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Connecting Organometallic Ni(III) and Ni(IV): Reactions of Carbon-Centered Radicals with High-Valent Organonickel Complexes

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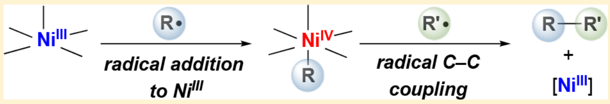
Supporting Information



ABSTRACT: This paper describes the one-electron interconversions of isolable Ni^{III} and Ni^{IV} complexes through their reactions with carbon-centered radicals (R•). First, model Ni^{III} complexes are shown to react with alkyl and aryl radicals to afford Ni^{IV} products. Preliminary mechanistic studies implicate a pathway involving direct addition of a carbon-centered radical to the Ni^{III} center. This is directly analogous to the known reactivity of Ni^{II} complexes with R•, a step that is commonly implicated in catalysis. Second, a Ni^{IV}−CH$_3$ complex is shown to react with aryl and alkyl radicals to afford C−C bonds via a proposed S$_H$2-type mechanism. This pathway is leveraged to enable challenging H$_3$C−CF$_3$ bond formation under mild conditions. Overall, these investigations suggest that Ni$^{II/III/IV}$ sequences may be viable redox pathways in high-oxidation-state nickel catalysis.

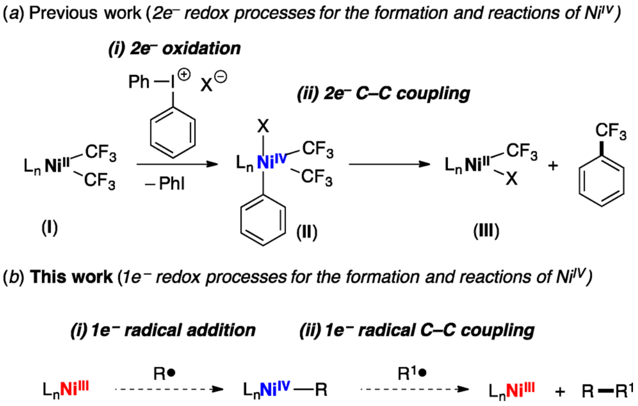
INTRODUCTION

Nickel-catalyzed cross-coupling reactions have emerged as powerful synthetic methods for the mild and selective construction of carbon−carbon and carbon−heteroatom bonds.[1] The vast majority of these transformations are proposed to involve organometallic Ni^{II} and/or Ni^{III} intermediates.[1b−f,2] Higher oxidation state Ni^{IV} species were historically believed to be inaccessible in these types of catalytic transformations.[1,2] However, recent studies have shown that organonickel(IV) complexes can be formed at or below room temperature using common oxidants.[3] As such, there is increasing interest in understanding the generation and reactivity of such Ni^{IV} complexes in order to interrogate their potential role(s) in catalysis.[4]

To date, studies of organometallic Ni^{IV} complexes have largely focused on two-electron redox processes that form and/or consume these species.[3] As one example, our group has demonstrated that the net two-electron oxidative addition of diaryliodonium salts to Ni^{II} complex **I** affords Ni^{IV} intermediates of general structure **II** (Scheme 1a, i).[3d] Furthermore, **II** was shown to undergo two-electron C−C bond-forming reductive elimination to afford PhCF$_3$ and Ni^{II} product **III** (Scheme 1a, ii). However, a hallmark of nickel catalysis is the accessibility of one-electron redox events, particularly those involving carbon-centered radicals.[1b−f,2] For instance, one of the most common elementary steps in Ni-catalyzed cross-coupling reactions involves the formation of a Ni^{III}−alkyl intermediate via the addition of a carbon-centered radical to a Ni^{II} center.[1c,2] Thus, an important outstanding question for the field is whether Ni^{IV} intermediates can be formed and/or consumed via analogous single-electron reactions with carbon-centered radicals.

As shown in Scheme 1b, we identified two such reactions for investigation: (i) the addition of carbon-centered radicals to Ni^{III} intermediates to form Ni^{IV} products and (ii) the reaction of organometallic Ni^{IV} complexes with carbon-centered radicals to afford C−C coupling products. Herein, we demonstrate the feasibility of both of these transformations using tris(pyrazolyl)-borate-ligated Ni model complexes in combination with thermally generated carbon-centered radicals. Furthermore, we show that the latter pathway enables challenging carbon−carbon coupling reactions that are not feasible via conventional two-electron inner-sphere C−C bond-forming reductive elimination pathways at Ni.

Scheme 1. (a) Previous Work, Two-Electron Redox Processes to Form/Consume Organometallic Ni^{IV} Complexes; (b) This Work, One-Electron Redox Processes Involving Carbon-Centered Radicals That Form/Consume Organometallic Ni^{IV} Complexes



RESULTS AND DISCUSSION

Accessing Ni^{IV} via Carbon-Centered Radical Addition to Ni^{III} Complexes. Recent reports have shown that organometallic Ni^{IV} complexes can be prepared via the net two-electron oxidation of Ni^{II} precursors with oxidants including diary-

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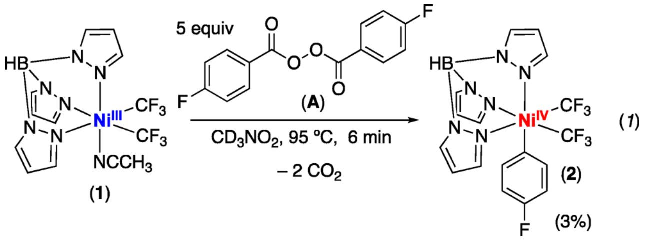
liodonium salts, aryl diazonium salts, and CF_3^+, O^+, Cl^+, and F^+ reagents (for example, Scheme 1a, i).[3,5] These transformations have close analogies to sequences that form high-valent palladium and platinum species.[6] In contrast, the generation of Ni^{IV} intermediates via the reaction of Ni^{III} precursors with carbon-centered radicals has not been demonstrated. This is of particular interest because both Ni^{III} complexes and carbon-centered radicals are common intermediates in Ni-catalyzed cross-coupling. Hence, this pathway, if feasible, could potentially be leveraged in catalytic transformations.

To probe the feasibility of this transformation, we chose the Ni^{III} complex $TpNi^{III}(CF_3)_2(MeCN)$ (**1**, eq 1) as a model system because our previous work has shown that it is stable and isolable from the 1e$^-$ oxidation of $[TpNi^{II}(CF_3)_2]^-$ with $AgBF_4$.[7,8] Additionally, the relevant Ni^{IV} product $TpNi^{IV}(CF_3)_2(Ph)$ (a close analogue of **2**, eq 1) has been independently formed from the reaction of $[TpNi^{II}(CF_3)_2]^-$ with diaryliodonium salts.[3d] We targeted a method for generating carbon-centered radicals that is compatible with both the organometallic Ni^{III} starting material and the organometallic Ni^{IV} product. The most common carbon-centered radical-forming reactions involve thermolysis, photolysis, reduction, or oxidation of an appropriate precursor.[9] However, high-valent Ni complexes like **1** and **2** generally decompose rapidly at high temperatures, as well as in the presence of light and/or reductants.[3d,5] On the basis of these considerations, we selected diacyl peroxides $[(RCOO)_2]$ as the radical source. These reagents are known to generate carbon-centered radicals under relatively mild conditions (heating at ≤95 °C),[10] without the requirement for light or reductants.[11]



We first studied the reaction of **1** with bis(4-fluorobenzoyl)peroxide (**A**), which has a $t_{1/2}$ of ∼1 h at 90 °C (eq 1).[10] Heating the reaction mixture for 15 min at 95 °C resulted in the complete consumption of **1**[12] along with the formation of **2** in a maximum yield of ∼3% (after 6 min). This result suggests the feasibility of the proposed radical addition reaction. However, attempts to improve the yield of **2** by changing the temperature, concentration, or solvent were unsuccessful. A control reaction showed that **1** is unstable at 95 °C, even in the absence of peroxide. Heating at 95 °C for 15 min resulted in complete consumption of **1** and the formation of a mixture of products including Tp_2Ni^{II} and HCF_3. This suggests that the low yield of **2** is at least partially due to the instability of the Ni^{III} starting material.

Vicic has reported that Ni^{III} complexes bearing a perfluoronickelocyclopentane ligand are significantly more stable than their trifluoromethyl analogues.[13] As such, we next targeted the analogous reaction of **3**. Complex **3** was synthesized via the reaction of $[TpNi^{II}(C_4F_8)]^-$ with 1 equiv of $AgBF_4$ and was isolated in 57% yield after purification by chromatography on silica gel (Figure 1A). In contrast to **1**, elemental analysis and X-ray crystallography indicate that this is a five-coordinate Ni^{III} complex. This is further confirmed by EPR spectroscopic

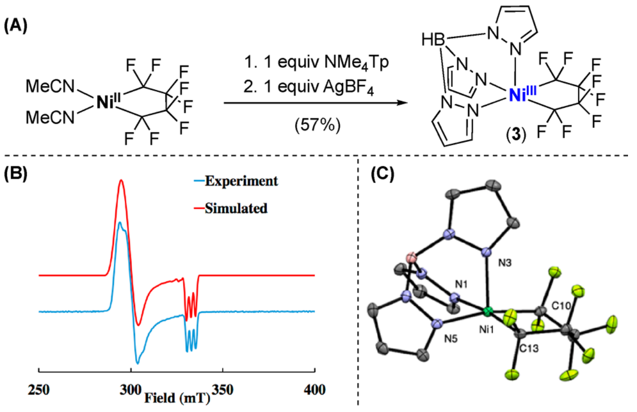
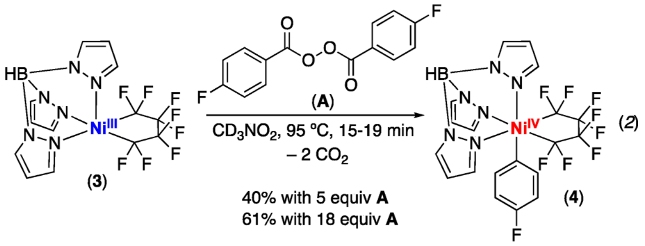


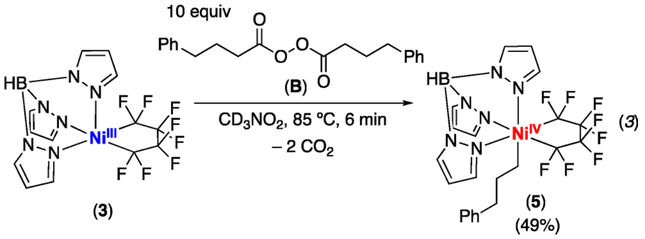
Figure 1. (a) Synthesis of complex **3**. (b) Experimental (blue) and simulated (red) EPR spectra of **3**. $G_x = 2.28$; $G_y = 2.22$; $G_z = 2.01$; $A_N = 22$ G. (c) X-ray crystal structure of **3**. Selected bond lengths (Å): Ni1−N3, 2.0314(14); Ni1−N1, 1.9917(14); Ni1−N5, 1.9692(14); Ni1−C13, 1.976; Ni1−C13, 1.9420(17). Thermal ellipsoids are drawn at 50% probability.

analysis (at 100 K in a toluene glass), which shows hyperfine coupling to a single nitrogen.

As predicted, **3** exhibits significantly enhanced thermal stability relative to **1**. Minimal decomposition was observed upon heating a CD_3NO_2 solution of **3** for 15 min at 95 °C.[14] This suggests that complex **3** should be more compatible with the thermolytic conditions required for R• generation from **A**. Indeed, the treatment of **3** with 18 equiv of **A** at 95 °C for 19 min produced $TpNi(C_4F_8)(4\text{-F-}C_6H_4)$ (**4**) in 61% yield, as determined by ^{19}F NMR spectroscopy (eq 2).[15] Product **4** was purified by column chromatography on silica gel and was isolated in 31% yield as a light orange solid. This octahedral Ni^{IV} complex was characterized by X-ray crystallography (Figure 2a), elemental analysis, and ^1H, ^{19}F, and ^{13}C NMR spectroscopy.



We also examined the reaction of **3** with bis(4-phenylbutyryl)peroxide (**B**).[16] The treatment of **3** with 10 equiv of **B** for 6 min at 85 °C afforded the Ni^{IV} alkyl product **5** in 49% yield, as determined by ^{19}F NMR spectroscopy (eq 3).[17] Product **5** was isolated in 17% yield after purification by column chromatography on silica gel, and it was characterized via ^1H, ^{11}B, ^{13}C, and ^{19}F NMR spectroscopy as well as by X-ray crystallography (Figure 2b).[18]



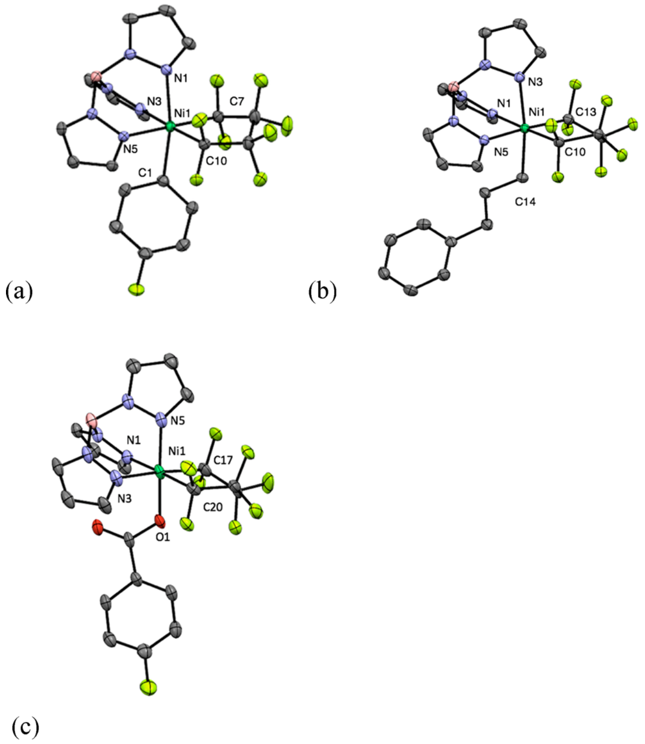
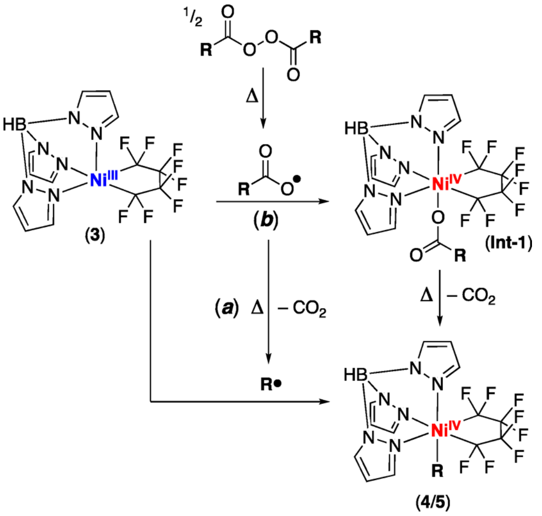


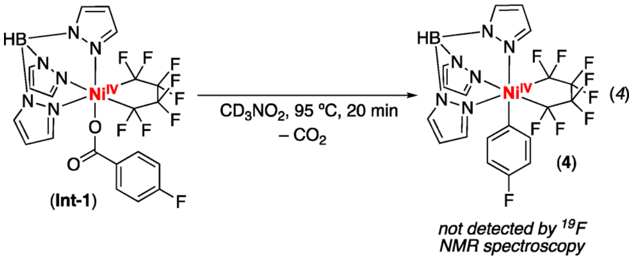
Figure 2. (a) X-ray crystal structure of **4**. Selected bond lengths (A) and angles of **4**: Ni1−N1, 2.089(2); Ni1−N3, 1.980(2); Ni1−C1, 2.031(2); Ni1−C10, 1.978(2); Ni1−C7, 1.967(2); N1−Ni1−C1, 169.31(9)°. (b) X-ray crystal structure of **5**. Selected bond lengths (Å) and angles of **5**: Ni1−N3, 2.1033(13); Ni1−N1, 1.9966(13); Ni1−N5, 1.990(2); Ni1−C13, 1.9787(15); Ni1−C10, 1.9860(16); Ni1−C14, 2.0581(15); N3−Ni1−C14, 171.76(6)°. Thermal ellipsoids are drawn at 50% probability, and hydrogen atoms are omitted for clarity. (c) X-ray crystal structure of **Int-1**. Selected bond lengths (Å) and angles of **Int-1**: Ni1−N5, 1.945(4); Ni1−Ni3, 2.012(4); Ni1−N1, 2.006(4); Ni1−O, 1.862(3); Ni1−C20, 1.999(8); Ni1−C17, 2.010(8); N5−Ni1−O1, 178.02(14)°. Thermal ellipsoids are drawn at 50% probability, and hydrogen atoms and disorder are omitted for clarity.

We envision at least two possible pathways for the conversion of **3** to **4**/**5**. The first involves the decarboxylative formation of R• and subsequent addition of this aryl/alkyl radical to **3** (Scheme 2, *a*). The second involves the addition of initially generated RCO_2• to **3** to form **Int-1** and subsequent decarboxylation at this Ni^{IV} carboxylate to form **4**/**5** (Scheme 2, *b*). To interrogate this latter possibility, we independently synthesized the Ni^{IV} carboxylate complex **Int-1** (with R = *p*-FC_6H_4).[19] **Int-1** was characterized by ^1H and ^{19}F NMR spectroscopy (where it exhibits resonances that are clearly distinct from those of **4**) as well as by X-ray crystallography (Figure 2c).

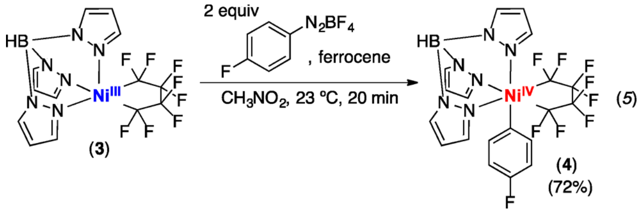
With characterization data for **Int-1** in hand, we reexamined the reaction between **3** and **A**. The crude ^{19}F NMR spectrum of this transformation shows that **Int-1** is formed in approximately 9% yield after 5 min, after which point it rapidly decays. However, this experiment does not establish whether **Int-1** is an intermediate or just a side product formed during this transformation. To distinguish these possibilities, a CD_3NO_2 solution of **Int-1** was heated at 95 °C for 20 min (the conditions for the reaction between **3** and **A** to form **4**). This resulted in 67% conversion of **Int-1** to a mixture of products (predominantly 4-fluorobenzoic acid in 55% yield, as determined by ^{19}F NMR spectroscopy).[20] However, no trace of **4** was detected under these conditions (eq 4). This strongly suggests that pathway b is not operating in this system.

Scheme 2. Possible Pathways for Conversion of 3 to 4/5





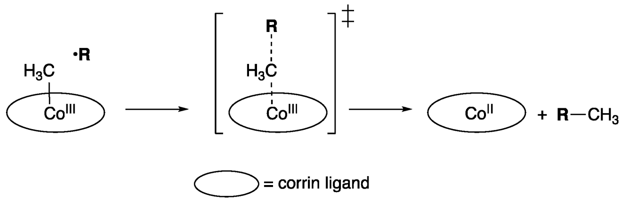
If pathway a were operating, then analogous reactivity would be expected using a different source of R•. The combination of aryl diazonium salts and ferrocene is well-known as an alternative route to aryl radicals.[21] As such, we next explored the reaction of Ni^{III} complex **3** with 2 equiv of 4-fluorophenyldiazonium tetrafluoroborate in the presence of 2 equiv of ferrocene (eq 5). Notably, complex **3** does not react with 4-fluorophenyldiazonium tetrafluoroborate over the course of an hour at room temperature. However, upon the addition of ferrocene, Ni^{IV}-aryl product **4** was formed in 72% yield after just 20 min.[22]



To rule out nonradical pathways, we also conducted radical scavenger experiments using the oxidatively stable radical trap β-nitrostyrene.[23] We initially confirmed that this reagent does not react with **3** over the time scale of the experiments. When the reaction of **3** with peroxide **A** was performed in the presence of β-nitrostyrene (1 equiv relative to **A**), the yield of **4** dropped dramatically, from 61 to 19%. Similar results were observed using peroxide **B**, with the yield of **5** decreasing from 49 to 14%. This is consistent with the formation (and competitive trapping) of alkyl radicals in the conversion of **3** to **4**/**5**. Collectively, the experiments outlined above are most consistent with pathway a in Scheme 2, involving thermal O–O bond scission, decarboxylation to form R•, and finally capture of R• at **3** to generate Ni^{IV} product **4** or **5**.

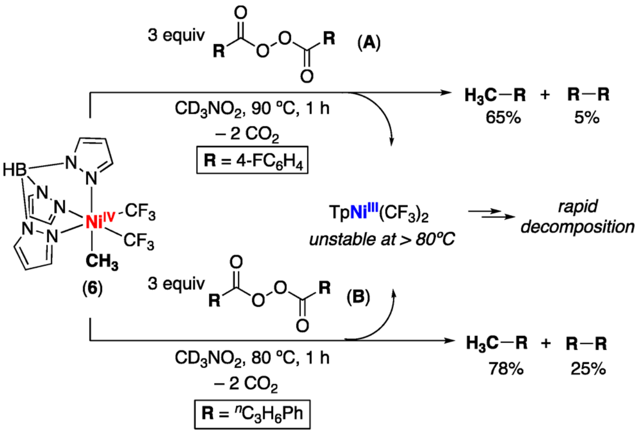
One-Electron Carbon–Carbon Coupling Reactions at Ni^{IV}. We next sought to evaluate the reactivity of Ni^{IV}–alkyl complexes with carbon-centered radicals to generate C–C bonds. Such pathways have precedent in the context of alkyl–Co^{III} systems[24,25] but seldom are considered in high-valent Ni catalysis.[4] In particular, methyl–Co^{III} corrinoid cofactors are well-known to react with exogeneous R• to afford R–CH_3 via an S_H2-type pathway (Scheme 3).[24]

Scheme 3. Reaction of Co^{III}–CH_3 Adducts with R• to Form R–CH_3



To initially probe the viability of this transformation at Ni^{IV}, we evaluated the reactivity of several different Ni^{IV}–alkyl complexes with R• (generated from the thermolysis of **A** or **B**). These studies revealed that the Ni^{IV}–CH_3 complex **6** exhibits the best balance between reactivity with R•, thermal stability, and synthetic accessibility (Scheme 4). Notably, this is similar to the Co systems, in which the methyl variants are typically thermally stable yet highly reactive with carbon-centered radicals.[24] As such, complex **6** was selected as the model system for more detailed studies.[26]

Scheme 4. Reaction of Carbon-Centered Radicals with 6 (Yields Based on 6 as the Limiting Reagent)

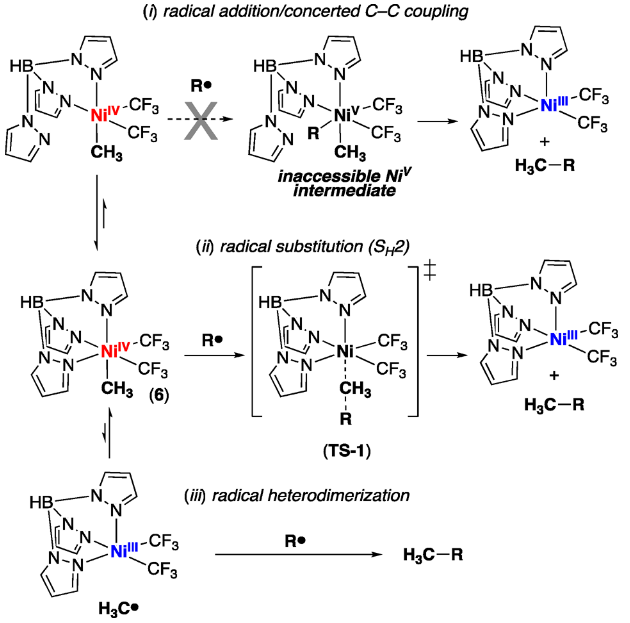


Heating a solution of **6** with 3 equiv of peroxide **A** at 90 °C for 1 h resulted in the formation of 4-fluorotoluene in 65% yield along with 5% of 4,4′-difluorobiphenyl, as determined by ^{19}F NMR spectroscopic analysis (Scheme 4).[27,28] Notably, 44% of **A** (or ~1.3 equiv relative to **6**) was consumed in this reaction. Similarly, the reaction of **6** with 3 equiv of **B** at 80 °C for 1 h afforded *n*-butyl benzene in 78% yield, as determined by ^{1}H NMR spectroscopy. Notably, 67% of **B** (or ~2 equiv relative to **6**) was consumed in this reaction. In this case, the radical homocoupling product 1,6-diphenylhexane was also detected in 25% yield (Scheme 4). However, neither methane nor ethane was observed in either reaction.

The Ni product of the reaction between **6** and R• is expected to be $TpNi^{III}(CF_3)_2$. However, $TpNi^{III}(CF_3)_2$ is unstable at temperatures ≥80 °C. As such, the reactions with **A** (conducted at 90 °C) and **B** (conducted at 80 °C) afforded complex mixtures of Ni byproducts that proved challenging to characterize.[29] Analysis of these crude mixtures by ^{11}B NMR spectroscopy revealed the presence of Tp_2Ni.[30]

Scheme 5 shows three pathways that could account for the formation of R–CH_3 in this reaction.[31] The first (Scheme 5, i) involves preequilibrium dissociation of an arm of the Tp ligand followed by radical addition and subsequent concerted inner-sphere C–C coupling. Notably, this radical addition/concerted reductive elimination sequence is frequently proposed in reactions of carbon-centered radicals with lower oxidation state coordinatively unsaturated Ni centers.[1c,2] However, it is highly unlikely in the current system, because it requires the formation of a nickel intermediate with a formal +5 oxidation state. The second pathway (Scheme 5, ii) involves outer-sphere radical coupling via a radical substitution (S_H2) pathway.[32] Here, R• reacts directly with the methyl ligand via a transition state of general structure **TS-1**. This pathway is analogous to that proposed for the reaction of methyl–Co^{III} corrinoid cofactors with R• (Scheme 3). Finally, this transformation could proceed via the heterodimerization of R• and methyl radicals formed through spontaneous Ni^{IV}–CH_3 homolysis (Scheme 5, iii).

Scheme 5. Potential Mechanisms for C–C Coupling Reactions between 6 and R•



The product distribution of these reactions provides initial evidence against the homolysis/radical heterodimerization pathway (mechanism *iii*). Unstabilized carbon-centered radicals are known to dimerize with low selectivity and at near diffusion-limited rates.[33] However, the reaction of **6** with **A** and **B** forms the cross-coupled product H_3C–R in much higher yield (65 and 78%, respectively) than R–R or H_3C–CH_3 (5 and 25% yield, respectively).[34,35]

To further interrogate the viability of mechanism *iii*, we monitored the thermolysis of **6** in the presence of 5 equiv of the

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radical scavenger β-nitrostyrene. If mechanism *iii* were operating, any free $H_3C\bullet$ that is generated should be rapidly captured by β-nitrostyrene, resulting in fast decomposition of **6**. In contrast, in the event of mechanism *ii*, **6** should be stable in the presence of this reagent. As shown in Figure 3, heating a solution of **6** in the presence of β-nitrostyrene had minimal impact on the decay of **6**. In marked contrast, the addition of **A** or **B** resulted in rapid loss of **6** (with concomitant formation of the respective C−C coupled product). Collectively, the experiments outlined above are most consistent with mechanism *ii*.

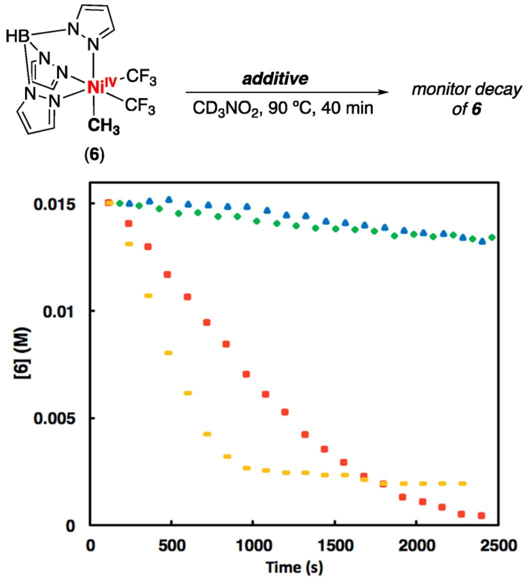


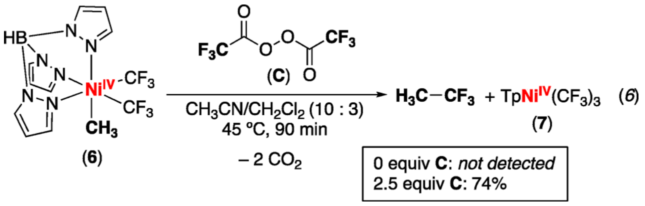
Figure 3. Thermal decomposition of **6** (0.015 M in CD_3NO_2) in the presence of various additives. Blue triangles = no additive. Green diamonds = β-nitrostyrene (0.075 M, 5 equiv relative to **6**). Red squares = **A** (0.045 M, 3 equiv relative to **6**). Yellow rectangles = **B** (0.045 M, 3 equiv relative to **6**).

Mechanism *ii* is fundamentally different than traditional $2e^-$ inner-sphere C−C bond-forming reductive elimination reactions. As such, we hypothesized that it might enable the formation of $C(sp^3)-CF_3$ bonds, which are challenging to forge via direct inner-sphere pathways.[3c,7,36] For example, heating **6** for 18 h at 100 °C in MeCN yields <5% of H_3C-CF_3. Instead, other decomposition pathways outcompete H_3C-CF_3 coupling.[37] This result is consistent with the known difficulties associated with direct inner-sphere $C(sp^3)-CF_3$ coupling.

However, in contrast, the treatment of **6** with 2.5 equiv of bis(trifluoroacetyl)peroxide (**C**) at just 45 °C for 90 min resulted in rapid decay of the Ni^{IV} starting material along with the concomitant formation of H_3C-CF_3 and $TpNi^{IV}(CF_3)_3$ **7** in 74 and 63% yield, respectively (eq 6).[38] Control reactions show that H_3C-CF_3 is not formed at this temperature unless both **6** and **C** are present. This represents a rare example of metal-mediated $C(sp^3)-CF_3$ coupling.[36,39] In our system, this transformation appears to be enabled by the accessibility of a $1e^-$ outer-sphere pathway.

SUMMARY AND CONCLUSIONS

In summary, this Article describes the first detailed study of the reactivity of high-valent organonickel complexes with carbon-centered radicals (R•). These studies demonstrate that Ni^{IV} compounds can be formed from the reaction of Ni^{III} complexes with R•. They also reveal that Ni^{IV}−methyl complexes can engage R• to form various types of C−C bonds. Preliminary mechanistic studies are most consistent with a pathway involving an S_H2-type reaction of R• with the $Ni^{IV}-CH_3$ ligand. In contrast, inner-sphere coupling and radical heterodimerization mechanisms are deemed unlikely. This unconventional C−C bond-forming pathway was found to enable $C(sp^3)-CF_3$ coupling, a reaction that is highly challenging through traditional inner-sphere reductive elimination at Ni centers. Overall, these investigations suggest that, with the appropriate choice of ligand, $Ni^{II/III/IV}$ sequences involving carbon-centered radicals could be targeted for the formation of challenging bonds. Future work in our laboratory will seek to extend these insights to the development of new catalytic methods.



ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.9b02411.

Crystallographic Information File for compound **3** (CIF)
Crystallographic Information File for compound **4** (CIF)
Crystallographic Information File for compound **5** (CIF)
Crystallographic Information File for compound **7** (CIF)
Crystallographic Information File for compound **Int-1** (CIF)
Experimental details, compound characterization, spectra, and safety considerations (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Zhou, J.; Fu, G. C. Cross-couplings of unactivated secondary alkyl halides: room-temperature nickel-catalyzed Negishi reactions of alkyl bromides and iodides. *J. Am. Chem. Soc.* **2003**, *125*, 14726. (b) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. Nickel-catalyzed cross-couplings involving carbon-oxygen bonds. *Chem. Rev.* **2011**, *111*, 1346. (c) Hu, X. Nickel-catalyzed cross coupling of non-activated alkyl

halides: a mechanistic perspective. *Chem. Sci.* **2011**, *2*, 1867. (d) Montgomery, J. Organonickel Chemistry. In *Organometallics in Synthesis: Fourth Manual*; Lipshutz, B. H., Ed.; Wiley: Hoboken, NJ, 2013; p 319. (e) Tasker, S. Z.; Standley, E. A.; Jamison, T. F. Recent advances in homogeneous nickel catalysis. *Nature* **2014**, *509*, 299. (f) Ananikov, V. P. Nickel: the "spirited horse" of transition metal catalysis. *ACS Catal.* **2015**, *5*, 1964. (g) Zuo, Z.; Ahneman, D. T.; Chu, L.; Terret, J. A.; Doyle, A. G.; MacMillan, D. W. C. Merging photoredox with nickel catalysis: coupling of u-carboxyl sp^3-carbons with aryl halides. *Science* **2014**, *345*, 437. (h) Green, R. A.; Hartwig, J. F. Nickel-catalyzed amination of aryl chlorides with ammonia or ammonium salts. *Angew. Chem., Int. Ed.* **2015**, *54*, 3768. (i) Wang, Z.; Yin, H.; Fu, G. C. Catalytic enantioconvergent coupling of secondary and tertiary electrophiles with olefins. *Nature* **2018**, *563*, 379. (j) MacQueen, P. M.; Tassone, J. P.; Diaz, C.; Stradiotto, M. Exploiting ancillary ligation to enable nickel-catalyzed C-O cross-couplings of aryl electrophiles with aliphatic alcohols. *J. Am. Chem. Soc.* **2018**, *140*, 5023. (k) Lee, S.-C.; Liao, H.-H.; Chatupheeraphat, A.; Rueping, M. Nickel-catalyzed C-S bond formation via decarbonylative thioetherification of esters, amides, and intramolecular recombination fragment coupling of thioesters. *Chem. - Eur. J.* **2018**, *24*, 3608.

(2) (a) Tsou, T. T.; Kochi, J. K. Reductive coupling of organometals induced by oxidation. Detection of metastable paramagnetic intermediates. *J. Am. Chem. Soc.* **1978**, *100*, 1634. (b) Tsou, T. T.; Kochi, J. K. Mechanism of biaryl synthesis with nickel complexes. *J. Am. Chem. Soc.* **1979**, *101*, 7547. (c) Jones, G. D.; McFarland, C.; Anderson, T. J.; Vicic, D. A. Analysis of key steps in the catalytic cross-coupling of alkyl electrophiles under Negishi-like conditions. *Chem. Commun.* **2005**, 4211. (d) Breitenfeld, J.; Ruiz, J.; Wodrich, M. D.; Hu, X. Bimetallic oxidative addition involving radical intermediates in nickel-catalyzed alkyl-alkyl Kumada coupling reactions. *J. Am. Chem. Soc.* **2013**, *135*, 12004. (e) Diccianni, J. B.; Katigbak, J.; Hu, C.; Diao, T. Mechanistic characterization of (Xantphos)Ni(I)-mediated alkyl bromide activation: oxidative addition, electron transfer, or halogen-atom abstraction. *J. Am. Chem. Soc.* **2019**, *141*, 1788.

(3) (a) Klein, H.-F; Bickelhaupt, A.; Jung, T.; Cordier, G. Syntheses and properties of the first octahedral diorganonickel(IV) compounds. *Organometallics* **1994**, *13*, 2557. (b) Carnes, M.; Buccella, D.; Chen, J. Y. C.; Ramirez, A. P.; Turro, N. J.; Nuckolls, C.; Steigerwald, M. A stable tetraalkyl complex of nickel(IV). *Angew. Chem., Int. Ed.* **2009**, *48*, 290. (c) Camasso, N. M.; Sanford, M. S. Design, synthesis, and carbon-heteroatom coupling reactions of organometallic nickel(IV) complexes. *Science* **2015**, *347*, 1218. (d) Bour, J. R.; Camasso, N. M.; Sanford, M. S. Oxidation of Ni(II) to Ni(IV) with aryl electrophiles enables Ni-mediated aryl-CF_3 coupling. *J. Am. Chem. Soc.* **2015**, *137*, 8034. (e) Zhou, W.; Schultz, J. W.; Rath, N. P.; Mirica, L. M. Aromatic methoxylation and hydroxylation by organometallic high-valent nickel complexes. *J. Am. Chem. Soc.* **2015**, *137*, 7604. (f) Martinez, G. E.; Ocampo, C.; Park, Y. J.; Fout, A. R. Accessing pincer (bis)carbene Ni(IV) complexes from Ni(II) via halogen and halogen surrogates. *J. Am. Chem. Soc.* **2016**, *138*, 4290. (g) Schultz, J. W.; Fuchigami, K.; Zheng, B.; Rath, N. P.; Mirica, L. M. Isolated Organometallic Ni(III) and Ni(IV) complexes relevant to carbon-carbon bond-formation reactions. *J. Am. Chem. Soc.* **2016**, *138*, 12928. (h) Chong, E.; Kampf, J. W.; Ariafard, A.; Canty, A. J.; Sanford, M. S. Oxidatively induced C-H activation at high-valent nickel. *J. Am. Chem. Soc.* **2017**, *139*, 6058. (i) Rovira, M.; Roldán-Gómez, S.; Martin-Diaconescu, V.; Whiteoak, C. J.; Company, A.; Luis, J. M.; Ribas, X. Trifluoromethylation of a well-defined square-planar aryl-Ni(II) complex involving Ni(III)-CF_3 and Ni(IV)-CF_3 intermediate species. *Chem. - Eur. J.* **2017**, *23*, 11662. (j) Watson, M. B.; Rath, N. P.; Mirica, L. M. Oxidative C-C bond formation reactivity of organometallic Ni(II), Ni(III), and Ni(IV) complexes. *J. Am. Chem. Soc.* **2017**, *139*, 35.

(4) (a) Aihara, Y.; Chatani, N. Nickel-catalyzed direct alkylation of C-H bonds in benzamides and acrylamides with functionalized alkyl halides via bidentate chelation assistance. *J. Am. Chem. Soc.* **2013**, *135*, 5308. (b) Aihara, Y.; Chatani, N. Nickel-catalyzed direct arylation of $C(sp^3)$-H bonds in aliphatic amides via bidentate chelation assistance. *J. Am. Chem. Soc.* **2014**, *136*, 898. (c) Aihara, Y.; Tobisu, M.; Fukumoto, Y.; Chatani, N. Ni(II)-catalyzed oxidative coupling between $C(sp^2)$-H in benzamides and $C(sp^3)$-H in toluene derivatives. *J. Am. Chem. Soc.* **2014**, *136*, 15509. (d) Omer, H. M.; Liu, P. Computational study of Ni-catalyzed C-H functionalization: factors that control the competition of oxidative addition and radical pathways. *J. Am. Chem. Soc.* **2017**, *139*, 9909. (e) Li, Y.; Zou, L.; Bai, R.; Lan, Y. Ni(I)-Ni(III) vs. Ni(II)-Ni(IV): mechanistic study of Ni-catalyzed alkylation of benzamides with alkyl halides. *Org. Chem. Front.* **2018**, *5*, 615. (f) Patel, U. N.; Jain, S.; Pandey, D. K.; Gonnade, R. G.; Vanka, K.; Punji, B. Mechanistic aspects of pincer Ni(II)-catalyzed C-H bond alkylation of azoles with alkyl halides. *Organometallics* **2018**, *37*, 1017.

(5) (a) Meucci, E. A.; Camasso, N. M.; Sanford, M. S. An organometalllic Ni^{IV} complex that participates in competing transmetalation and $C(sp^2)$-O bond-forming reductive elimination reactions. *Organometallics* **2017**, *36*, 247. (b) D'Accriscio, F.; Borja, P.; Saffon-Merceron, N.; Fustier-Boutignon, M.; Mézailles, N.; Nebra, N. C-H bond trifluoromethylation of arenes enabled by a robust, high-valent nickel(IV) complex. *Angew. Chem., Int. Ed.* **2017**, *56*, 12898.

(6) (a) Bayler, A.; Canty, A. J.; Ryan, J. H.; Skelton, B. W.; White, A. H. Arylation of palladium(II) and platinum(II) by diphenyliodonium triflate to form metal(IV) species, and a structural analysis of an isomer of $PtIMe_2Ph(bpy)$ (bpy = 2,2'-bipyridine). *Inorg. Chem. Commun.* **2000**, *3*, 575. (b) Furuya, T.; Ritter, T. Carbon-fluorine reductive elimination from a high-valent palladium fluoride. *J. Am. Chem. Soc.* **2008**, *130*, 10060. (c) Ball, N. D.; Kampf, J. W.; Sanford, M. S. Aryl-CF_3 bond-forming reductive elimination from palladium(IV). *J. Am. Chem. Soc.* **2010**, *132*, 2878. (d) Dubinsky-Davidchik, I.; Goldberg, I.; Vigalok, A.; Vedernikov, A. N. Selective aryl-fluoride reductive elimination from a platinum(IV) complex. *Angew. Chem., Int. Ed.* **2015**, *54*, 12447. (e) Daryanavard, M.; Armstrong, D.; Lough, A. J.; Fekl, U. The first palladium(IV) aryldiazenido complex: relevance for C-C coupling. *Dalton Trans.* **2017**, *46*, 4004. (f) Yamamoto, K.; Li, J.; Garber, J. A. O.; Rolfes, J. D.; Boursalian, G. B.; Borghs, J. C.; Genicot, C.; Jacq, J.; van Gastel, J.; Neese, F.; Ritter, T. Palladium-catalysed electrophilic aromatic C-H fluorination. *Nature* **2018**, *554*, 511.

(7) Bour, J. R.; Camasso, N. M.; Meucci, E. A.; Kampf, J. W.; Canty, A. J.; Sanford, M. S. Carbon-carbon bond-forming reductive elimination from isolated nickel(III) complexes. *J. Am. Chem. Soc.* **2016**, *138*, 16105.

(8) For related oxidations of $[Ni(II)(CF_3)_2]$ complexes using $AgBF_4$, see: (a) Zhang, C.-P.; Wang, H.; Klein, A.; Biewer, C.; Stirnat, K.; Yamaguchi, Y.; Xu, L.; Gomez-Benitz, V.; Vicic, D. A. A five-coordinate nickel(II) fluoroalkyl complex as a precursor to a spectroscopically detectable Ni(III) species. *J. Am. Chem. Soc.* **2013**, *135*, 8141. (b) Tang, F.; Rath, N. P.; Mirica, L. M. Stable bis(trifluoromethyl)nickel(III) complexes. *Chem. Commun.* **2015**, *51*, 3113.

(9) Fossey, J.; Lefort, D.; Sorba, J. *Free radicals in organic chemistry*; Wiley: New York, 1995; p 307.

(10) Cooper, W. The effect of structure of diacyl peroxides on the rates of initiation of the polymerization of styrene. *J. Chem. Soc.* **1951**, 3106.

(11) Tp-supported high-valent organonickel complexes are light sensitive and thus unstable under photolytic conditions.

(12) The consumption of **1** was determined by ^{11}B NMR spectroscopic analysis of the crude reaction mixture.

(13) Yu, S.; Dudkina, Y.; Wang, H.; Kholin, K. V.; Kadirov, M. K.; Budnikova, Y.; Vicic, D. A. Accessing perfluoroalkyl nickel(II), (III), and (IV) complexes bearing a readily attached $[C_4F_8]$ ligand. *Dalton Trans.* **2015**, *44*, 19443.

(14) Heating **3** at 100 °C for 12 h resulted in complete decomposition of the starting material to form a mixture of nickel-containing products including $NiTp_2$.

(15) The yield of **4** appears to be limited by the competitive decomposition of this Ni^{IV} product at 95 °C. Analysis of the crude reaction between **A** and **3** revealed that only 11% (~1.8 equiv relative to Ni) of the initial **A** was consumed at the time of maximum Ni^{IV} yield. The remaining mass balance of the reaction was fluorobenzene and 4-fluorobenzoic acid, presumably formed through H-atom abstraction

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from the solvent (see Figure S3). Using fewer equivalents of **A** resulted in lower yields of **4** (11% yield with 1 equiv, 40% yield with 5 equiv).

(16) Diacyl/aroylperoxides are potentially explosive materials and should be handled with appropriate precautions (see the Supporting Information for details).

(17) The yield of **5** appears to be limited by the competitive decomposition of this Ni^{IV} product at 85 °C. Analysis of the crude reaction mixture by ^1H NMR spectroscopy and GCMS revealed the formation of 1,6-diphenyl hexane and allylbenzene. The allylbenzene is formed during the thermal decomposition of **5** via an apparent net *β*-hydride elimination.

(18) Complex **5** was isolated in 17% yield through the reaction of **3** with 5 equiv of **B** at 85 °C for 6 min. Notably, diacyl peroxides are potentially explosive compounds and should be handled with caution. The equivalents of **B** were reduced to mitigate risk on the preparatory scale.

(19) See the Supporting Information, pp S7 and S8, for the synthesis and characterization of **Int-1**.

(20) The nature of the primary nickel-containing product of this reaction is currently unclear. The ^{11}B NMR rules out the formation of $NiTp_2$ or free unbound Tp.

(21) Galli, C. Radical reactions of arenediazonium ions: easy entry into the chemistry of the aryl radical. *Chem. Rev.* **1988**, *88*, 765.

(22) Similarly, complex **1** reacts with 4-fluorophenyldiazonium tetrafluoroborate and ferrocene to yield **2** in 52% yield under these conditions.

(23) A key consideration in the choice of radical scavenger is its stability to the highly oxidizing conditions of this reaction. For example, the use of TEMPO as a radical scavenger resulted in violent decomposition of the peroxides. On this basis, we selected the electron deficient Michael acceptor *β*-nitrostyrene. Barton, D. H. R.; Togo, H.; Zard, S. R. The invention of new radical chain reactions. Part X. High-yield radical addition reactions of -nitroolefins. An expedient construction of the 25-hydroxy-vitamind D_3 side chain from bile acids. *Tetrahedron* **1985**, *41*, 5507.

(24) (a) Mosimann, H.; Krautler, B. Methylcorrinoids methylate radicals- their second biological mode of action? *Angew. Chem., Int. Ed.* **2000**, *39*, 393. (b) Woodyer, R. D.; Li, G.; Zhao, H.; van der Donk, W. A. New insight into the mechanism of methyl transfer during the biosynthesis of fosfomycin. *Chem. Commun.* **2007**, *0*, 359. (c) Ding, W.; Li, Q.; Jia, Y.; Ji, X.; Qianzhu, H.; Zhang, Q. Emerging diversity of the cobalamin-dependent methyltransferases involving radical-based mechanisms. *ChemBioChem* **2016**, *17*, 1191. (d) Bridwell-Rabb, J.; Drennan, C. L. Vitamin B 12 in the spotlight again. *Curr. Opin. Chem. Biol.* **2017**, *37*, 63.

(25) Analogous outer-sphere radical C−C coupling mechanisms are commonly proposed for iron(II)/(III)-catalyzed transformations. For examples, see: (a) Hatakeyama, T.; Hashimoto, T.; Kondo, Y.; Fujiwara, Y.; Seike, H.; Takaya, H.; Tamada, Y.; Ono, T.; Nakamura, M. Iron-catalyzed Suzuki-Miyaura coupling of alkyl halides. *J. Am. Chem. Soc.* **2010**, *132*, 10674. (b) Hatakeyama, T.; Okada, Y.; Yoshimoto, Y.; Nakamura, M. Tuning chemoselectivity in iron-catalyzed Sonogashira-type reactions using a bisphosphine ligand with peripheral steric bulk: selective alkynylation of nonactivated alkyl halides. *Angew. Chem., Int. Ed.* **2011**, *50*, 10973. (c) Daifuku, S. L.; Al-Afyouni, M. H.; Snyder, B. E. R.; Kneebone, J. L.; Neidig, M. L. A combined Moössbauer, magnetic circular dichroism, and density functional theory approach for iron cross-coupling catalysis: electronic structure, in situ formation, and reactivity of iron mesityl-bisphosphines. *J. Am. Chem. Soc.* **2014**, *136*, 9132. (d) Przyojski, J. A.; Veggeberg, K. P.; Arman, H. D.; Tonzetich, Z. J. Mechanistic studies of catalytic carbon-carbon cross-coupling by well-defined iron NHC complexes. *ACS Catal.* **2015**, *5*, 5938.

(26) Complex **6** was prepared in 40% yield via the reaction of $NMe_4[TpNi^{II}(CF_3)_2]$ with excess methyl iodide and 1.3 equiv of 2,6-difluorobenzendiazonium tetrafluoroborate (see the Supporting Information, pp S9 and S10). This Ni^{IV} complex was characterized via ^1H, ^{13}C, ^{19}F, and $^1H/^{19}F$ HMBC NMR spectroscopy as well as elemental analysis. Complex **6** exhibits relatively high thermal stability, with <10% decomposition after 1 h at 90 °C in CD_3NO_2. This high thermal stability is likely due to the high barrier for $CH_3{-}CF_3$ coupling via inner-sphere reductive elimination.

(27) A similar yield (58%) was obtained on the basis of ^1H NMR spectroscopic analysis of the crude reaction mixture, confirming that the methyl is not solvent-derived.

(28) The ethyl analogue, $TpNi^{IV}(CF_3)_2(CH_2CH_3)$, reacts with 6 equiv of **A** under analogous conditions to afford 4-fluoroethylbenzene in 7% yield. However, it is important to note that this complex is not very stable at the reaction temperature, and it decomposes competitively at 90 °C to form ethylene and CF_3H. See the Supporting Information, p S29, for more details.

(29) Attempts to isolate Ni-containing products from the crude reaction mixtures with **A** and **B** (by column chromatography on silica or recrystallization) were unsuccessful.

(30) Tp_2Ni was also the major identifiable nickel-containing compound in the thermal decomposition of **1**.

(31) A reviewer suggested that an alternate pathway for the reactions in Scheme 4 and eq 6 could involve the transmetalation of a methyl group from **6** to reduced nickel byproducts and subsequent C−C coupling from a lower valent Ni center. While we cannot definitively rule out this possibility, we note that this would require a $H_3C{-}CF_3$ bond-forming reductive elimination reaction from a lower valent Ni intermediate. This transformation currently does not have precedent from group 10 metal centers. See ref 7.

(32) Ingold, K. U.; Roberts, B. P. *Free radical substitution reactions: Bimolecular homolytic substitutions at saturated multivalent atoms*; Wiley: New York, 1971.

(33) The dimerization of localized and sterically accessible carbon-centered radicals, such as $\bullet CH_3$ and •Ph, is thought to be nearly barrierless. Costentin, C.; Savéant, J.-M. Origin of activation barriers in the dimerization of neutral radicals: A "nonperfect synchronization" effect. *J. Phys. Chem. A* **2005**, *109*, 4125.

(34) Ethane was not detected by ^1H NMR spectroscopy. However, potential loss of ethane to the headspace of the reaction vessel could not be mitigated due to the hazards associated with eliminating reaction vessel headspace in gas-evolving reactions. The mass balance of other methyl-containing products sets the maximum yield as 17 and 11%.

(35) The H-atom abstraction products fluorobenzene and *n*-propylbenzene were observed in 30% and <2% yield, respectively.

(36) Inner-sphere $C(sp^3){-}CF_3$ coupling has recently been proposed to occur from $Cu^{III}(CF_3)_3(CH_3)$ complexes. S_H2 mechanisms involving the direct attack of $\bullet CF_3$ on $Cu^{III}(CH_3)$ were not discussed. See: (a) Tan, X.; Liu, Z.; Shen, H.; Zhang, P.; Zhang, Z.; Li, C. Silver-catalyzed decarboxylative trifluoromethylation of aliphatic carboxylic acids. *J. Am. Chem. Soc.* **2017**, *139*, 12430. (b) Paeth, M.; Tyndall, S. B.; Chen, L.-Y.; Hong, J.-C.; Carson, W. P.; Liu, X.; Sun, X.; Liu, J.; Yang, K.; Hale, E. M.; Tierney, D. L.; Liu, B.; Cao, Z.; Cheng, M.-C.; Goddard, W. A.; Liu, W. $C(sp^3)$-CF_3 reductive elimination from well-defined Cu(III) complexes. *J. Am. Chem. Soc.* **2019**, *141*, 3153.

(37) In marked contrast, the analogous phenyl complex $TpNi^{IV}(CF_3)_2(Ph)$ undergoes high yielding inner-sphere $Ph{-}CF_3$ coupling at 55 °C over 14 h. See ref 3d for details.

(38) **7** is likely formed through the addition of $\bullet CF_3$ to $TpNi(CF_3)_2$ which is more stable at these lower temperatures.

(39) Levin, M. D.; Chen, T. Q.; Neubig, M. E.; Hong, C. M.; Theulier, C. A.; Kobylianskii, I. J.; Janabi, M.; O'Neil, J. P.; Toste, F. D. A catalytic fluoride rebound mechanism for $C(sp^3)$-CF_3 bond formation. *Science* **2017**, *356*, 1272.