Abstract: We herein showcase the ability of NHC-coordinated dinuclear NiII–NiI complexes to override fundamental reactivity limits of mononuclear (NHC)NiI0 catalysts in cross-couplings. This is demonstrated with the development of a chemoselective trifluoromethylselenolation of aryl iodides catalyzed by a NiI dimer. A novel SeCF3-bridged NiI dimer was isolated and shown to selectively react with Ar–I bonds. Our computational and experimental reactivity data suggest dinuclear NiI catalysis to be operative. The corresponding NiI0 species, on the other hand, suffers from preferred reaction with the product, ArSeCF3, over productive cross-coupling and is hence inactive.

Despite the widespread existence of multinuclear metal sites in naturally occurring catalysts (enzymes), man-made homogeneous catalysis is dominated by mononuclear metal cores. This might be due to our still limited understanding of the underlying synergism and reactivity of multimetallic assemblies. A prominent example is nickel, which is of significant current synthetic interest and predominantly investigated as a monomer in synthesis,[2a,b,5] although it is featured in higher-order clusters in several enzymes.[3] Whereas the greater sustainability of nickel is advantageous, its high reactivity and mechanistic diversity can make it difficult to tame this metal in a synthetic context, impacting in particular chemoselectivity—a key requirement for applications in synthesis. The relative instabilities of NiI0 intermediates and their comparably low propensities towards transmetalation as required in traditional NiII/NiI catalysis have been identified as an origin of this reactivity behavior, leading to side reactions, undesired side products, multiple potentially reactive species, as well as catalyst deactivation.[2a,b,5]

We hypothesized that dinuclear Ni catalysis could be particularly advantageous in this context as the elementary steps, that is, oxidative addition and transmetalation, would be formally reversed, circumventing the intermediacy of poorly reactive NiI0 species that are prone to side reactions (Figure 1). Our group recently showed this concept to be viable for palladium.[6] However, whereas NiI0 complexes have been successfully synthesized,[7] detected in catalytic transformations employing typical NiI complexes,[8] used as precatalysts,[9] or implicated as mechanistic intermediates,[10] unambiguous mechanistic support and a rationale for the direct catalytic involvement of NiI dimers in cross-couplings have not been reported.

Building on our research in the area of PdI dimer catalysis,[6] which led to the development of a catalytic trifluoromethylselenolation of aryl iodides,[6c] we herein describe our efforts in exploring whether such a dinuclear catalysis concept is feasible also with the less precious and more sustainable element nickel.

The SeCF3 group features several agrochemically and pharmaceutically important properties in terms of the resulting membrane permeability and bioavailability.[11] Consequently, there have been numerous activities in devising synthetic methods to access this compound class.[12] The direct catalytic incorporation of the SeCF3 moiety is of particular interest as it may be used for late-stage manipulations of molecules. The latter concept has, however, rarely been realized,[13] it has been accomplished for aryl diazonium salts under Cu catalysis,[14] and a coupling of aryl iodides with (Me2N)2SeCF3 catalyzed by a dinuclear PdI complex has been developed by our group.[6c]

We started our investigations with assessing as to whether NiI0(cod), in combination with the NHC ligand 1,3-bis(2,6-disopropylphenyl)imidazolin-2-ylidene (SIPr) could trigger the trifluoromethylselenolation of aryl halides. In the pres-
ence of this catalyst and ligand, 4-idoanisole (1) was converted into the corresponding ArSeCF_3 product in 59% yield (Figure 2). The analogous aryl bromide and chloride did not give the ArSeCF_3 product. In all cases, the formation of the corresponding biaryl and dehalogenation were observed. The remainder was unreacted starting material. The latter observation may appear surprising at first given that Ni^0 complexes are typically highly reactive, catalyzing even cross-couplings of unactivated aryl ethers or aryl fluorides. However, the formation of biaryl species hints toward a possible explanation. Thus, such biaryl products can be an indication of a change in catalyst, arising from a ligand exchange between [L_Ni^0(Ar)(X)] intermediates to form [L_Ni^0(Ar)_2] and [L_Ni^0(X)_2]. Ultimately, biaryls are obtained upon reductive elimination. The resulting [L_Ni^0] species may then undergo comproportionation with [Ni^0(X)_2] to [Ni^0]. We speculated that the lack of significant conversion with ArBr and ArCl may be associated with the intermediacy of [Ni^0], rather than [Ni^0].

Given that we saw significantly more conversion with ArI but mainly biaryl formation with ArBr (Figure 2), we surmised that Ni^0 species are formed in these cases and take over as the active catalyst for ArI, but may not be reactive enough for ArBr. To test this, we subjected our newly synthesized SeCF_3-bridged Ni^0 dimer 4 (1 equiv) to ArI and ArBr (10 equiv). Whereas trifluoromethylselenolation was indeed observed for ArI (and 80% of the total available SeCF_3 was incorporated into ArI), there was no conversion for ArBr (Figure 2). Importantly, no biaryl species were detected in these reactions, suggesting that the Ni^0 complex does not simply serve as a precursor to Ni^0. Moreover, our kinetic studies under the same conditions gave first order in Ni^0 dimer 4, in agreement with a direct reaction between the dimer and the aryl iodide. These data strongly suggest that Ni^0 is a competent trifluoromethylselenolation species, and hence also likely a competent species in catalysis when generated from the iodine-bridged Ni^0 dimer 3 in the presence of (Me)_2NiSeCF_3. Separate studies showed that a facile displacement of the iodine bridges in 3 with (Me)_2NiSeCF_3 takes place to give 4, in analogy to our previously developed Pd-Pd chemistry.

Pleasingly, with 10 mol % of [(SIPr)Ni]^0(1)), (3) and (Me)_2NiSeCF_3 (1.5 equiv) in benzene at 45°C, a range of aryl iodides were successfully transformed into the corresponding ArSeCF_3 products (Table 1). A number of electron-rich and electron-poor aryl iodides were functionalized in good to excellent yields. The method proved to be compatible with various functional groups, such as ketone (5a and 5d), methoxy (5f), and amine (5i) moieties, as well as the pharmaceutically interesting unprotected indole motif (5e).

We hypothesized that the formally less electron-rich Ni^0 dimer might offer a platform for selective functionalizations and tested its potential to also trigger chemoselective catalytic C-SeCF_3 bond formations. Pleasingly, we observed exclusive functionalization of C–Se bonds in the presence of C–Br and C–Cl bonds (Table 1, bottom). These data showcase the superiority of an isolated dinuclear Ni^0 complex as a catalyst in the chemoselective SeCF_3 functionalization of aryl iodides without the formation of side products. In this context, it was unclear why a Ni^0 dimer would be the preferred reactive species in C–SeCF_3 couplings over Ni^0. To address this, we turned to computational studies.

We initially assessed the feasibility of a [Ni^0] catalyst to oxidatively add to PhI, PhBr, and PhCl with DFT methods. The activation barriers for oxidative addition follow the expected trend, that is, ΔG^*> follows ArI < ArBr < ArCl. We previously demonstrated that another important factor for the efficiency and scope of Ni-catalyzed functionalizations is the likelihood of the catalyst reacting with the desired product. In our case, an activated C–SeCF_3 moiety was
installed, which could also be prone to oxidative addition to [Ni]. Interestingly, we observed that the oxidative addition of PhSeCF₃ to [Ni₀] is characterized by a substantially lower activation barrier than addition of PhI, PhBr, and PhCl (Figure 3 and Table S1 in the Supporting Information). Depending on the level of theory (we considered M06L, M06, and PBE0-D3), addition of PhSeCF₃ is favored by ΔG° = 4.0 to 6.6 kcal mol⁻¹ over addition of PhI. These data suggest that [Ni₀] should preferentially react with the product PhSeCF₃ as soon as it is formed, rather than with the aryl halide substrate. The thereby generated [(SIPr)Ni²⁺(SeCF₃)]⁻(Ar) could then undergo side reactions, for example, the commonly occurring ligand exchange between two such Ni²⁺ species to ultimately generate biaryl. In line with this, our experimental studies indeed gave the corresponding biaryls (7%) when we subjected 20 mol% of Ni₀(cod)₂/SIPr to ArSeCF₃ in benzene at 45°C for 30 min. Thus the reason for the ineffectiveness of Ni²⁺ was found to be more reactive than the doubly SeCF₃-bridged Ni²⁺ 4 and also favorably adds via the triplet transition state, leading to the conversion of another equivalent of ArI into ArSeCF₃ (see the Supporting Information). The overall transformation was calculated to be exergonic (ΔG° = −10.1 kcal mol⁻¹ at M06L), and as such, to be thermodynamically driven.

As a mechanistic alternative, a Ni²⁺ monomer pathway might be followed. If open-shell Ni²⁺ monomers were to be involved, we would expect EPR activity. However, our EPR investigations of the reaction mixture of the catalytic SeCF₃ coupling of aryl iodides with 3, the substoichiometric reaction of Ni²⁺ dimer 4 with ArI (as shown in Figure 2), as well as the Ni²⁺ dimer itself in solution showed no EPR signals.
Lastly, we set out to investigate why the Ni\textsuperscript{II} dimer allows for productive catalysis, while Ni\textsuperscript{III} does not. To address this, we computationally studied the relative preference for oxidative addition to the product ArSeCF\textsubscript{3}, relative to ArI, ArBr, and ArCl once again. We employed a range of DFT methods (see the Supporting Information for details), and all consistently predicted the same reactivity trend. Interestingly, whereas Ni\textsuperscript{II} clearly preferred addition to the product ArSeCF\textsubscript{3} by $\Delta G^+ = 6.3$ kcalmol\textsuperscript{-1} (with M06L), for Ni\textsuperscript{III}–Ni\textsuperscript{II}, a different reactivity pattern is seen, substantially favoring addition to the aryl halide over the product (by $\Delta G^+ = 9.0$ kcalmol\textsuperscript{-1} at M06L; see Figure 3). As such, remarkably, nickel in oxidation state I follows a different selectivity pattern than nickel in oxidation state 0.\textsuperscript{[20]}

In conclusion, we have reported compelling data in support of NHC-derived dinuclear Ni(II) catalysis in cross-couplings with aryl iodides. The first iodine- (3) and SeCF\textsubscript{3}-bridged (4) Ni\textsuperscript{II} dimers were synthesized, fully characterized, and complex 4 was shown to react directly with aryl iodides. Using the Ni\textsuperscript{II} dimer as the catalyst avoids the formation of undesired biaryl side products through the suppression of alternative pathways and circumvents mononuclear Ni\textsuperscript{II} intermediates, which are prone to side reactions. Selective functionalization of C–I bonds over C–Br, C–Cl, and alternative functional groups was possible. The corresponding Ni\textsuperscript{III} species was found to be inferior and inactive owing to its propensity to preferentially react with the product, ArSeCF\textsubscript{3}. Our computational and experimental data suggest fundamentally different reactivity trends, that is, for Ni\textsuperscript{II}: ArSeCF\textsubscript{3} $\rightarrow$ ArI $\rightarrow$ ArBr $\rightarrow$ ArCl and for Ni\textsuperscript{III}–Ni\textsuperscript{II}: ArI $\rightarrow$ ArBr $\rightarrow$ ArCl $\rightarrow$ ArSeCF\textsubscript{3}. These data provide an example of the superior reactivity of dinuclear Ni\textsuperscript{II} over mononuclear Ni\textsuperscript{III} catalysis and showcase the potential and importance of precisely controlling and harnessing the distinct metal oxidation states in catalysis.

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Conflict of interest

The authors declare no conflict of interest.

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