metal–alkyl species are well-documented.¹²

In the alkene cross-coupling reaction, we used NMR and Mössbauer spectroscopies to show that the vast majority of the iron (>95%) is present as reduced $Fe(acac)_2$, which could in principle react with transient alkyl radicals to form an iron(III) alkyl species.^{6b} Though these putative iron(III) alkyls were not observed by Mössbauer spectroscopy, their concentration could be too low to detect. In order to understand and control the HAT alkene reactions, it is important to evaluate the reactivity of such metal species, even when they are not experimentally observed. Here, we describe the results of mechanistic experiments and DFT computations that increase our understanding of several key steps in the HAT alkene cross-coupling by iron-acac catalysts. They illuminate unanticipated mechanistic features that are likely to be applicable to the broader class of HAT alkene reactions with Mn, Fe, and Co. Therefore, the results are likely to be useful for analysis and improvement of related reactions such as hydropyridylation (Minisci reaction), hydroamination, hydroazidation, hydrohydrazination, hydrocyanation, hydration, and hydrogenation.^{1b}

RESULTS

Formation of the Reactive Hydride Species. In an earlier paper^{6b} some of us developed a new catalyst, $[(acac)_2 Fe(\mu-OEt)]_2$, which is much more active than the Fe(acac)₃ precatalyst. Its higher activity was attributed to the ability of the ethoxide to react directly with silanes to give an iron hydride. It was interesting that the rate of the catalytic reaction depended on the hydride donor used: it was faster when using the monoalkoxysilane PhSi(OEt)H₂, but slower using PhSiH₃ or PhSi(OEt)₂H. Obradors and Shenvi have described an analogous rate increase using PhSi(OiPr)H₂. However, it was not clear whether this silane is a more active hydride donor or whether the monoalkoxysilane somehow modifies the iron catalyst. To resolve this question, we performed the catalytic reaction with equal amounts of PhSiD₃ and PhSi(OEt)H₂. Product analysis by mass spectrometry showed that this reaction gave less than 5% deuteration of the product (Scheme 4 and Figure S25), which contrasts with the





complete deuteration observed when $PhSiD_3$ is used as the sole silane.¹⁴ This result demonstrates that the monoalkoxysilane more rapidly generates the reactive hydride that ends up in the product.

The reaction trajectory for hydride transfer with a slightly truncated model system $[(acac)_2Fe(\mu-OMe)]_2$ was explored using density-functional theory (DFT) calculations with the BPW91* functional, which has been shown to be suitable for variable spin states for 3d transition metals.¹⁵ The geometries were optimized in the gas phase, and then the electronic energies were corrected for thermal (PV) and entropy (TS) effects at 298 K, dispersion forces, solvation in ethanol, and solution standard state (see Computational Details in the Supporting Information), to give standard-state free energies.

First, we resolved the electronic structure of the iron(III) alkoxide starting material. We considered all possible spin states for iron(III) (S = 1/2, 3/2, and 5/2, which are conventionally termed low-, intermediate-, and high-spin, respectively). Details are in the Supporting Information (section 2.A). The calculations show that the dimeric starting material is most stable as an open-shell singlet ($S_{\text{total}} = 0$), from antiferromagnetically coupled ions with local spins $S_{\text{Fe}} = 5/2$. The $S_{\text{total}} = 5$ state lies only 0.3 kcal/mol higher, consistent with the weak antiferromagnetic coupling observed experimentally.¹⁶ Splitting into monomeric [Fe^{III}(acac)₂(OMe)] is feasible, since the two high spin monomer molecules are only 6.5 kcal/mol higher in energy than the dimer.

For the hydride product, we also considered both monomeric and dimeric structures, since hydrides are often found to be bridging in iron compounds.¹⁷ In this case, the three monomeric spin isomers are calculated to be more stable than the corresponding dimers (Supporting Information section 2.B). The optimized structure of monomeric [Fe^{III}(acac)₂H] is spin-state-dependent. The low-spin state has a square pyramidal geometry at iron with the strong transinfluence hydride in the axial position, while the intermediate-

and high-spin states have trigonal bipyramidal iron with the hydride in the axial and equatorial positions, respectively. All three spin states have energies within 1.2 kcal/mol of one another. Dimeric species $[(acac)_2Fe^{III}(\mu-H)]_2$, in each spin state and with parallel or antiparallel spins on the two sites, were found to be higher in energy than the corresponding monomers by at least 5 kcal/mol. At catalytic concentrations of iron that are much lower than the standard state of 1 M, the dimer would be even more unfavorable. We also considered the potential for solvent ethanol to coordinate to a monomeric iron(III) hydride complex. However, the calculations show that binding of ethanol is weak: the octahedral EtOH adducts are not lower in energy in either the doublet or quartet state (Supporting Information section 2.C).

With the alkoxide and the hydride complexes modeled, we compared the thermodynamics and kinetics for hydride transfer from Si to Fe (details in Supporting Information section 2.D). The reaction of monomeric $[Fe^{III}(acac)_2(OMe)]$ (S = 5/2) with PhSiH₃ to form the aforementioned $[Fe^{III}(acac)_2H]$ (S = 3/2) along with PhSi(OMe)H₂ is uphill by 5.4 kcal/mol. Adding the energy of splitting the alkoxide dimer, the hydride product lies a total of 8.6 kcal/mol above the starting materials. The transition state for H transfer from PhSiH₃ to Fe (**TS1**) on the sextet PES lies 24.9 kcal/mol above the starting materials (see Figure 1) in free energy. The



Figure 1. Relative free energies of the starting materials $(1/2[Fe^{III}(OMe)(acac)_2]_2 + PhSiH_3)$, of the corresponding monomeric $[Fe^{III}(OMe)(acac)_2]$ intermediate, and the reaction coordinate over TS1 to give $[Fe^{III}H(acac)_2]$ and PhSi(OMe)H₂.

corresponding TS along the quartet PES lies at a higher ΔG value (34.4 kcal/mol, see Supporting Information section 2.D). In light of the small barriers for other steps (see below), this alkoxide/hydride exchange is predicted to be the turnover-limiting step in the catalytic cycle. We measured the initial rate for the catalytic reaction at 40 °C to be $6.5 \pm 0.7 \times 10^{-5}$ M/s, which leads to an estimate of the experimental ΔG^{\ddagger} as 22.8 \pm 0.2 kcal/mol. Thus, the computed barrier of 24.9 kcal/mol is similar to that observed experimentally.

The calculated trajectory of this step is interesting (Figure 2). First, the iron-bound alkoxide approaches the Si atom



Figure 2. Partially optimized structures (at fixed Si \cdots O distances) of three representative points along the reaction pathway of precatalyst activation by PhSiH₃.

opposite from the phenyl group (pseudotrigonal bipyramidal with the incoming O considered as a bond). Then, the geometry at silicon undergoes a Berry pseudorotation to yield, at the transition state, a geometry close to an ideal square pyramid with a Si-H bond placed axially and then eventually forms a new trigonal bipyramidal geometry with the transferring H atom and another H atom in the pseudoaxial positions and the Ph and OMe substituents together with the third H atom in the pseudoequatorial plane. From here, there is simultaneous transfer of hydride to Fe and OMe to Si to smoothly yield the products.

The nature of this transition state helps to explain the greater activity when moving from PhSiH₃ to PhSi(OR)- H_2 .^{6b,13} The calculations, carried out with R = Me for simplicity, reveal a greater driving force for the alkoxysilane, as hydride transfer from the monoalkoxysilane is 4.1 kcal/mol less endergonic (Supporting Information section 2.E).¹⁸ This driving force comes from the greater hydridicity of the H atom (calculated Mulliken charges on the H atoms are -0.087 in PhSiH₃, -0.118 in PhSi(OMe)H₂ and -0.153 in PhSi- $(OMe)_2H$). The geometry of TS1 shows that one additional alkoxide group may be accommodated in the axial position of the square pyramidal geometry of the TS. Indeed, reoptimization of TS1 after replacement of one silane H atom with OMe gave a transition state corresponding to a barrier that is 3.6 kcal/mol lower in energy, which compares reasonably well to the $\Delta\Delta G^{\ddagger}$ = 1.4 kcal/mol derived from the competition experiment in Scheme 4.¹⁴ However, use of the dialkoxysilane PhSi(OR)₂H as hydride donor, even though presumably leading to a thermodynamically even more favorable transformation, would place an additional OR group in an equatorial position of the square pyramid where it would be destabilized by a steric clash with the other equatorial substituents. In this way, the computational investigation of the hydride transfer to the Fe atom elucidates the empirically observed silane trends. In light of this result, it seems likely that appropriate silanes can be designed in the future to accomplish faster hydride transfer for catalytic reactions.

Hydrogen Atom Transfer from Fe–H to Alkene. In the HAT alkene reactions, a key step is the transfer of a hydrogen atom from a metal-hydride complex to an alkene;^{1b} therefore, we sought ways to experimentally probe this step for the intermolecular alkene cross-coupling. Thus, we studied the HAT alkene cross-coupling of TBS-protected 3-methylbut-3en-1-ol with benzyl acrylate under the conditions of Lo et al., using Fe^{III}(acac)₃ as the precatalyst (Scheme 5).^{6a} In this

Scheme 5. Deuterium Transfer to Product Indicates that HAT Is Not Reversible



reaction, the metal-bound hydrogen in the putative hydride is derived from phenylsilane; thus, its fate can be probed by using PhSiD₃ in place of PhSiH₃. ¹H and ¹³C NMR analysis of the product (Figures S1 and S2) show that the cross-coupled product has regiospecific D incorporation (Scheme 5), which agrees with previous work.^{6a} In addition, it is important to consider whether the H atom transfer is reversible, because M-H additions from isolated hydride species to alkenes were shown to be reversible by Halpern, Bullock, and Norton.¹⁹ Since the radical generated from the M-D compound would be singly deuterated, reversible HAT would lead to partially deuterated alkene starting material at low conversion. Therefore, a catalytic reaction run under normal conditions was stopped at 3 min (30% conversion), and analysis by NMR spectroscopy and mass spectrometry (Figures S1-S5) showed that no D was incorporated into the remaining starting material. Therefore, the initial hydrogen atom addition to the alkene is irreversible, which agrees with our qualitative rationale for the normal isotope effect previously observed upon substitution of PhSiD₃ for PhSiH₃.

The pathway for HAT from the transient iron(III) hydride to the donor alkene was evaluated by DFT using isobutene as model H atom acceptor (Figure 3; see details in Supporting



Figure 3. HAT pathway for ground-state $[Fe^{II}H(acac)_2]$ reaction with isobutene to give $[Fe^{II}(acac)_2]$ and *tert*-butyl radical.

Information section 2.F). This reaction yields a *tert*-butyl radical and $[Fe^{II}(acac)_2]$, which was treated as the experimentally known quintet ground state. Hence, the reaction can take place on a single potential energy surface (PES), i.e., is spin-allowed, starting from either the intermediate-spin (S = 2 - 1/2 = 3/2) or high-spin (S = 2 + 1/2 = 5/2) hydride complex, whereas the HAT from the low-spin system would be spin-forbidden. The barrier for the spin-allowed reaction along the quartet surface is extremely low: we were able to optimize a transition state (**TS2**) that lies only 4.7 kcal/mol higher in free energy, making this step extremely rapid. A rate constant of $2.2 \times 10^9 \text{ s}^{-1} \text{ M}^{-1}$ can be calculated from the Eyring equation, though one should note that the geometry optimization uses the electronic energy; therefore, the saddle point on the free energy surface might be

slightly different. In any case, this finding supports our conclusion above that HAT to the alkene is unlikely to be the turnover-limiting step as proposed earlier.^{6b} HAT from Fe to the alkene was calculated to be exergonic by 26 kcal/mol, which agrees with the experimental finding that HAT occurs irreversibly under the cross-coupling conditions.

The iron product from HAT, $[Fe^{II}(acac)_2]$, is known to form weak adducts with monodentate donor molecules, including EtOH.²⁰ Indeed, trans- $[Fe^{II}(acac)_2(EtOH)_2]$ has been isolated and crystallographically characterized.^{6b} We measured the variation of the chemical shift of the ¹H NMR resonance for [Fe^{II}(acac)₂] in benzene as a function of [EtOH], and the curve (Figure S20) yielded an association constant of $3.2 \pm 0.2 \text{ M}^{-1}$ at 80 °C, corresponding to ΔG° = -0.8 ± 0.1 kcal/mol. However, in this weak-binding regime, the stoichiometry is not evident from the binding curve. DFT calculations on the EtOH coordination process (Supporting Information section 2.G) gave a ΔG of +1.3 kcal/mol for formation of $[Fe^{II}(acac)_2(EtOH)]$ and -0.6 kcal/mol for $[Fe^{II}(acac)_2(EtOH)_2]$. The excellent agreement validates the DFT calculations and explains why a single binding curve was observed (the second EtOH molecule binds more tightly than the first).

These energetics suggest that the speciation of $[Fe^{II}(acac)_2]$ in pure EtOH solvent (17 M) at 298 K is ca. 99% 6-coordinate *trans*- $[Fe^{II}(acac)_2(EtOH)_2]$ and 1% 4-coordinate $[Fe^{II}(acac)_2]$, with only trace amounts of 5-coordinate $[Fe^{II}(acac)_2(EtOH)]$. Hence, both the unsolvated $[Fe^{II}(acac)_2]$ and the alcohol complex *trans*- $[Fe^{II}(acac)_2(EtOH)_2]$ are readily accessible reactive species for the ethanolic reactions to be explored in the remainder of this study.

Behavior of the Initial Alkyl Radical. The product of HAT to the alkene is an alkyl radical. Though this alkyl radical may add to the acceptor alkene directly, our experience with OMRP and the previous suggestions of assistance by the persistent radical effect³ encouraged us to evaluate the possibility of its reversible binding to $[Fe^{II}(acac)_2]$, which would give an alkyliron(III) complex (eq 1).

$$[Fe^{II}(acac)_2] + R^{\bullet} \rightleftharpoons [Fe^{III}(acac)_2R]$$
⁽¹⁾

We calculate that the formation of the quartet state of the iron(III) *tert*-butyl complex is exergonic by 1.5 kcal/mol (Figure 4 and Supporting Information section 2.H), whereas the low- and high-spin states are found at higher energy. For this reason, the formation of the iron(III) alkyl complex can serve to decrease the concentration of the radical in solution. Thus, our computations indicate the potential for a weak



Figure 4. Reaction coordinates of two *tert*-butyl radical reactions: (left) trapping by $[Fe^{II}(acac)_2]$; (right) addition to methyl acrylate.

persistent radical effect that "protects" the intermediate alkyl radical from bimolecular radical coupling.

The cross-selectivity of the alkene cross-coupling reaction arises because the nucleophilic alkyl radical (in the computations, modeled as a *tert*-butyl radical) reacts most rapidly with electron-poor alkenes. The relative rates for reaction of such radicals with alkenes are well-known in the literature.²¹ In this specific case, a radical is expected to react more than 10³ times more rapidly with an acrylate ester than with a simple alkene.²² According to our calculations, the addition of tert-butyl radical to methyl acrylate has a barrier (TS3) of only 8.4 kcal/mol, and has a favorable $\Delta G = -15$ kcal/mol (Figure 4 and Supporting Information section 2.I) as expected for the formation of a stabilized radical. Therefore, this C-C bond forming reaction is also expected to be irreversible. Because the acrylate radical is more stable, it is expected to form a weaker bond to the iron atom. This proposition was explored using the simpler propionate radical $CH_3CH^{\bullet}(COOMe)$ as a model for the produced radical. The formation of an Fe-C bond between this radical and iron(II) to give [Fe^{III}(acac)₂-(CHMeCOOMe)] in the preferred quartet state is calculated to be endergonic by 0.6 kcal/mol (Supporting Information section 2.J). The O-bound isomer was calculated to be 4 kcal/mol higher in energy than the Cbound isomer. Therefore, the acrylate radical should not benefit from the persistent radical effect at catalytic concentrations of iron. Additional calculations of the Fe-C bond strength in [Fe^{III}(acac)₂(CHMeCOOMe)] were also conducted with other functionals to validate our computational method (see Supporting Information section K).

Trapping of the Acrylate Radical through the Previously Proposed Stepwise ET/PT Mechanism. The acrylate radical, which derives from the attack of the initial alkyl radical on the acceptor alkene, is a key species in the catalytic cycle. Its conversion into the product requires one proton and one electron. The regioselectivity of deuterium transfer from EtOD to the product^{6a} indicates that the proton derives from ethanol. In the previously proposed mechanism for the cross-coupling reactions, the trapping takes place through a two-step mechanism: initial electron transfer from the iron(II) species to the acrylate radical to yield an acrylate anion, which accepts proton transfer from ethanol to generate the product and the iron(III) ethoxide (this stepwise mechanism "ET/PT" is shown as (a) in Scheme 6). We tested this idea using both computations and experiments.

Since mechanism (a) is initiated by electron transfer (ET) from iron(II) to the acrylate radical, we tested its feasibility by determining the thermodynamics of ET from iron(II) to the acrylate radical. Cyclic voltammetry of [Fe^{II}(acac)₂] in ethanol (the solvent used in the catalytic reaction) showed an irreversible oxidation wave at moderate scan rates (\leq 500 mV/s), with the cathodic peak current being much smaller than the anodic peak current (Figure 5, black trace). We attribute the irreversibility to the limited stability of $[Fe^{III}(acac)_2]^+$ in solution. The instability of related ironacetylacetonate species has been reported previously,²³ and we have observed that oxidation of $[Fe^{II}(acac)_2]$ in air gives $[Fe^{III}(acac)_3]^{6b}$ with ligand redistribution.^{20c} Fortunately, increasing the scan rate to 2 V/s improved chemical reversibility $(i_{pc} \sim i_{pa})$, enabling the calculation of a half-wave potential $(E_{1/2})$ of -0.48 V vs Fc^{+/0} (Figure 5, blue trace). DFT calculations (SI, section 2.L) predicted this potential to be -0.42 V, which supports this value (and

Scheme 6. Mechanisms for Quenching the Product Radical





Figure 5. Cyclic voltammetry of $[Fe^{II}(acac)_2]$ (3 mM) in EtOH with NBu₄BF₄ (0.1 M) as supporting electrolyte, showing the Fe^{III/II} redox couple at -0.48 V. The greater reversibility at faster scan rate suggests that the iron(III) species is unstable.

provides another successful validation of the computational protocol).

$$trans-[FeII(acac)_{2}(EtOH)_{2}] + MeCH^{\bullet}(COOMe)$$

$$\rightarrow trans-[FeIII(acac)_{2}(EtOH)_{2}]^{+} + MeCH(COOMe)^{-}$$
(2)
$$E_{total} = E_{enolate radical/anion} - E_{Fe(III)/Fe(II)}$$

Judging the thermodynamics of ET requires one to compare
this value to the potential for the acrylate radical/anion couple
The redox potential of
$$CH(CH_3)CO_2CH_3^{\bullet/-}$$
, a close relative
of the product radical, has been measured to be -1.04 V vs
 $Fc^{+/0}$ in acetonitrile.²⁴ With the caveat that this literature value
is in a different solvent, this analysis suggests that ET from
iron(II) to the radical is unfavorable, with *E* of roughly -0.56
V (uphill by 13 kcal/mol). Our DFT calculations predict that
it is even more uphill (35.0 kcal/mol) in ethanol (Supporting
Information section 2.L). Thus, ET would be expected to
introduce a substantial barrier to the ET/PT two-step
mechanism that potentially keeps it from being kinetically
competent.

Concerted Proton-Coupled Electron Transfer. In mechanism (b) of Scheme 6, we consider the hypothesis that there could be inner-sphere electron transfer from iron to the radical during proton transfer from ethanol. This process has been termed concerted proton–electron transfer (CPET), which is a subset of PCET reactions that are concerted.²⁵ In these concerted PCET reactions, the proton and the electron are transferred in a single elementary step, with a barrier that is lower than that for either proton transfer or electron transfer.²⁶ This situation is termed multisite concerted PCET, ^{25b} because the proton and electron come from different locations. We

examined this concerted PCET process in a truncated substrate using DFT calculations (Figure 6 and Supporting Information section 2.M). Approach of the model propionate radical CH₃CH[•](COOMe) to iron(II) compound trans- $[Fe^{II}(acac)_2(EtOH)_2]$ gave transfer of the proton and electron to yield acrylate and the iron(III) compound trans- $[Fe^{III}(acac)_2(OEt)(EtOH)]$, through transition state TS4 lying only $\Delta G_{PCET}^{\ddagger} = 9.4$ kcal/mol above the energy of the starting materials. This low barrier corresponds to a very rapid rate at room temperature and importantly is lower than the barrier for the ET/PT mechanism above. In the concerted PCET transition state (TS4), the O-H distance is 1.14 Å, much longer than 0.97 Å in the starting material, and the incipient C---H bond distance is 1.456 Å. The long distances, as well as the low spin density (-0.021 vs 0.000 in the starting)complex) and Mulliken charge (+0.38 e^- , identical to that in the starting Fe^{II} complex) on the transferring proton are characteristic of a synchronous proton-electron transfer.²



Figure 6. Reaction coordinate for concerted PCET from $[Fe^{II}(acac)_2(EtOH)_2]$ to $CH_3CH^{\bullet}(COOMe)$.

In addition to the productive concerted PCET described above, we also used DFT to evaluate concerted PCET from $[Fe(acac)_2(EtOH)_2]$ to the *tert*-butyl radical, which models a side reaction that would give the net hydrogenation of the donor alkene without C-C bond formation. The calculated transition state energy is 7.3 kcal/mol, which is slightly lower than that for the productive concerted PCET (9.4 kcal/mol). However, the rate law for the side reaction is $k_{\text{PCET},t\text{Bu}}[t\text{Bu}^{\bullet}]^{-1}$ $[(acac)_2 Fe^{II}(EtOH)_2]$, while the rate law for the C-C coupling is $k_{CC}[tBu^{\bullet}]$ [alkene]. Since the concentration of the trapping alkene is much higher than the Fe concentration, the rate of the reaction with the alkene would be similar despite the lower rate constant. Using the Eyring equation, we calculate a rate constant for the CPET side reaction of 3×10^7 M^{-1} s⁻¹ at 298 K for a rate law $k_{PCET,tBu}[tBu^{\bullet}]^{-1}$ $[(acac)_2 Fe^{II}(EtOH)_2]$. The rate constant for the C–C bond formation, in contrast, would be $4 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ for a rate law $k_{\rm CC}[tBu^{\bullet}]$ [alkene]. Importantly, this model predicts that the C-C coupling of tert-butyl radical to acceptor alkene should become less favorable as the reaction progresses due to the decrease in the relative concentration of trapping alkene. Monitoring the product distribution in the standard coupling reaction at 60 $^{\circ}C$ indicates that indeed the reduction of donor alkene is a competing side reaction and occurs only later in the reaction as the acceptor olefin is consumed (Figure S21). This explains why the reaction yield for cross-coupling is often enhanced by using superstoichiometric amounts of the acceptor alkene,6b because then the concentration of acceptor alkene does not drop precipitously in the later part of the reaction.

A second question concerns why the acrylate product radical undergoes concerted PCET rather than continuing to add to further acrylate substrate. In this case, we must compare $k_{\text{PCET,R}} [\mathbb{R}^{\bullet}] [\text{Fe}^{\text{II}}] \text{ and } k_{\text{p}} [\mathbb{R}^{\bullet}] [\text{alkene}], \text{ where } \mathbb{R}^{\bullet} \text{ is the acrylate}$ radical and k_p is the propagation rate constant of the acrylate monomer polymerization. The calculations for the CH₃CH[•](COOMe) model predict $\Delta G^{\ddagger}_{PCET,R}$ of 9.4 kcal/ mol (see above), while the calculation of the model product radical addition to methyl acrylate predicts a barrier ΔG^{\ddagger}_{p} = 10.9 kcal/mol (Supporting Information section 2.N). Due to the skewed relative concentrations, the calculated rates are again close, and in agreement, Lo et al. observed side products from multiple additions of acceptor alkene.^{6b} Clearly, there is a delicate balance between the concerted PCET and alkene addition rates, and the success of the catalytic cross-coupling rests on the tuning of these two processes for the two different radicals.

Kinetic Isotope Effects. If PCET to the acrylate radical (either concerted or stepwise with slow PT) were turnoverlimiting, then there would be a kinetic isotope effect between reactions in EtOH versus EtOD. The kinetic isotope effect for the overall catalysis was measured by comparing separate standard catalytic reactions in EtOH and EtOD (Scheme 7, top). The initial rates at 40 °C were $6.5 \pm 0.7 \times 10^{-5}$ M/s and $6.2 \pm 1.2 \times 10^{-5}$ M/s, respectively; thus, there is no kinetic isotope effect. This suggests that PCET is not the turnoverlimiting step in the cycle. We also used a competition experiment in order to isolate the KIE of the step involving transfer of the H from ethanol (which we call the product isotope effect "PIE"). Performing the catalytic reaction in a 1:1 mixture of EtOH and EtOD (Scheme 7, bottom) gave a product with $21 \pm 1\%$ D incorporation, which indicates a PIE of 3.8 \pm 0.1. The difference in the KIE and PIE values²⁸ indicates that the PCET step is not turnover-limiting, but rather lies after the turnover-limiting step. This is consistent with a low-energy transition state for transfer of H to the propionate radical.

Protonation of Iron-Bound Intermediates. In addition, we considered mechanism (c), in which the product radical





forms a bond to iron(II) to give an intermediate that is susceptible to protonation. As noted above, a putative alkyliron(III) intermediate lies at higher energy than the free radical + iron(II), but it could be a kinetically competent intermediate if the subsequent protonation occurs with a low barrier. For the sake of computational efficiency, in addition of keeping propionate as a model alkyl, MeOH was used as model alcohol in these calculations (Supporting Information section 2.O). Relaxed PES scans, for both quartet and sextet spin states and considering up to two MeOH molecules, identified reasonable pathways leading from this alkyl complex to products. Protonation of the C-bound enolate (Supporting Information section 2.P) required a transition state with an electronic energy more than 20 kcal/mol higher than CH₃CH[•](COOMe), MeOH, and [Fe^{II}(acac)₂] or led to Fe-C homolysis and subsequent concerted PCET through a transition state indistinguishable from that in mechanism (b). Therefore, we rule out this mechanistic possibility.

In contrast, the higher-energy *O*-bound enolate (Supporting Information section 2.Q) revealed feasible pathways (Scheme 8). A first possibility consists of the direct proton transfer to the enolate C atom, generating the product as shown as (c1). This was calculated to be difficult, with the optimized TS lying at nearly 20 kcal/mol above $[Fe^{II}(acac)_2]$, MeOH, and CH₃CH[•](COOMe). The high activation barrier is attributed

Scheme 8. Variants of Mechanism (c) Intramolecular Proton Transfer to O-Bound Ester Enolate



to the unfavorable hybridization change of the C atom from sp^2 to sp^3 , with loss of the enolate π delocalization. Direct proton transfer to the enolate O atom, leading to the ester enol tautomer of the desired product, is expected to be unfavorable because it requires a strained 4-membered ring, as shown in (c2) in Scheme 8.

However, the computed activation barriers drop dramatically by including an additional methanol (mechanism (c3) in Scheme 8) as a "proton shuttle" as shown for other systems.²⁹ Despite the assistance from additional alcohol molecules, the product of protonation lies 11.0 kcal/mol above $[Fe^{II}(acac)_2]$, MeOH and CH₃CH[•](COOMe). The pathway would then be completed by the exergonic ester enol tautomerization. So, the protonation pathway requires an intermediate that is slightly higher in energy than the PCET barrier (see Supporting Information section 2.Q), but it is close enough for consideration.

Experimentally Testing Concerted versus Stepwise PCET to a Model Alkyl Radical. In order to experimentally test the conditions under which the putative active species can achieve multisite concerted PCET or stepwise PCET to an alkyl radical, we used azobis(isobutyronitrile) (AIBN) as a source of the cyanoisopropyl radical. Transfer of a proton and an electron would lead to isobutyronitrile $(Me_2C(CN)-H)$, by forming a new C-H bond of 92 kcal/mol.³⁰ In control experiments without $[Fe^{II}(acac)_2]$, heating AIBN with 20 equiv of EtOH at 80 °C in acetonitrile yields undetectable amount of Me₂C(CN)-H by ¹H NMR spectroscopy, and the main product is the radical homocoupling product (Me₂C(CN)- $C(CN)Me_2$ (Figure S15). In contrast, the same reaction with 2 equiv of $[Fe^{II}(acac)_2]$ per AIBN (one per radical) gave an 86 \pm 3% yield of Me₂C(CN)-H. and substituting ethanol-OD and ethanol- d_6 result in Me₂C(CN)-D with 88 ± 2% and 89 ± 2% deuterium incorporation (quantified by ¹H NMR, Figures S12-S14). Thus, the combination of $Fe(acac)_2$ and EtOH indeed generates a competent system for PCET.

In order to distinguish whether it is a coordinated acid that performs PCET, we repeated these experiments with $Et_3NH^+BF_4^-$, where the acid cannot coordinate to Fe. Importantly, the triethylammonium cation is a stronger acid than ethanol (K_a is more than 10¹⁰ higher).³¹ Addition of Et₃NH⁺BF₄⁻ to a heated acetonitrile solution of AIBN as a control experiment gives only 1% of Me₂C(CN)-H (Figure S22). Repeating this experiment with 1 and 20 equiv of $Fe(acac)_2$ gave $25 \pm 2\%$ and $54 \pm 5\%$ yield of $Me_2C(CN)$ -H, respectively. These yields are lower than the ones observed with ethanol, indicating that there is a pathway in ethanol that requires coordination: we attribute this to concerted PCET from $[Fe(acac)_2(EtOH)_2]$. However, PCET is still observed when using the Et₃NH⁺ salt, which indicates that there is a second pathway: we attribute this to a stepwise PCET pathway. In the present case, this second pathway cannot correspond to one of the mechanism (c) variants, because the proton donor cannot coordinate the metal center. However, there may be an intermolecular variant consisting of proton transfer from outer sphere Et₃NH⁺ to the C- or N-bound Fe^{III} cyanoisopropyl complex. An intermolecular proton transfer from outer sphere Et₃NH⁺ to an cyanopropyl radical that is Nbound to copper(I) has been documented recently using a similar strategy.³²

DISCUSSION

Hydride Species in HAT Alkene Reactions. A number of stoichiometric hydrogenation and cyclization reactions are mediated by isolable transition metal hydride species. The seminal observation of chemically induced dynamic nuclear polarization (CIDNP) and an inverse kinetic isotope effect from the reduction of styrene with HMn(CO)₅ established hydrogen atom transfer (HAT) from a metal hydride to an alkene and indicated that HAT is reversible.^{19a} Further observation of inverse isotope effects from 2-cyclopropylpropene reacting with HCr(CO)₃Cp and the observation of CIDNP from HFe(CO)₂Cp in diene hydrogenation demonstrated reversible hydrogen atom transfer from first row transition metal hydrides to alkenes.^{19b,33} Two characteristics of these literature reactions of isolable hydride complexes were as follows: (1) HAT was reversible. (2) HAT was the ratelimiting step. This is presumably related to the fact that these reactions use stable hydride complexes with relatively high metal-hydrogen bond energies. For example, the metalhydride BDE values of HCr(CO)₃Cp, HMn(CO)₅, cis-HMn(CO)₄PPh₃, and HFe(CO)₂Cp have been reported to be 62, 68, 69, and 68 kcal/mol, respectively.^{19b,34}

Our studies indicate that the unobserved iron(III) hydride species that are involved in room-temperature catalytic alkene coupling have amazingly weak M-H bonds that are quite different than the previously studied systems. The DFT calculated gas-phase bond dissociation enthalpy of (acac)₂Fe^{III}-H at 298 K from the quartet ground state is only 17.3 kcal/mol (Supporting Information section 2.R). As a result of this very weak M-H bond, hydrogen atom addition from the hydride complex to the alkene is irreversible, which contrasts with the reversible hydrogen atom additions in the above systems with M-H bond energies greater than 60 kcal/ mol.^{19a-c} This difference in reversibility was previously proposed on the basis of kinetic isotope effect studies^{6b} and is supported here by isotopic labeling experiments that rule out reversibility and by computational studies that show the hydrogen atom transfer (HAT in Scheme 9) to be thermodynamically favorable by more than 25 kcal/mol in

Scheme 9. Mechanism for Iron-Catalyzed Intermolecular Cross-Coupling of Alkenes, Supported by Experiments and Computations



DOI: 10.1021/jacs.9b02117 J. Am. Chem. Soc. XXXX, XXX, XXX–XXX free energy. The barrier for this exergonic HAT is much lower than the barriers for the previously studied reversible systems with isolable hydrides, as expected from the Hammond principle. This low barrier explains the rapid rate of the ironcatalyzed cross-coupling reaction despite the undetectably low concentration of the transient hydride species during catalysis.

The observation that the choice of silane and iron alkoxide drastically influence the catalytic reaction rate, combined with the agreement between calculated and observed barries of 22-24 kcal/mol, indicate that the turnover determining transition state (TDTS in Scheme 9) is the generation of the key acacsupported iron(III) hydride complex. Its steady-state concentration would be too small for spectroscopic detection (see calculation in Supporting Information section 2.S). Because the transient Fe-H species has not been possible to observe, we used DFT to computationally define the most likely geometry, energy, and reactivity. The computations indicate that the mononuclear hydride is lower in energy than multimetallic hydrides and is highly reactive. As noted by a reviewer, a sufficiently reactive polynuclear hydride is a conceivable intermediate, but bridging hydrides typically have lower reactivity than terminal hydrides.³⁵ Interestingly, all three possible spin states of the mononuclear hydride complex have very similar energies and geometries, which suggests that crossover from one state to the other may be facile. We have suggested that electronic flexibility of this type may facilitate catalytic reactions, by providing multiple opportunities for low barriers.³⁶

The low barrier for this hydride addition conflicts with our earlier conclusion that this is the turnover-limiting step in the catalytic cycle.^{6b} Other data also conflict with this idea: here we show that the overall catalytic reaction rate depends on the choice of silane and the presence of ethoxide, implicating the transfer of hydride from the silane to iron as the turnover-limiting step. This concords with the high-energy hydride species and is supported by calculations which indicate that the exchange of hydride and ethoxide has a relatively high activation barrier.

Proton-Coupled Electron Transfer (PCET) from an Iron(II)-Ethanol Complex. There are a variety of different HAT alkene reactions, but despite the different products, all involve HAT from a metal hydride that should result in formation of a metal center in which the formal oxidation state is reduced by one.^{1b} In order to reoxidize the metal, it is natural that chemists have postulated electron transfer from the reduced metal to the radical.^{1b} However, alkyl radicals are weak oxidizing agents.³⁷ Therefore, we explored the feasibility of several potential pathways.

Earlier work on the HAT alkene cross-coupling reaction proposed that electron transfer (ET) is followed by a separate proton transfer (PT) step. However, in the Fe^{III/II} case studied here, the iron(II) species has too little reducing power to accomplish the proposed ET step. Of course, the ET step does not need to be favorable to be part of the catalytic cycle: if the barrier is small, then an uphill reaction can be followed by a more exergonic step that consumes the high-energy intermediate. However, the reorganization energy of the ester radical to anion was determined to be 26 kcal/mol,²⁴ which would add a substantial kinetic barrier to the unfavorable thermodynamics of the proposed electron transfer reaction. The experimentally determined overall barrier from our experiments on the catalytic reaction described in Scheme 5 at 40 °C is 22.8 ± 0.2 kcal/mol. These results suggest that the proposed ET step in the ET/PT mechanism (mechanism (a)) may not be kinetically competent and that other mechanisms should be considered, in which ET and PT are concerted or involve binding of substrates.³⁸

Here, we use "PCET" as a general term for movement of proton and electron between reagents, "HAT" to indicate movement of proton and electron from the same site (e.g., transfer from the iron(III)-hydride to the donor alkene), and "concerted PCET" to indicate the concerted transfer of proton and electron from different sites (e.g., transfer of the electron from iron(II) and the proton from coordinated alcohol in the quenching of the product radical).^{25b} PCET has long been discussed in reactions that oxidize organic compounds, particularly in bioinorganic chemistry,^{26,39} but the involvement of concerted PCET in organic reduction reactions has been studied more recently.⁴⁰ Initial attention in the synthetic community came from the realization that coordination to a metal can lower the BDFE of the O-H bond, enabling the use of abundant H[•] sources like water and alcohols in place of traditional H[•] sources like tin hydrides. Cárdenas, Cuerva, Flowers, and Mayer have shown that H₂O complexes of titanium(III) and samarium(II) are particularly effective H[•] donors due to their strong reducing ability and formation of strong M–O bonds, and computations indicate that the proton and electron transfer to the radical are concerted.⁴¹ Chirik and others have expanded this concept to include N-H bonds as reductants.⁴² However, we are not aware of previous studies where concerted PCET from metal-alcohol complexes has been linked to catalytic HAT alkene cross-coupling reactions.

In the HAT alkene cross-coupling reactions studied here, the incorporation of deuterium from EtOD shows that the alcoholic OH proton is the source of the new C-H bond $(92^{43} \text{ or } 90 \text{ kcal/mol for the model H-CH(Me)(COOMe)})$ system according to our DFT calculations (Supporting Information section 2.P2). This new bond is much weaker than the O-H bond in ethanol (104 kcal/mol).^{6a,b} However, our computations indicate that coordination of the ethanol to $Fe^{II}(acac)_2$ lowers the O–H bond dissociation free energy from 104 to 74 kcal/mol (see Supporting Information section 2.P3). We experimentally confirmed the PCET ability of the iron(II) ethanol complex by showing that it reacts with the cyanoisopropyl radical formed by AIBN, forming a C-H bond that is 92 kcal/mol.³⁰ Therefore, the predominant iron(II) during the catalytic HAT alkene cross-coupling reaction binds EtOH, enabling the alcohol to become a competent PCET reductant. We calculate a low-lying transition state for a synchronous multisite PCET. The normal kinetic isotope effect of 3.8 for this step (from competition experiments that target this step of the mechanism) is consistent with concerted PCET.

Mayer has noted that two-step PT/ET or ET/PT sequences tend to occur when there are similar acidities for the two sites or similar redox potentials for the two sites, respectively.^{25b} Here, the coordinated ethanol is expected to be much more acidic than the ester product, and the Fe^{III/II} potential is substantially more positive than that of the ester-based radical/ anion couple, consistent with the preference for concerted PCET. Similar considerations have been made by Cárdenas and Cuerva for Ti^{III}-water complexes, leading to the conclusion that proton and electron transfers are concerted.^{41a,c} We speculate that other HAT alkene reactions catalyzed by different metals may similarly use concerted PCET as a "shortcut" that avoids unfavorable ET in a range of HAT alkene reactions. For example, formal hydroamination by nitro compounds,^{4k} hydrohydrazidation of alkenes,^{4a-c} coupling of diazoalkanes to alkenes,⁴⁴ and radical cyclization of alkenes and ketones⁴⁵ all involve postulated ET/PT sequences that might be concerted instead, and thus these mechanisms deserve study in this context. However, related HAT additions to quinone methides would give a radical that is much easier to reduce, and therefore a stepwise ET/PT mechanism could be more likely.⁴⁶

Consideration of Fe(III) Alkyl and Enolate Intermediates. The formation of bonds between metals and radicals is well-established in related OMRP reactions. For example, the 4-coordinate diaminebis(phenolate)iron(II) system, which is isoelectronic with Fe(acac)2, reversibly traps polystyrene and poly(methyl methacrylate) chains and controls polymer growth by an OMRP mechanism.47 In the case studied here, there is weak binding of the initial alkyl radical to iron(II), which lowers its concentration and prevents extensive homocoupling. In contrast, the acrylate radical (formed after reaction with the alkene) is more stable and forms an accordingly weaker bond to iron(II). Our calculations indicate that the BDFE of the iron(III)-acrylate radical adduct is negative; therefore, this radical is not protected through the PRE and could be preferentially quenched through concerted PCET from $[Fe^{II}(acac)_2(EtOH)_2]$. Thus, the differential metal-carbon bond strength in the transient organometallic complex potentially represents another control strategy for HAT alkene reactions.

Though the iron(III) complex that comes from iron(II) and the acrylate product radical has a very low concentration, it is susceptible to protonation by the alcohol present, but only as the O-bound enolate. This iron(III) adduct with the radical proceeds to product with very low barriers using a protonshuttle pathway, though it has a relatively high barrier mandated by the high energy of the enol tautomer of this ester. Our experimental comparison of coordinating (EtOH) and noncoordinating (Et₃NH⁺) acids is most consistent with the idea that both the protonation of the enolate and the concerted PCET can occur, and this is compatible with the similar calculated barriers for these two pathways.

Our results also help to analyze the selectivity of the catalytic reaction and how it avoids undesired pathways. For example, the product acrylate radical could add to a second acceptor alkene to give polymerized products. The two likely pathways to quench the product radical presented in this work (concerted PCET and intermolecular protonolysis of Obound enolate complex) are in competition with the polymerization process. Therefore, understanding the factors governing the rate of the product radical quenching step will be a key to outcompete the undesired side reaction in the ironcatalyzed alkene cross-coupling reaction. Future studies will explore a range of alcohols that could provide higher selectivity and yield.

CONCLUSIONS

Though HAT alkene reactions are typically viewed as free radical reactions in which the metal's main role is radical generation, our experimental and computational studies on the iron-catalyzed alkene cross-coupling demonstrate the intimate involvement of iron species throughout the catalytic cycle. These function not only to donate H^{\bullet} from an iron-hydride complex but also to form Fe–C bonds that decrease the

concentration of free radicals as well as Fe–O bonds that make alcohols into good H^{\bullet} donors.

Our results show many of the characteristics of the metal center that are required during catalysis, which should be useful for rational design of catalysts. One is the high reactivity of the metal-hydride species, which gives rapid and irreversible transfer of a hydrogen atom to the donor alkene. The use of weak-field ligands in the acac-iron system gives a very weak Fe^{III}-H bond that transfers H[•] rapidly to the alkene, and the lack of reversibility prevents chain transfer or β -hydride elimination. Second, our calculations and experiments have showed that there are concurrent multiple low-energy pathways for quenching the radical with alcohol and iron(II). The large normal PIE is consistent with concerted PCET from an iron(II)-alcohol complex and is also consistent with iron binding of the radical to iron(II) to form an O-bound enolateiron(III) complex that has formally transferred an electron to the radical. In the latter case, subsequent irreversible protonation yields the product.

We show that the iron(III) hydride is important, but after it loses H[•], the iron(II) product is also influential. It is a reducing agent but not in the traditional sense. It gives an alcohol complex that is an excellent H[•] donor through PCET. Alternatively, it can bind radicals to form a variety of species including an iron(III)-enolate complex which can be protonated to release the product. The alcohol, which was previously viewed as merely the proton source for the intermediate enolate, is now also implicated as a central player in key mechanistic steps.

We highlight the new insights into the mechanism above in Scheme 9, which we propose as a more accurate picture of the mechanism for alkene cross-coupling by Fe-acac catalysts. These insights into the energetics of various mechanistic steps may be applicable to various HAT alkene coupling reactions such as hydropyridylation, hydroamination, hydroazidation, hydrohydrazination, hydrocyanation, hydration, and hydrogenation that were recently reviewed^{1b} and therefore provide motivation and methods for mechanistic work on other HAT alkene reactions.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.9b02117.

Experimental, spectroscopic, and computational details (PDF)

Crystallographic information file for $[Fe(acac)_2(\mu-OEt)]_2$ (CIF)

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Notes

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