

Attenuation of Ni(0) Decomposition: Mechanistic Insights into AgF-Assisted Nickel-Mediated Silylation

Venkadesh Balakrishnan,[†] Vetrivelan Murugesan,[†] Bincy Chindan, and Ramesh Rasappan^{*}Cite This: *Inorg. Chem.* 2022, 61, 1438–1446

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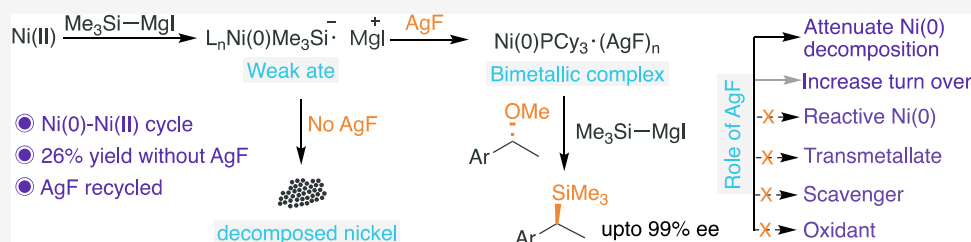
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ABSTRACT: In nickel-mediated Kumada cross-coupling reactions, low valent active nickel complexes are often generated in situ and the ligands usually govern the reactivity or stability of these complexes. However, the decomposition of active nickel complexes is inevitable if the subsequent reaction is sluggish. While we recently developed AgF-assisted nickel catalysis to cross-couple methyl ethers and silylmagnesium reagents, the intriguing catalytic role of AgF and the actual active nickel species remains elusive. Recently, both Ni(0) and Ni(I) intermediate complexes are identified as active species in Kumada cross-coupling reactions. Control experiments in combination with ³¹P nuclear magnetic resonance (NMR) suggest that AgF attenuates the decomposition of in situ generated Ni(0) species. The plausible Ni(0) and Ni(I) intermediate complexes were synthesized, and experimental findings are consistent with the actual catalytic cycle being Ni(0)/Ni(II) rather than Ni(I)/Ni(III).

INTRODUCTION

Nickel-mediated Kumada cross-coupling reactions involving Grignard reagents have emerged as an appealing and powerful method to forge C–C and C–X bonds in organic synthesis.^{1–5} Commonly, Ni(II) pre-complexes are employed in these reactions. However, the mechanism may not follow a single universal pathway; in fact, mechanisms involving the intermediacy of different low valent complexes are reported.^{6–19} These active and in situ generated low valent nickel complexes are highly unstable and decompose if the subsequent oxidative addition is sluggish, commonly observed for unreactive electrophiles. Recently, we developed AgF-assisted nickel-mediated enantiospecific silylation of methyl ethers that offered a rapid and efficient strategy to construct benzylic organosilanes (Scheme 1c).²⁰ Despite the profound effect of catalytic AgF in this reaction, the underlying mechanism, which can explain the role of AgF, remains elusive. We proposed a hypothetical Ni(0) intermediate along with a possible Ni(I) intermediate²⁰ since the recent literature on Kumada cross-coupling reactions revealed Ni(0) as well as Ni(I) intermediacy complexes. The formation of Ni(I) is also reported recently in the use of Grignard reagents by Cárdenas²¹ and Fu⁸ (Scheme 1a). At the same time, Kambe and Jarvo reported the Ni(0) active species in the Kumada cross-coupling reactions (Scheme 1b).^{6,22} While the use of stoichiometric AgF as an oxidant or to generate electropositive metal is well understood, the catalytic application of AgF is not

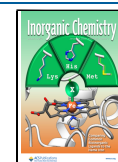
well studied. Identifying the actual intermediates and mechanistic pathway could broaden the current scope of chemistry even in other catalytic transformations.

We carried out a systematic mechanistic study to identify the nature of the process, and the possible intermediate Ni(I) and Ni(0) complexes were prepared and studied using ³¹P NMR, UV, and CV techniques to identify the resting state of the catalyst and the actual catalytic cycle (Ni(0)/Ni(II) vs Ni(I)/Ni(III)). Kinetic studies were also performed to gain insight into the transition state and the rate-limiting step. A series of control experiments were carried out to probe the role of AgF in the catalytic cycle since the silver salts are known to perform multiple roles, including as a scavenger to either halides^{23,24} or free ligand (PCy₃),²⁵ as an oxidant,^{26–28} or as a transmetallating agent to generate organosilver intermediate.^{23,29}

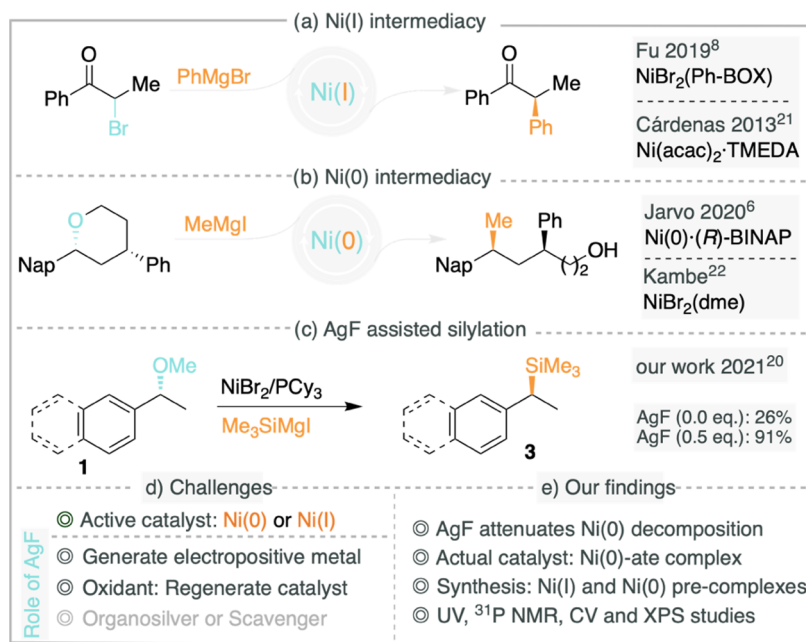
Initial studies were focused on the identification of the active catalyst and the resting state of the nickel complex. Although Ni(II)Br₂-diglyme/PCy₃ complex **4a** was employed as a pre-catalyst, the active catalyst could be either Ni(0) or Ni(I) complex. The moisture and air-sensitive dimeric [Ni(0)-

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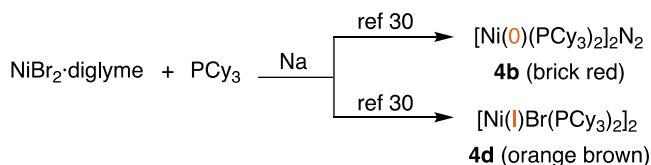


Scheme 1. Kumada Cross-Coupling Reactions

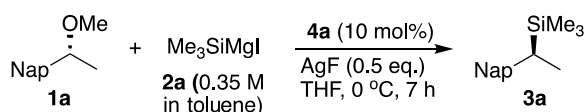


(PCy₃)₂]₂N₂ **4b** and [Ni(I)Br(PCy₃)₂]₂ **4d** complexes^{30–36} were prepared (Scheme 2) from **4a** and studied using various

Scheme 2. Synthesis of Ni(0) and Ni(I) Complexes



spectroscopic techniques. Complex **4a** gave the cross-coupled product **3a** in excellent yield in the presence of 0.5 equiv of AgF (entry 1). Complex **4f** (DPEPhos instead of PCy₃) also offered product **3a** in a moderate yield (entry 2). The pre-complexes **4b** and **4d** were also employed in the cross-coupling of **1a** under the optimized condition²⁰ and observed the formation of **3a** albeit, in a lower yield (entries 3 and 4, Table 1), and partial decomposition of these complexes may be at play. In the absence of AgF, however, only 26% of **3a** was observed (entry 5). We observed poor conversion when AgF was replaced with AgBr or AgI or CsF or LiF (entries 6–9). The ³¹P NMR spectrum of [Ni(0)(PCy₃)₂]₂N₂ **4b** (brick red) is shown in Figure 1a, where the complex resonates at 46.0 ppm. The dimer **4b** may exist in equilibrium with its monomer (η^6 -toluene)Ni(0)(PCy₃) **4c** (orange); however, no change in color or dissociation of PCy₃ was observed in ³¹P NMR (Figure 1a), indicating that the monomer was not present in toluene.³¹ We also sparged argon to the **4b** solution, resulting in [Ni(PCy₃)₃], which has a phosphine resonance of 45.03 ppm, as described in the literature.³⁰ As expected, the mixture from Ni(II) complex **4a** and Me₃SiMgI·TMEDA (0.35 M in toluene) gave a signal at 46.7 ppm (Figure 1b), an imperceptible downfield shift from the Ni(0) complex **4b**. Fortunately, the same signal appeared when the Ni(0) complex **4b** was treated with Me₃SiMgI·TMEDA (Figure 1c). We corroborate the peak at 46.7 ppm to a weak nickel(0)-ate complex [Ni(0)_L_nMe₃Si[−]MgI⁺] **4e**, which is in equilibrium

Table 1. Oxidative Addition of **4b** and **4d**^a

entry	deviation from above	yield (%)
1	none	91
2	4f instead of 4a	65
3	4b instead of 4a	40
4	4d instead of 4a	27
5	without AgF	26
6	AgBr instead of AgF	59
7	AgI instead of AgF	56
8	CsF instead of AgF	34
9	LiF instead of AgF	36

^a0.2 mmol **1a**, **4a** (10 mol%), 0.30 mmol Me₃SiMgI·TMEDA **2a** (0.35 M in toluene), AgF (0.5 equiv), 0.15 M THF, 7 h.

with Ni(0) complex **4b**, similar ate complexes are reported in the literature for Fe(0),³⁷ Ni(0),³⁸ and Pd(0) complexes.^{39–41} Notably, we found a downfield shift, which corresponds to what has already been reported in the literature for the Pd(0)-ate complex.⁴⁰

We performed cyclic voltammetry studies to gather more evidence supporting the formation of the ate complex.⁴⁰ The Ni(0) complex **4b** showed oxidation at $E_{Ox}^P = 0.48$ V vs ferrocene. When Me₃SiMgI·TMEDA was added to this Ni(0) complex, we observed a cathodic shift ($E_{Ox}^P = 0.38$ vs ferrocene), as expected; a similar cathodic shift has been reported in the literature for ate complex formation.⁴⁰ We also measured UV spectrum for Ni(0) **4b**, Ni(I) **4d**, and Ni(II)Br₂/PCy₃ **4a** complexes (Figure 1g). The Ni(0) complex **4b** had two absorption bands at 410 and 475 nm, and the addition of Me₃SiMgI to this complex **4b** (generating a weak Ni(0)-ate complex **4e**) did not alter the spectra (SI-23). Ni(I) complex **4d** also had two broad absorption bands at 310 and 355 nm.

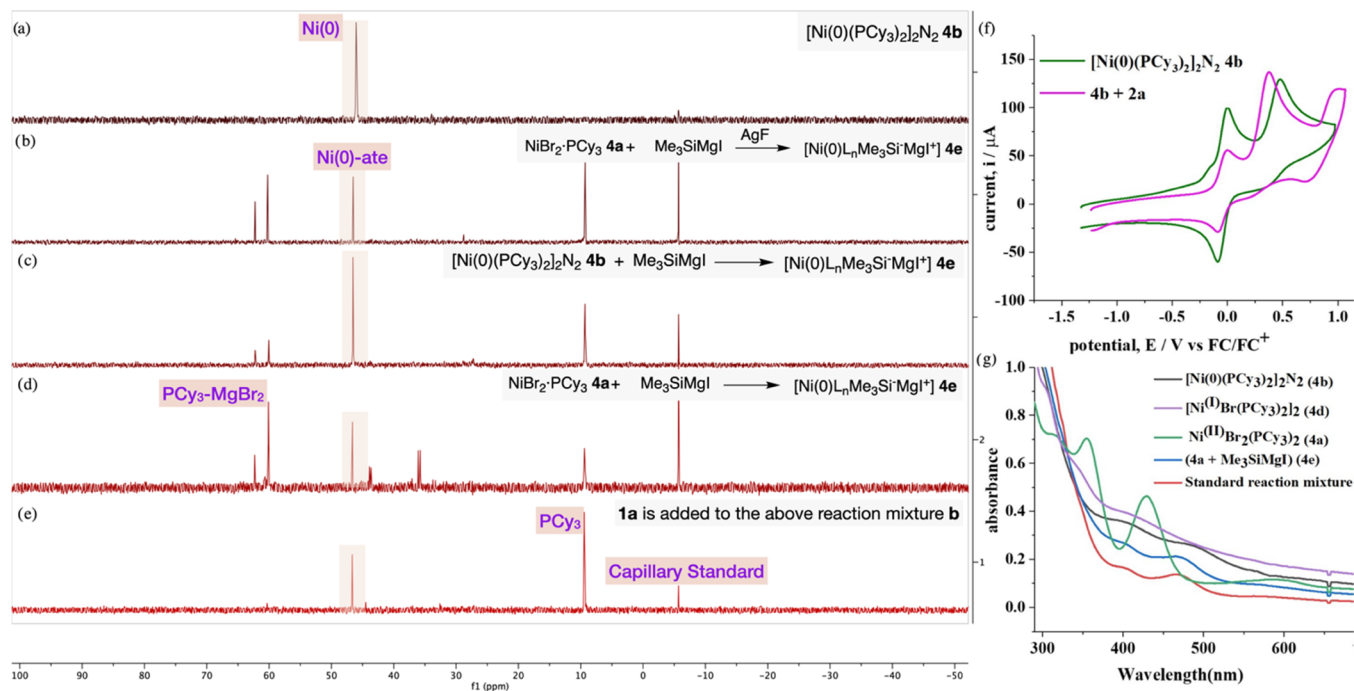


Figure 1. (a–e) ^{31}P NMR Studies. (f) CV of Ni(0) 4b and $\text{Me}_3\text{Si-Ni}(\text{O})$ -ate complex. (g) UV studies.

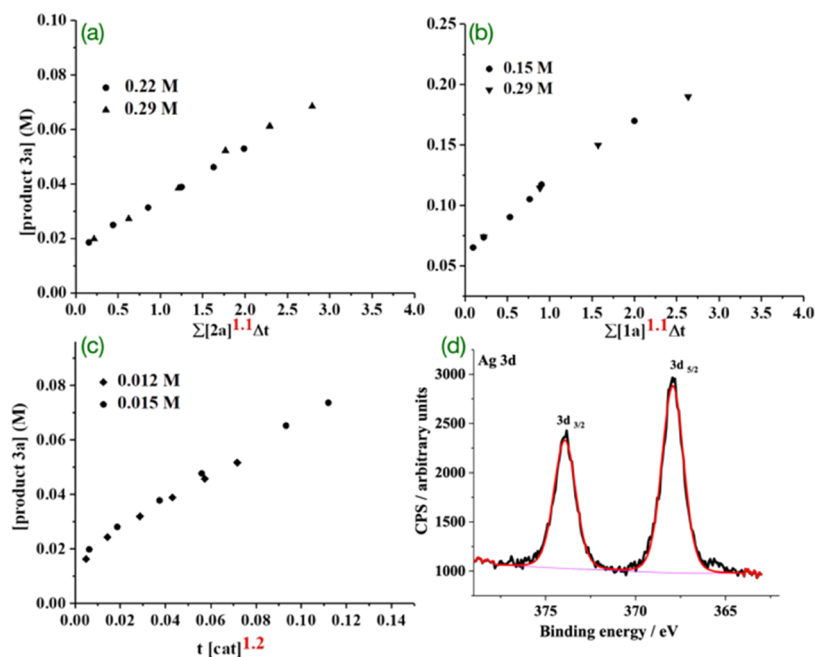


Figure 2. Product concentration profile against variable time normalized in (a) Grignard 2a, (b) 1a, and (c) catalyst 4a. (d) XPS spectra of recovered AgF.

The pre-complex $\text{Ni}(\text{II})\text{Br}_2/\text{PCy}_3$ 4a had two d–d transition bands at 435 and 355 nm. Upon the addition of Me_3SiMgI to 4a, the two bands at 435 and 355 nm disappeared and consequently formed the Ni(0)-ate complex 4e with two absorption bands at 410 and 475 nm.

The standard reaction mixture (Figure 1g) also exhibited these two bands. Hence, ^{31}P NMR studies with additional CV studies support the intermediacy Ni(0)-ate complex 4e as the predominant resting state. It is worth mentioning that Borys and Hevia reported the formation of Ni(0)-ate complex when the Ni(0) complex was mixed with organolithium.³⁸ We also

observed the formation of Ni(0)-ate complex 4e when Me_3SiMgI and Ni(I) complex 4d was mixed (see SI-24 for UV and SI-32 for ^{31}P NMR).⁶ Kinetic analysis of the reaction was performed using variable-time normalization analysis (VTNA) developed by Burés.⁴² The obtained profiles of the experiments with differing concentration of one reactant will only overlay if the time axis is replaced by $\sum[\text{reactant}]^\alpha \Delta t$ (α – correct order). Order of 1.2, 1.1, and 1.1 was found for the catalyst 4a, alkyl ether 1a, and Grignard 2a, implying that they are involved in the rate-limiting step (Figure 2).

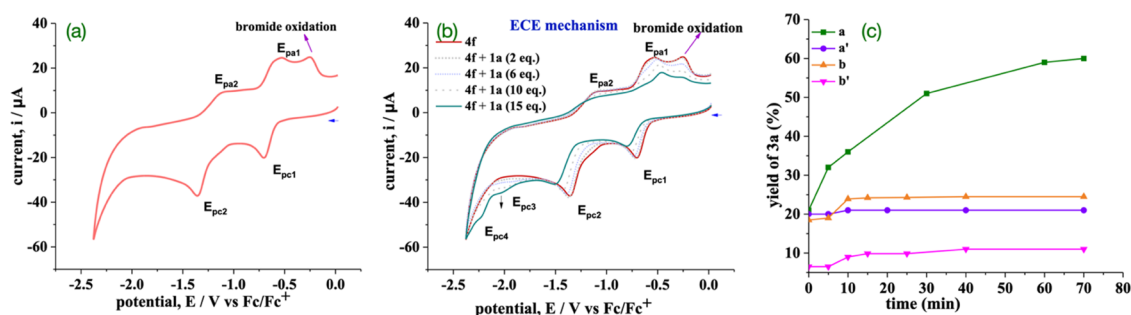
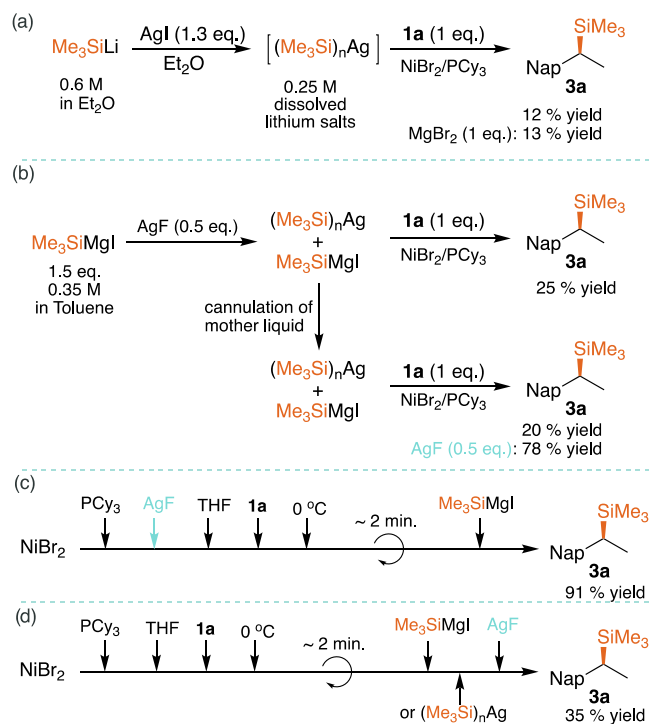


Figure 3. Cyclic voltammogram of (a) NiBr₂/DPEphos **4f**. (b) Gradual addition of **1a** to **4f**. (c) Reaction profile of (a) standard reaction with AgF, (a') standard reaction without AgF, (b) standard reaction at $-40\text{ }^{\circ}\text{C}$ with AgF, and (b') standard reaction at $-40\text{ }^{\circ}\text{C}$ without AgF.

These results draw attention to the possibility of Ni(0)/Ni(II) catalytic cycle; however, the involvement of Ni(I)/Ni(III) in the catalytic cycle cannot be excluded since the recent literature provides evidence for the formation of transient Ni(I) species via comproportionation of Ni(0) and Ni(II) species^{43–45} or disproportionation of Ni(II) species.⁴⁶ Moreover, the pre-Ni(I) complex **4d** also afforded the cross-coupled product **3a** albeit in lower yield (Table 1). Further support was accessed from CV experiments. The use of cyclic voltammogram to identify the intermediate species has been reported in the literature.^{47–49} The Ni(II)Br₂/PCy₃ complex **4a** gave only a single cathodic peak with no associated anodic peak, probably due to the formation of unstable low valent nickel;⁵⁰ thus, the complex **4a** cannot be used in this study. Under these circumstances, equally efficient or similar ligands have been employed in CV in place of optimal ligand.⁵¹ Fortunately, NiBr₂/DPEphos **4f** (equally effective as **4a**) exhibited two chemically reversible reductions E_{pc1} (-0.70V) and E_{pc2} (-1.36V), as well as anodic reoxidation peaks E_{pa1} (-0.51V) and E_{pa2} (-1.1V) (Figure 3a).⁵² When we subjected Ni(II) complex **4f** to the electrochemical reduction with a gradual increase in the amount of methyl ether **1a** (sequentially added), the magnitude of reoxidation peak was progressively decreased (Figure 3b), indicating the depletion of [Ni(0)] in the medium. This is consistent with the fact that the electrochemically generated Ni(0) species underwent oxidative addition with methyl ether **1a** (**1a** alone gets reduced at E_{pc4} : -2.21V), which in turn gets reduced at E_{pc3} (-2.05V) following an ECE type of mechanism (see SI-09).^{39,47,49} A shift with the decrease in intensity of cathodic peak potentials is due to the consumption of Ni(II) complex **4f** with the concomitant formation of a new Ni(II) complex.⁴⁹

Role of AgF. The use of silver salts as a halide scavenger or oxidant has been well explored in cross-coupling reactions. The formation of transient organosilver species^{23,29} and bimetallic (M-Ag)^{24,53} complexes is also reported in the literature. We noticed a low yield when using the silylsilver reagent produced from silyllithium, and AgI had no effect on the yield (Scheme 3a). Under optimized conditions, the in situ formation of silylsilver and the subsequent reaction were investigated (Scheme 3b). As shown in Scheme 3b, we observed only 25% of **3a** using the in situ generated silylsilver reagent. Fortunately, the yield was restored when additional AgF was added (at the end of sequential addition). It is worth noting the critical nature of sequential addition; AgF must be added at the beginning of the sequence (Scheme 3c). We noticed a decrease in yield when AgF was added after the addition of Me₃SiMgI·TMEDA or when the AgF was added concurrently with Me₃SiMgI·TMEDA (Scheme 3d). These experiments rule

Scheme 3. Cross-Coupling with Silylsilver Reagents

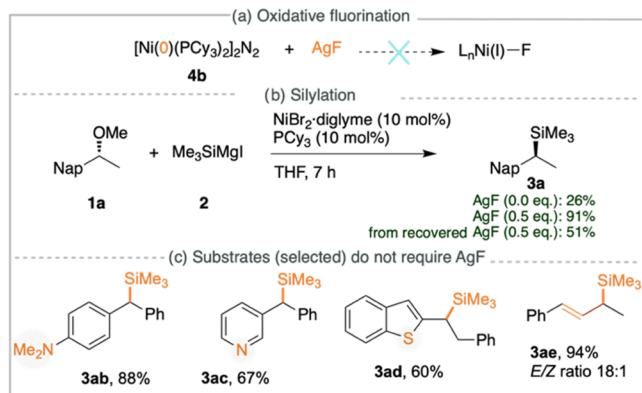


out the possibility of silylsilver reagent as the actual coupling partner.

In contrast to the superstoichiometric loading of AgF,^{26–28} the current method can offer complete conversion with the substoichiometric amount of AgF. Notably, substrates **1ab–ae** (Scheme 4)²⁰ do not require AgF. We also recovered and recycled the AgF that gave the cross-coupled product in 51% yield (Scheme 4).²⁴ The XPS spectrum (Figure 2d) of the crude material obtained by cannulation of the mother liquor away from the standard reaction revealed that the binding energy corresponds to AgF (SI-22). Thus, the oxidative fluorination²⁸ of the intermediate nickel complex is unlikely (Scheme 4). Despite the fact that the reaction requires substoichiometric AgF or is AgF-independent, and we recovered/recycled AgF, the role of AgF in catalyst turnover cannot be totally eliminated.

Under the optimized condition, we noticed that the amount of PCy₃ is inversely proportional to the conversion of starting material **1a** and the yield. When 20 mol % of PCy₃ (instead of 10 mol %) was employed in the standard reaction, the yield was decreased to 72% (from 91%), and the yield was restored with the increasing amount of either AgF or MgBr₂ (SI-20).

Scheme 4. Role of Catalytic AgF



However, the role of AgF as a scavenger to the unbound PCy₃ cannot be the primary reason for the improved conversion since ³¹P NMR showed a strong signal for the formation of complex MgIBr–PCy₃ (60.2 and 62.2 ppm, Figure 1b–d; see SI-29). Further, the pre-complexes [Ni(0)(PCy₃)₂]₂N₂ **4b** and [Ni(I)Br(PCy₃)₂]₂ **4d** were subjected to oxidative addition with **1a** in the absence of Me₃SiMgI, and the results are summarized in Table 2. When Ni(0) complex **4b** was

Table 2. Oxidative Addition of **4b** and **4d**^a

entry	condition	1a	5a
1	4b , AgF (0.5 equiv), 0 °C	98	<1
2	4b , AgF (0.5 equiv), 50 °C	57	40
3	4b , MgBr ₂ ·OEt ₂ , 0 °C	58	41
4	4d , AgF (0.5 equiv)/MgBr ₂ ·OEt ₂	99	ND ^b

^a0.2 mmol **1a**, 1.0 equiv NiX_n, additive 1.0 equiv, 0.15 M THF/toluene (1:9), 7 h. ^bCarried out at 0 and 50 °C.

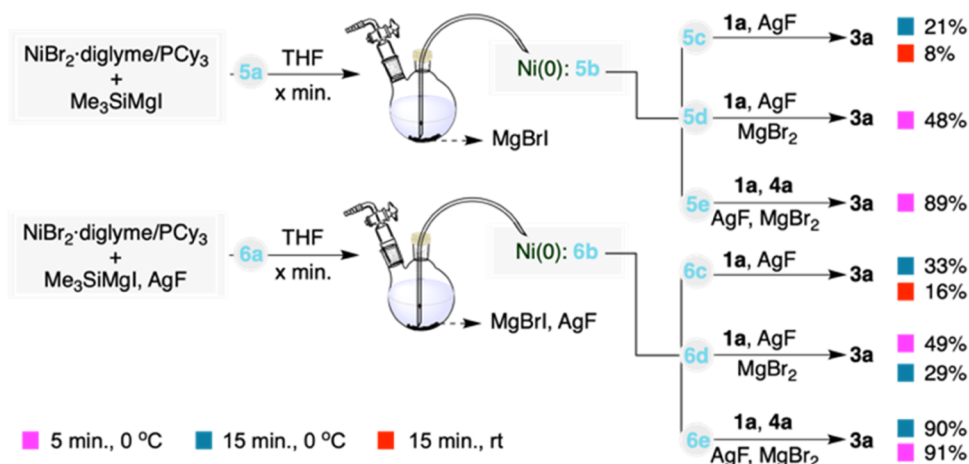
employed along with either AgF (50 °C) or MgBr₂ (0 °C), the reduced product **5a** was observed in moderate yield (entries 1–3). However, Ni(I) complex **4d** does not undergo oxidative addition under similar conditions (entry 4) (rules out Ni(I)–Ni(III) cycle). These data support the activation of **1a**

by MgBr₂, and the Ni(I) complex **4d** is not an active catalyst. The activation of methyl ether **1a** by magnesium halides is also evident from ³¹P NMR; upon the addition of methyl ether **1a** to Ni(0) complex **4e** (Figure 1e vs Figure 1b or Figure 1c), the concentration of unbound PCy₃ (9.4 ppm) increased while completely suppressing the MgIBr–PCy₃ complex.

Although MgIBr promotes oxidative addition, still AgF accelerated the overall catalytic cycle. The reaction profile is shown in Figure 3c; in the absence of AgF, maximum yields of 26% (at 0 °C) and 9% (at –40 °C) were observed within 10 min of the reaction. In contrast, the reaction was accelerated in the presence of AgF: 36% (at 0 °C) and 24% (at –40 °C) yields were observed within 10 min. The formation of in situ NiF₂ is unlikely since the pre-catalyst NiF₂ was ineffective to deliver the cross-coupled product **3a**. To gain further insight into the role of AgF, a series of control experiments were carried out (SI-27). As shown in Scheme 4, in the absence of AgF, we noticed that incomplete consumption of **1a** (26% of **3a** and 70% of **1a**), the addition of excess Me₃SiMgI did not improve the reaction, and the decomposition of Ni(0) species may be at play. Further insight into the literature revealed that the sluggish oxidative addition might lead to the decomposition of active metal species (e.g., Ni(0)L_n) into nickel black.^{6,54} We performed the standard reaction in the absence of AgF to rule out the potential of nickel black reactivation by AgF. After 15 min of stirring, 0.5 equiv of AgF was applied, and the yield could not be enhanced beyond 21%, ruling out the potential of nickel black reactivation by AgF.

Control experiments were designed to identify the role of AgF in the prevention of Ni(0) decomposition (possibly to nickel black).^{6,54} The active Ni(0) complexes **5b** and **6b** were prepared by the reaction of Ni(II)Br₂/PCy₃ and Me₃SiMgI in the absence (Scheme 5, **5a**) and presence (Scheme 5, **6a**) of AgF. The mother liquor (**5b** and **6b**) from these heterogeneous mixtures were cannulated into various reaction mixtures containing **1a** with additional AgF (Scheme 5, **5c**, **6c**), MgBr₂/AgF (Scheme 5, **5d**, **6d**), or NiBr₂/PCy₃ **4a** (Scheme 5, **5e**, **6e**). If the in situ preparation of active Ni(0) complexes **5b** and **6b** was carried out for 5 min, then they had equal reactivity in the subsequent reactions (Scheme 5, **5d** (48%) vs **6d** (49%) and **5e** (89%) vs **6e** (91%)). However, prolonging the preparation of Ni(0) had a difference in its activity, and the Ni(0) prepared in the presence of AgF offered better yield, although the yields were low (Scheme 5, **5c** (21, 8%) vs **6c**

Scheme 5. Control Experiments



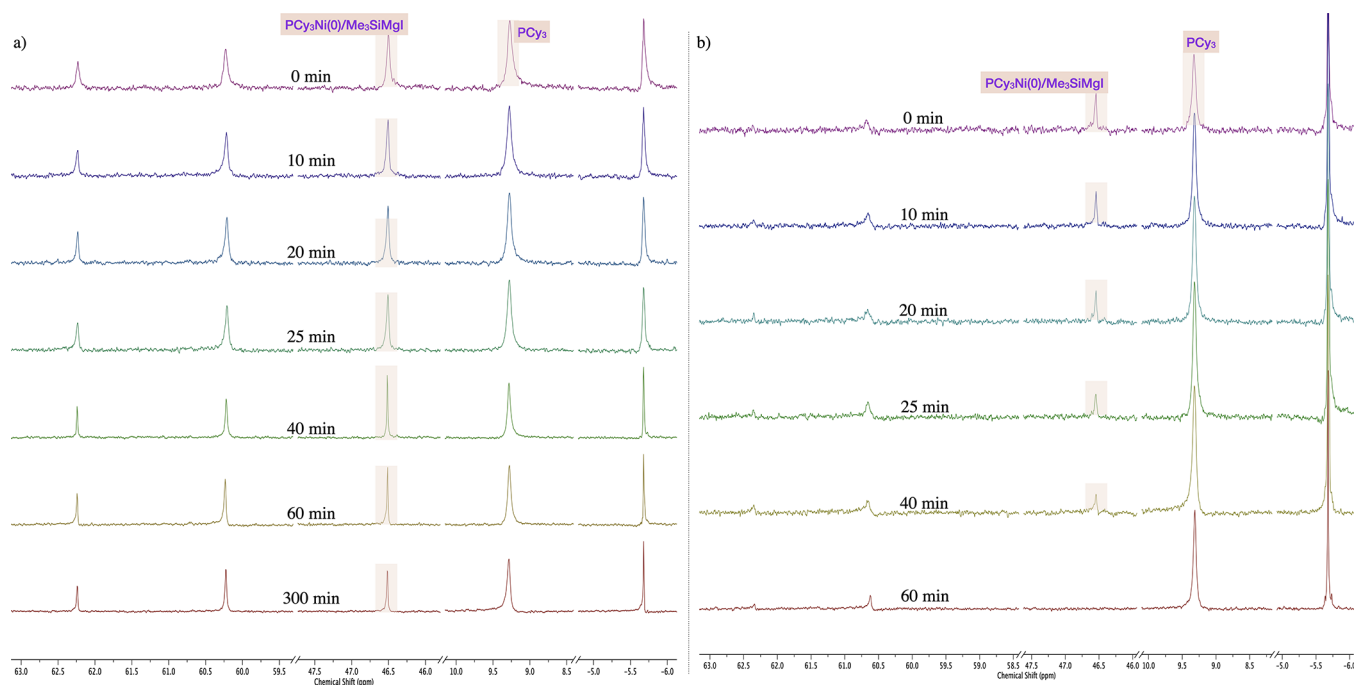


Figure 4. Stability of **4e** in the (a) presence and (b) absence of AgF.

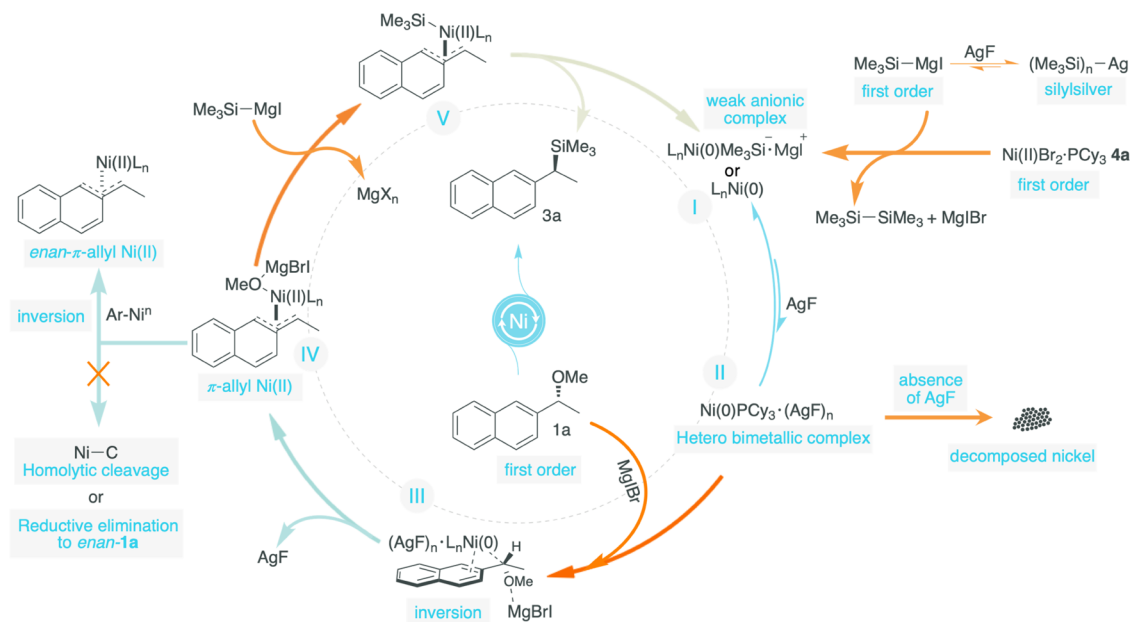


Figure 5. Mechanistic proposal.

(33, 16%)), which demonstrates the ability of AgF in the stabilization of the Ni(0) complex. The given yields are of the average of three individual runs. Further support was obtained from ^{31}P NMR, the in situ generated Ni(0) complex **4e** degrades significantly in the absence of AgF (Figure 4a vs Figure 4b and SI-25), and these experiments support the attenuation of Ni(0) degradation in the presence of AgF. The CV experiment for the mixture of **4b** and AgF showed an oxidation peak in the more positive region to that of **4b** alone (anodic shift), and this can be attributed to the formation of unidentified heterobimetallic Ni–Ag complex (SI-11). It is experimentally proven that silver salts generate heterobimetallic complexes with gold (Au–Ag)²⁴ and palladium (Pd–Ag);⁵³

it is also proven that Grignard reagents and halides form anionic-ate complexes with Fe(0)/Pd(0), which are highly reactive toward oxidative addition.^{37,39–41} Based on the above studies, one can conclude that AgF may form an unidentified bimetallic complex^{53,55} that attenuates the decomposition of the active Ni(0) complex **4e** and also accelerates the rate of oxidative addition.

A mechanistic proposal can be drawn as shown in Figure 5.^{56–58} Upon the addition of Me₃SiMgI to the pre-complex NiBr₂/PCy₃ **4a**, the Ni(0)-ate or Ni(0) complex I was generated with concomitant elimination of disilane and MgIBr,⁵⁹ and the generated Ni(0) intermediate I is in equilibrium with the Ni(0)(PCy₃)·(AgF)_n complex II, which

undergoes rapid decomposition in the absence of AgF. The intermediate **II** forms a π complex **III** with **1a**, which was further activated by MgBrI toward oxidative addition with an inversion in the configuration. A double inversion of intermediate **IV** could be responsible for the erosion of enantiospecificity.^{20,60} Transmetalation of intermediate **IV** with Me₃SiMgI led to intermediate **V**, which subsequently underwent stereospecific reductive elimination to deliver the cross-coupled product **3a**.

CONCLUSIONS

In summary, for the first time, we identified the role of AgF in the attenuation of Ni(0) degradation via the formation of an unidentified heterobimetallic Ni–Ag complex. The viable intermediate Ni(0) and Ni(I) complexes were synthesized and subjected to mechanistic investigations. Nickel's resting state could be Ni(0) or Me₃Si–Ni(0)-ate complex. Experimental data support the presence of Ni(0)/Ni(II) catalytic cycle. The in situ generated MgBrI promotes oxidative addition but is accelerated by AgF. Control experiments support the fact that the reaction is not purely nickel catalysis and excludes the role of AgF as a scavenger, oxidant, or source of organosilver intermediate.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.inorgchem.1c03108>.

Details of experimental methods and instrumentation; ¹H, ¹³C, ³¹P, and ²⁹Si NMR and UV–vis spectra; XPS and CV (PDF)

AUTHOR INFORMATION

Corresponding Author

Ramesh Rasappan – School of Chemistry, Indian Institute of Science Education and Research Thiruvananthapuram, Thiruvananthapuram 695551 Kerala, India; orcid.org/0000-0002-3209-3315; Email: rr@iisertvm.ac.in

Authors

Venkadesh Balakrishnan – School of Chemistry, Indian Institute of Science Education and Research Thiruvananthapuram, Thiruvananthapuram 695551 Kerala, India

Vetrivelan Murugesan – School of Chemistry, Indian Institute of Science Education and Research Thiruvananthapuram, Thiruvananthapuram 695551 Kerala, India

Bincy Chindan – School of Chemistry, Indian Institute of Science Education and Research Thiruvananthapuram, Thiruvananthapuram 695551 Kerala, India

Complete contact information is available at: <https://pubs.acs.org/doi/10.1021/acs.inorgchem.1c03108>

Author Contributions

[†]V.B. and V.M. contributed equally to this work. The manuscript was written through contributions of all authors. V.B. and V.M. performed the experiments, and B.C. conducted the CV study. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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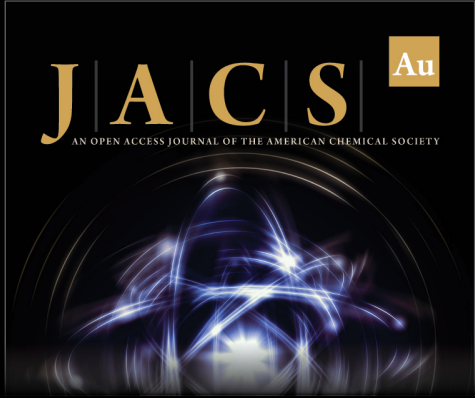
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