## **ORGANOMETALLICS**

# A Molecular/Heterogeneous Nickel Catalyst for Suzuki–Miyaura Coupling

Ryan J. Key,<sup>†</sup> John Meynard M. Tengco,<sup>‡</sup> Mark D. Smith,<sup>†</sup> and Aaron K. Vannucci<sup>\*,†</sup>

<sup>†</sup>Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208, United States <sup>‡</sup>Department of Chemical Engineering, University of South Carolina, Columbia, South Carolina 29208, United States

**Supporting Information** 

**ABSTRACT:** A molecular/heterogeneous catalyst motif based on an earth abundant nickel catalyst and SiO<sub>2</sub> support has been designed and synthesized. Characterization and catalytic testing indicate that the molecular nickel catalyst  $[(2,2':6',2''-terpyridine-4'-benzoic acid)Ni(II)]Cl_2$  attached to a high surface area SiO<sub>2</sub> support is the active cross-coupling catalyst and increased product yields are a result of increased molecular stability of the catalyst while attached to the SiO<sub>2</sub> support. This molecular/heterogeneous motif is easily



separated from reaction mixtures and can be recycled for multiple catalytic reactions. The catalyst is active for Suzuki– Miyaura catalysis at catalyst loadings as low as 0.1 mol %, and turnover numbers nearing 2000 have been achieved.

#### INTRODUCTION

Attaching molecular catalysts to heterogeneous supports can generate a catalyst motif that merges the benefits of homogeneous catalysis (high selectivity and activity) with heterogeneous catalysis (high stability/lifetime and ease of separations). Many reports have been dedicated to the study of molecular/heterogeneous catalysts for cross-coupling reactivity.<sup>1,2</sup> While multiple successes have been reported, primarily with Pd catalysts, a critical review examined the stability of molecular/heterogeneous catalysts.<sup>3</sup> The review concluded that many of the catalysts on oxide supports decomposed into homogeneous catalysts or metal nanoparticles, and thus extensive characterization of these catalysts.

Transition-metal catalyzed cross-coupling reactions, especially those catalyzed by palladium, are extensively used in a variety of synthesis routes.<sup>4,5</sup> Of these reactions, the Suzuki– Miyaura cross-coupling reaction is the most widely used for the formation of C–C bonds.<sup>6–8</sup> While palladium catalyzed Suzuki–Miyaura coupling reactions have become textbook,<sup>9</sup> development of new cross-coupling catalysts based on abundant first row transition metals is a continual growing research area.<sup>10–13</sup> In particular, over the past decade, interest has grown and great progress has been made in the field of nickel catalyzed cross-coupling reactions.<sup>14</sup> Furthermore, the ACS Pharmaceutical Round Table has called for increased use of nickel catalysts and encouraged the development of catalyst immobilization techniques.<sup>15</sup>

Nickel-based cross-coupling catalysts offer many advantages over palladium catalysts beyond nickel being a less expensive/ more sustainable metal. Nickel catalysts have shown the ability to activate less reactive carbon electrophiles such as aryl chlorides,<sup>16–18</sup> unactivated alkyl electrophiles,<sup>19,20</sup> tertiary

© XXXX American Chemical Society

alkyls,<sup>21,22</sup> and various C–O bonds.<sup>23–25</sup> Stereoselective Suzuki–Miyaura coupling with nickel catalysts bearing inexpensive ligands has also been achieved.<sup>26,27</sup> High-valent nickel complexes have even been isolated, showing that nickel has the redox range typically only observed with palladium catalysts.<sup>28–30</sup> Mechanistic insight on nickel catalyzed C–C cross-coupling has supported high-valent nickel intermediates in cross-coupling reactions.<sup>31,32</sup> Furthermore, innovative routes for nickel catalyzed cross-coupling have been reported. Reductive coupling between two carbon electrophiles has expanded the scope of sp<sup>2</sup>–sp<sup>3</sup> C–C coupling reactions.<sup>33–35</sup> Nickel catalysts have also found a prevalent role in photoredox cross-coupling catalysis.<sup>36–39</sup>

While nickel catalysts offer clear advantages, controlled reactivity and catalyst stability can still present issues. Compared to palladium catalysts, nickel catalysts exhibit a high degree of sensitivity to the choice of solvent and base during Suzuki cross-couplings.<sup>40</sup> In addition, Suzuki couplings typically require upwards of 5-10 mol % of catalyst loadings for efficient product formation.<sup>14</sup> Higher catalyst loadings can increase the rate of bimolecular decomposition pathways for nickel catalysts. Nickel dimers formed during bimolecular decomposition pathways have been shown to be inactive species formed during nickel catalyzed Suzuki coupling reactions.<sup>31</sup> Increased concentrations of catalyst can also lead to unwanted metal poisoning of products which is a major concern for pharmaceutical development.<sup>41</sup> In addition, a vast majority of nickel catalyzed cross-coupling reactions are performed in a homogeneous solution which makes postreaction separations and catalyst recycling difficult.

```
Received: February 7, 2019
```

Molecular/heterogeneous catalysts based on molecular nickel complexes<sup>42</sup> and heterogeneous nickel catalysts in solid polymer supports have been reported.43,44 An NHCcontaining nickel complex attached to Al<sub>2</sub>O<sub>3</sub> nanoparticles actually exhibited suppressed catalytic activity compared to the analogous homogeneous catalyst in solution.<sup>42</sup> Conversely, a heterogeneous nickel-containing polystyrene-cross-linking bisphosphine polymer catalytically outperformed the analogous homogeneous Ni-BINAP catalysts (BINAP = 2,2'-bis-(diphenylphosphino)-1,1'-binaphthyl).43 The homogeneous Ni-BINAP catalyst resulted in moderate yields of desired cross-coupled products due to bimolecular decomposition pathways.<sup>45</sup> Heterogeneous nickel polymers have also exhibited greater product selectivity for the hydrosilyation of alkynes compared to homogeneous catalysts.<sup>44</sup> It is hypothesized that the geometric confinement of the polymer network led to the increased observed selectivity.

To attempt to build on the successes of molecular/ heterogeneous nickel catalysts and address the issues of high catalyst loading in homogeneous solution (bimolecular deactivation, product contamination, and difficult catalyst recycling), we have designed and synthesized a molecular/ heterogeneous nickel-based catalyst system. This catalyst system starts with the molecular catalyst [(2,2':6',2''-terpyridine-4'-benzoic acid)Ni(II)]Cl<sub>2</sub>, which is a direct analogue of our previously reported (2,2':6',2''-terpyridine)Ni(II) catalyst that was shown to be an efficient catalyst for C-C and C-N photoredox cross-coupling.<sup>20,46</sup> The addition of the benzoic acid moiety to the terpyridine ligand allows for this catalyst to be attached to solid metal oxide supports for the generation of a molecular/heterogeneous catalyst system. Acidic moieties, such as COOH, have shown the ability to bind to metal oxides in order to attach molecular catalysts to solid oxide supports.<sup>2</sup> This system, illustrated in Figure 1, simplifies catalyst



Figure 1. Illustration of molecular/heterogeneous catalyst COOH-Nil SiO<sub>2</sub>.

separation from post-reaction mixtures and leads to good catalyst recyclability. This molecular/heterogeneous catalyst has been characterized and performs Suzuki–Miyaura cross-coupling catalysis at catalyst loadings as low as 0.1 mol %.

#### RESULTS AND DISCUSSION

The previously unreported complex  $[(2,2':6',2''-\text{terpyridine-4'-benzoic acid})Ni(II)]Cl_2$  (COOH-Ni) was synthesized by dissolving a 1:1 ratio of the 2,2':6',2''-terpyridine-4'-benzoic acid ligand and nickel dichloride in ethanol and allowing the solution to stir at reflux for 4 h. Post reflux, the green solid was washed with diethyl ether and dried. Crystals suitable for X-ray crystal analysis were grown by slow evaporation of dichloro-

methane. Elemental Analysis: Calculated for  $[NiC_{22}H_{15}N_3O_2-Cl_2]0.5H_2O$ : C 53.71%; H 3.07%; N 8.54%. Found: C 53.81%; H 3.03%; N 8.32%.

**COOH-Ni** crystallizes in the monoclinic system and is shown in Figure 2. The pattern of systematic absences in the



Figure 2. Illustration of molecular/heterogeneous catalyst COOH-Nil SiO<sub>2</sub>.

intensity data was consistent with the space group  $P2_1/n$ . The asymmetric unit consists of one  $NiCl_2(H_2O)(C_{22}H_{15}O_2)$ complex and one noncoordinated, partially occupied water molecule. Around the nickel center, the chloride and coordinated water ligands are disordered. Two sites were modeled as a disordered mixture of  $Cl^{-}/H_2O$ ; the third anion site was modeled with a split chloride position. Further details about the crystal structure can be found in the Supporting Information. The distance between the nickel center and the middle nitrogen atom of the (2,2':6',2''-terpyridine-4'-benzoic acid) ligand is 1.99 Å, and the distances from the nickel center to the two nitrogen atoms in the equatorial plane are 2.08 Å each. The average distance to the chloride atoms is 2.38 Å. These distances are all within 0.02 Å when compared to the previously reported crystal structure for the (2,2':6',2''- terpyridine)Ni(II) complex,<sup>20</sup> indicating the benzoic acid moiety does not significantly alter the electronic structure or geometry of the nickel metal center.

Functionalization of high surface area SiO<sub>2</sub> particles with the molecular catalyst was achieved by soaking the SiO<sub>2</sub> particles in a methanol solution containing the catalyst. This catalyst loading procedure is analogous to previously reported metal oxide derivatization by molecular complexes.<sup>48</sup> After soaking, the particles were filtered from solution, rinsed with cold methanol, dried, and then characterized. The resulting molecular/heterogeneous catalyst (COOH-NilSiO<sub>2</sub>) was characterized with ICP-MS and XRD. The paramagnetic nature of the nickel complex prevented accurate characterization through solid-state NMR spectroscopy. ICP-MS analysis indicated that COOH-NilSiO<sub>2</sub> contained 0.56 wt % nickel. This equates to  $3.9 \times 10^{-8}$  mol of catalyst per m<sup>2</sup> of silica support. X-ray diffraction analysis of COOH-NilSiO2 (Figure S2) did not show any evidence for crystalline nickel particles when compared to fresh SiO<sub>2</sub> particles. This result suggests that the molecular nickel catalyst, and not metallic nickel particles, is present on the  $SiO_2$  support. It is worth noting that the detection limit of the XRD instrument used is 1.0 nm crystalline particles.<sup>49,50</sup>

Further characterization of the COOH-NilSiO<sub>2</sub> catalyst was carried out through control reactions and catalytic optimization reactions as summarized in Tables 1-3. The Suzuki–

### Table 1. Optimization of Suzuki–Miyaura Cross-Coupling with COOH-NilSiO<sub>2</sub> Catalyst



<sup>*a*</sup>Standard conditions: 100 mg of COOH-NilSiO<sub>2</sub> ( $1.2 \times 10^{-6}$  mol of COOH-Ni), 0.68 mmol of iodotoluene, 0.82 mmol of benzene boronic acid, 1.7 mmol of K<sub>3</sub>PO<sub>4</sub>, 20 mL of dioxane. <sup>*b*</sup>Yields determined by GC–MS.

Miyaura coupling between 4-iodotoluene and benzeneboronic acid was chosen as the test reaction. Common reactions conditions-equivalents of substrates, base used, and solvent-were chosen for a general comparison to literature. The chosen standard reaction conditions (row 1, Table 1) contained 100 mg of COOH-NilSiO<sub>2</sub>, which is equivalent to  $1.2 \times 10^{-6}$  mol of the molecular COOH-Ni catalyst, 0.68 mmol of iodotoluene, 1.2 equiv of phenylboronic acid, and 2.5 equiv of K<sub>3</sub>PO<sub>4</sub> base. A 24 h reaction in dioxane solvent heated to reflux resulted in a 75% yield of the desired cross-coupled product. Reactions of 6 and 18 h resulted in 20% and 51% yields, respectively, while reactions performed for longer than 24 h did not result in a significant increase in product yield. Next, the equivalents of base needed to promote the reaction were varied. Bases are believed to be necessary to promote transmetalation reactions between the catalyst and the boronic acid substrates.<sup>51</sup> Conversely, Lewis acids have been shown to promote nickel catalyzed cross-coupling reactivity, and thus the acidity of the SiO<sub>2</sub> support may play a role in catalysis. As can be seen in Table 1, complete removal of the  $K_3PO_4$  base resulted in no observed cross-coupled products. The use of 1.25 equiv of base led to 72% product yield, consistent with 2.5 equiv. Lastly, increasing the concentration of base up to 5.0 equiv had a detrimental effect on products yields. Excess base has previously been shown to decrease nickel catalyzed crosscoupled yields.<sup>40</sup> The results for the base variance experiments, therefore, have determined a range of base concentrations suitable for this catalyst motif and indicate that the acidic sites on SiO<sub>2</sub> likely do not play a large role in promoting catalysis. To further examine if SiO<sub>2</sub> has any direct reactivity with the substrates, a reaction was performed with just SiO<sub>2</sub> added to

the reaction solution. No cross-coupled products or dimer formation was observed.

Metal oxides other than  $SiO_2$  were also examined. The **COOH-Ni** molecular catalyst loaded onto  $TiO_2$ ,  $ZrO_2$ , and  $Al_2O_3$  individually all lead to poor product formation. These results are likely attributed to how the metal oxide reacts to the dioxane solvent. Upon heating, the  $TiO_2$  particles immediately clumped up into rock-like particles that could not be broken up with vigorous stirring. These clumps greatly decreased the exposed surface area of the particles, thus limiting catalysis. Similar results were observed for  $Al_2O_3$  particles which immediately adhered to the walls of the round-bottom flask. Lastly,  $ZrO_2$  oxide particles formed a milky solution that turned yellow upon heating, indicating  $ZrO_2$  is not stable in hot dioxane.

To examine the possible benefit of utilizing the molecular/ heterogeneous catalyst **COOH-NilSiO**<sub>2</sub>, homogeneous catalytic reactions were performed using **COOH-Ni** as the catalyst in solution, and those results are shown in Table 2. A reaction

 Table 2. Catalytic Suzuki–Miyaura Cross-Coupling Results

 from Homogeneous Catalysts



<sup>*a*</sup>Standard conditions: 0.68 mmol of iodotoluene, 0.82 mmol of benzene boronic acid, 1.7 mmol of  $K_3PO_4$ , 20 mL of dioxane. <sup>*b*</sup>Yields determined by GC–MS. <sup>*c*</sup>tpy is 2,2':6',2''-terpyridine.

performed with 0.1 mol % COOH-Ni, roughly equivalent to the catalyst loading for COOH-NilSiO<sub>2</sub>, did not result in any observed cross-coupled product. Furthermore, a mixture of fresh SiO<sub>2</sub> particles and 0.1 mol % COOH-Ni catalyst did not result in any cross-coupled product formation, once again indicating that the preformed COOH-NilSiO<sub>2</sub> catalyst is necessary for efficient Suzuki-Miyaura cross-coupling. Increasing the homogeneous catalyst loading to 10 mol % did result in a 25% yield of cross-coupled product. These homogeneous catalysis results indicate that the molecular catalyst in homogeneous solution possesses the inherent activity to promote Suzuki cross-coupling, but catalyst lifetime may limit the overall product yields. The increased stability imparted on the molecular catalyst by attaching it to a heterogeneous support is a clear advantage that is obtained by using the molecular/heterogeneous COOH-NilSiO<sub>2</sub> catalyst.

As mentioned previously, nickel dimers formed from monomeric nickel catalysts have been shown to be inactive for Suzuki cross-couplings.<sup>31</sup> Potential nickel catalyst decomposition products were thus tested for possible catalytic activity with the results in Table 2. The  $[(\mu-Cl)Ni(tpy)]_2^{2+}$  dimer was examined in homogeneous solution, but no cross-coupled product was observed. In addition,  $[tpy_2Ni]Cl_2$  was also examined, and no cross-coupled products were obtained; however, deborylation products were observed. Rainey nickel was tested to examine if metal nickel particles exhibited catalytic activity. The metallic nickel produced little to no desired cross-coupled products, but some homocoupled product of the boronic acid substrate was observed. Thus, the monomeric **COOH-Ni** catalyst appears to be the only active Ni species for the desired Suzuki coupling, and preventing of the decomposition of this catalyst is essential for prolonged catalytic activity.

The results shown in Table 1 and Table 2 indicate that the COOH-NilSiO<sub>2</sub> catalyst isolates individual COOH-Ni molecules and helps prevent bimolecular decomposition of the catalyst, which can occur in homogeneous solution. Preventing the bimolecular decomposition of the catalyst increases catalyst lifetime, thus increasing cross-coupled product yields. Alternate decomposition routes, such as reduced nickel nanoparticle formation, or ligand-free nickel salt adhering to the SiO<sub>2</sub> support could possibly occur. Furthermore, these ligand-free nickel species could be active cross-coupling catalysts.<sup>3</sup> With this possibility in mind, a series of control reactions were performed to gain further insight into the active form of the nickel catalyst, and the results of these experiments are shown in Table 3.

 Table 3. Molecular/Heterogeneous Catalyst Identity

 Experiments



"Standard conditions: 100 mg of  $SiO_2$  supported catalyst unless otherwise noted, 0.68 mmol of iodotoluene, 0.82 mmol of benzene boronic acid, 1.7 mmol of K<sub>3</sub>PO<sub>4</sub>, 20 mL of dioxane. <sup>b</sup>Yields determined by GC–MS. <sup>c</sup>Two-step loading procedure as described in the experimental procedure. <sup>d</sup>One-step loading procedure as described in the experimental procedure.

Initially, two different procedures for loading the nickel catalyst onto the SiO<sub>2</sub> support, described in the Experimental Section, were examined. Row 1 of Table 3 is identical to row 1 of Table 1 and shows the results of the two-step loading procedure where the ligand was first bound to the SiO<sub>2</sub> surface, followed by addition of NiCl<sub>2</sub> salt to synthesize the **COOH-Nil** SiO<sub>2</sub> catalyst. This synthesis procedure resulted in 0.56 wt % of nickel on SiO<sub>2</sub> as confirmed by ICP-MS. Row 2 of Table 3 shows the results for the one-step loading method. This one-step method was performed by first isolating the molecular nickel catalyst, followed by loading the catalyst onto the support to also generate **COOH-NilSiO<sub>2</sub>**. This loading procedure resulted in 1.05 wt % of nickel on SiO<sub>2</sub>. As can be seen from Table 3, both loading procedures resulted in

comparable cross-coupled product yields. Assuming molecular integrity of the catalyst during the cross-coupling reactions, these results show that catalysts of this molecular/heterogeneous motif can be easily synthesized from mild loading procedures.

To examine the molecular integrity and possibility of ligandfree nickel species being active catalysts, a series of further experiments were performed. Table 2 shows that the homogeneous nickel catalyst and possible molecular decomposition products do not result in product yields nearly as high as using the COOH-NilSiO<sub>2</sub> catalyst; however, nonmolecular nickel particles could leach from the catalyst into solution. To test if any leached species could be the active catalyst, postreaction solutions were tested for catalytic activity. To perform this test, a catalytic cross-coupling reaction was performed using COOH-NilSiO<sub>2</sub> as the catalyst. After the initial reaction, the solid COOH-NilSiO<sub>2</sub> catalyst was filtered out of the solution and product yield was determined with GC-MS. Then extra substrates were added to the filtrate, and a second reaction was performed without the presence of solid COOH-NilSiO<sub>2</sub>. No additional products were obtained, indicating that the post-reaction filtrate did not contain any active crosscoupling species. This result is consistent with the catalyst recycle studies shown in Table 4 and discussed later.

The catalytic activity of nickel particles on the surface of the SiO<sub>2</sub> support was also explored. To examine reduced nickel nanoparticles as possible catalysts, we synthesized a 0.5 wt % nickel nanoparticle catalyst on the SiO<sub>2</sub> support using charge enhanced dry impregnation (CEDI).<sup>52</sup> The CEDI particles were then tested under the standard conditions from Table 1 and resulted in a 12% yield of the desired cross-coupled catalyst. Thus, reduced nickel nanoparticles can catalyze Suzuki cross-coupling reactivity, but the yields are  $5 \times$  lower than what is observed for the molecular/heterogeneous COOH-NilSiO<sub>2</sub> catalyst. To gain further insight into the reactivity of the CEDI particles, a mercury drop test was performed, as mercury has been shown to poison heterogeneous nanoparticle catalysts.<sup>53</sup> This test was carried out by placing 2 g of mercury into a reaction containing 100 mg of the CEDI catalyst. Table 3 shows that the addition of a mercury drop to the CEDI sample completely inhibited catalysis and no product yield was obtained. Conversely, adding mercury to a reaction containing the molecular/heterogeneous COOH-NilSiO<sub>2</sub> catalyst did not result in a significant change in observed product yield (75% vs 71%). The difference between the CEDI samples and the COOH-NilSiO<sub>2</sub> catalyst in response to mercury strongly suggests that nickel nanoparticles are not present as active catalysts during reactions catalyzed by COOH-NilSiO<sub>2</sub>.

Ligand-free nickel chloride salt was then examined for catalytic activity. The first experiment involved loading NiCl<sub>2</sub> salt onto the SiO<sub>2</sub> support prior to the reaction. Following the standard overnight loading procedure, the NiCl<sub>2</sub> loaded SiO<sub>2</sub> particles contained 5.4 wt % nickel compared to only 0.56 wt % nickel of the **COOH-NilSiO**<sub>2</sub> catalyst. The lower nickel weight percent loading of the **COOH-NilSiO**<sub>2</sub> catalyst could arise from the geometrically larger 2,2':6',2''-terpyridine-4'-benzoic acid ligand occupying more space on the SiO<sub>2</sub> support compared to NiCl<sub>2</sub> salt. Following the standard catalyst testing reaction, the NiCl<sub>2</sub>ISiO<sub>2</sub> particles did give a 17% cross-coupled product yield. Once again, this result shows that ligand-free nickel can act as a moderate catalyst for Suzuki cross-coupling, but the yields are not as high as the **COOH-NilSiO**<sub>2</sub> catalyst.

A mercury drop test was also performed on the NiCl<sub>2</sub>|SiO<sub>2</sub> catalyst, as shown in Table 3. In contrast to the CEDI nickel nanoparticles, mercury did not have an effect on the catalytic activity of NiCl<sub>2</sub>|SiO<sub>2</sub>, suggesting that the NiCl<sub>2</sub> salt may leach from the SiO<sub>2</sub> support during catalysis. Therefore, a reaction mixture containing 10 mol % NiCl<sub>2</sub> (approximately equivalent to the nickel mol % loading for 100 mg of NiCl<sub>2</sub>|SiO<sub>2</sub>) in the absence of SiO<sub>2</sub> was tested for catalytic activity. Statistically, the same yield of cross-coupled product was obtained from NiCl<sub>2</sub> in solution compared to NiCl<sub>2</sub>|SiO<sub>2</sub>. This result also shows that nearly 100× the concentration of NiCl<sub>2</sub> salt is required to obtain 5× less product compared to the molecular/ heterogeneous **COOH-NilSiO<sub>2</sub>** catalyst.

Table 4. Cross-Coupled Product Yields from Consecutive Reactions Using Recycled COOH-NilSiO<sub>2</sub>

	$\rightarrow - \bigcirc - \bigcirc \bigcirc$
experiment <sup>a</sup>	% yield
1	76
2	74
3	72
4	72
5	37
<sup>a</sup> Standard conditions used as described in Table 1.	

Lastly, the need for the benzoic acid moiety of the ligand was examined. Acidic moieties, such as COOH, have shown the ability to bind to metal oxides in order to attach molecular catalysts to solid oxide supports;<sup>47</sup> however, nickel catalysts have been shown to bind to activated silica through the nickel metal.<sup>54</sup> Following the standard overnight loading procedures, the solid SiO<sub>2</sub> support was soaked in a solution of (2,2':6',2''-terpyridine)Ni(II) (tpyNi). These particles were then examined for cross-coupling reactivity, but no catalysis or product formation was observed. This result indicates that the benzoic acid moiety is necessary to adhere the molecular catalyst to the surface of SiO<sub>2</sub>, and this result is consistent with the low loading homogeneous catalyst results in Table 1.

The results summarized above in Tables 1-3 all indicate that the molecular/heterogeneous cross-coupling catalyst COOH-NilSiO<sub>2</sub> is much more active compared to ligandfree nickel species and exhibits a greater lifetime than the COOH-Ni catalyst in homogeneous solution. The extended lifetime and solid nature of the COOH-NilSiO<sub>2</sub> catalyst should therefore be easily separated from reaction mixtures and be recyclable. In relation to the first aspect, the solid COOH-Nil SiO<sub>2</sub> catalyst was easily separated from product mixtures through filtration without the need for column chromatography. To test the recyclability, the used, filtered catalyst was rinsed, dried, and added to a fresh reaction solution. This procedure was repeated for multiple reactions, and Table 4 shows the results of those trials. The molecular/heterogeneous COOH-NilSiO<sub>2</sub> catalyst exhibited consistent catalyst activity and product formation over the course of four consecutive reactions. The percent yields reported in Table 4 equate to 1700 catalytic turnovers before catalyst deactivation is observed in the fifth reaction. These experiments were repeated, and catalyst deactivation was once again observed during the fifth reaction. We hypothesize that loss of nickel catalyst from the surface of the SiO<sub>2</sub> support over the course of five reactions and filtrations hits a critical point by the fifth reaction and product formation begins to drop due to low nickel catalyst loadings.

Post-reaction analysis of the molecular/heterogeneous **COOH-NilSiO**<sub>2</sub> catalyst was performed with ICP-MS and XRD. Once again, XRD patterns showed no evidence of Ni nanoparticle formation on the surface of the SiO<sub>2</sub> support. This result, in conjunction with the results from Tables 2 and 3, supports that the molecular **COOH-Ni** catalyst attached to the SiO<sub>2</sub> support is responsible for the observed catalytic activity. ICP-MS analysis of the used catalyst showed that only 78 mg/g of the original 687 mg/g of nickel remained on the SiO<sub>2</sub> support. This leaching of the catalyst is not ideal and is the likely cause for eventual catalyst deactivation. Though this result also corroborates that the molecular catalyst on the SiO<sub>2</sub> support is the active catalyst and molecular nickel catalyst in homogeneous solution quickly deactivates.

To ensure that the molecular/heterogeneous catalyst  $COOH-Ni|SiO_2$  is generally capable of Suzuki–Miyaura cross-coupling reactions, a substrate scope for this catalyst was examined. Figure 3 shows that coupling of 4-*tert*-butyl-



Figure 3. Catalytic Suzuki–Miyaura cross-coupling aryl iodides and aryl boronic acids. 34 mM aryl iodide, 41 mM boronic acid in 20 mL of 1,4-dioxane. % yields are isolated yields and based on limiting reagent.

benzeneboronic acid with 4-iodotoluene gave comparable yields to the coupling of benzeneboronic acid with 4iodotoluene. A strong electron donating methoxy group on the boronic acid increased yields of the cross-coupled product up to 92%. This catalyst was also amenable to coupling boronic acids with an electron withdrawing  $CF_3$  group. The coupling reaction involving 4-fluorobenzeneboronic acid resulted in 80% yield, showing this catalyst exhibits functional group tolerance to pharmaceutically important fluorine atoms. No coupling at the fluoro position was observed. Boronic acids with a functional group *ortho* to the acid were also successfully coupled as product 6 was obtained in 50% yield. Naphthylboronic acids and aryl iodides were also tolerated as evidenced by products 7 and 8.

Next, the cross-coupling of various aryl halides with aryl boronic acids was examined. Entry 9 (Figure 4) shows the general trend of reactivity for COOH-NilSiO<sub>2</sub> toward aryl halides. Aryl iodides were generally more efficient coupling partners compared to aryl bromides, while no reactivity was



**Figure 4.** Catalytic Suzuki–Miyaura cross-coupling aryl boronic acids and aryl halides. 34 mM aryl halide, 41 mM boronic acid in 20 mL of 1,4-dioxane. % yields are isolated yields and based on limiting reagent.

observed with aryl chlorides. This reactivity trend is consistent with previously reported nickel catalysts containing tridentate polypyridyl ligands.<sup>20</sup> Good yields were, however, obtained from aryl bromide coupling partners with electron withdrawing groups in both the *para* and *meta* positions (entries 10–12). Aryl iodides containing the electron donating methoxy group were also successfully coupled to form products 13 and 14. Although, electron donating groups on the boronic acid are more tolerated by this catalyst compared to electron donating groups on the aryl halide. Product 13 was only obtained in 58% yield starting with phenylboronic acid and 4-methoxyiodobenzene, while a closely related product (entry 3, Figure 3) was obtained in 92% yield through coupling of 4-methoxyphenylboronic acid and 4-iodotoluene. Coupling involving iodonaphthalene was also successful (product 15).

#### CONCLUSIONS

A molecular/heterogeneous catalyst system for Suzuki-Miyaura cross-coupling has been designed, synthesized, and characterized. The catalyst is composed of an earth-abundant Ni molecular catalyst and an inexpensive amorphous SiO<sub>2</sub> support. The catalyst exhibits activity at low catalyst loadings (approximately 0.1 mol % based on the molecular nickel catalyst) and good functional group tolerance. Control reactions tested possible homogeneous and heterogeneous catalyst decomposition species for catalytic activity. All of the control reactions showed that potential catalyst decomposition species were either not as active or not as robust as COOH-Nil  $SiO_{2}$  and these decomposition species could not account for the observed catalytic activity of COOH-NilSiO<sub>2</sub>. Eventual catalyst leaching from the surface of the support leads to catalyst deactivation, though the catalyst is easily recycled and turnover numbers of 1700+ were observed before deactivation. This loss of the molecular catalyst from the solid support shows the need to design new molecular/heterogeneous systems with stronger immobilization of the catalyst onto the support.55 Obtaining good yields of cross-coupled products from a low-loading of a nonprecious metal catalyst, however, shows promise for future studies for this catalyst motif for cross-coupling reactions.

#### EXPERIMENTAL SECTION

**Materials.** All reagents were used as received from the manufacturer and were used without any further purification.  $[(\mu-Cl)Ni(tpy)]_2$  was prepared by previously reported methods.<sup>20</sup> The silica oxide support used throughout was Aerosil 300 (A300, Evonik). A300 is amorphous SiO<sub>2</sub> with a 300 m<sup>2</sup>/g surface area and an average particle size of 20 nm.

Instrumentation. X-ray diffraction (XRD) analysis was carried out with a benchtop powder X-ray diffractometer (Rigaku Miniflex-II with a silicon strip detector, D/teX Ultra, capable of detecting nanoparticles down to 1.0 nm) with Cu K $\alpha$  radiation ( $\lambda$  = 1.5406 Å), operated at 15 kV and 30 mA. Powder samples were loaded on a zerobackground holder, and scans were made from the  $20-80^{\circ} 2\theta$  range, with a scan rate of  $3.0^{\circ} 2\theta$ /min. Inductively coupled plasma-mass spectrometry (ICP-MS, Finnigan ELEMENT XR double focusing magnetic field) analysis was used for the analysis of nickel present on silica with rhenium as internal standard. A quartz torch and injector (Thermo Fisher Scientific) and a 0.2 mL/min Micromist U-series nebulizer (GE, Australia) were used for sample introduction. GC-MS (Shimadzu QP-2010S) analysis was performed with a 30 m long Rxi-5 ms (Restek) separation column with a 0.25 mm id, and the oven temperature program was 40 °C for 0.5 min, followed by a 10 °C/min ramp to 280 °C and held for 2 min. Mass spectrometer electron ionization was at 70 eV, and the spectrometer was scanned from 1000 to 50 m/z at low resolution. NMR spectroscopy was performed using a Bruker Advance III HD 300. Data were processed using Bruker TopSpin software. <sup>1</sup>H NMR spectroscopy was performed using a 300 MHz instrument using deuterated chloroform or deuterated methylene chloride as the solvent with a calibrated peak at 7.26 or 5.32 ppm, respectively. <sup>13</sup>C NMR was conducted on a 300 MHz instrument set to a frequency of 75 MHz using chloroform or methylene chloride as the solvent and a calibrated solvent peak at 77.33 or 54.00 ppm. Details of the single crystal X-ray crystallography can be found in the Supporting Information.

Synthesis of [(2,2'.6',2''-Terpyridine-4'-benzoic acid)Ni(II)]-Cl<sub>2</sub>. To a round-bottom flask, 0.100 g (0.28 mmol) of 2,2'.6',2''terpyridine-4'-benzoic acid was dissolved in 100 mL of ethanol and heated to 60 °C. To this solution, 0.067 g of NiCl<sub>2</sub>·6H<sub>2</sub>O (0.28 mmol) was added and stirred for 3 h. The solution was then placed on the rotary evaporator and evaporated to dryness. The solid was washed several times with ethanol and diethyl ether. The resulting green solid was then isolated and dried in an oven overnight. Yield: 0.125 g, 0.113 mmol. Elemental Analysis for [NiC<sub>22</sub>H<sub>15</sub>N<sub>3</sub>O<sub>2</sub>Cl<sub>2</sub>]-0.5H<sub>2</sub>O: Calculated: C 53.71%; H 3.07%; N 8.54%. Actual: C: 53.81%; H: 3.03%; N: 8.32%.

**Synthesis of tpy<sub>2</sub>Ni.** To a round-bottom flask, 150 mg of (2,2': 6',2"-terpyridine)Ni was dissolved in 20 mL of acetonitrile. To this solution, 23 mg of potassium *tert*-butoxide was added, and the solution was stirred at room temperature for 24 h. The resulting brown solution was dried on the rotary evaporator to produce a brown solid. Yield: 0.105 g, 0.20 mmol. ESI MS two most prominent peaks 166 m/z ( $C_{17}H_{14}N_4Ni^{2+}$ , tpyNi(MeCN)) and 262 m/z ( $C_{30}H_{22}N_6Ni^{2+}$ , tpy<sub>2</sub>Ni<sup>2+</sup>), matching previously reported data for tpy<sub>2</sub>Ni.<sup>56</sup>

**Preparation of COOH-NilSiO<sub>2</sub>.** Two-step method: To a 500 mL media bottle, 1.00 g of Aerosil A300 SiO<sub>2</sub> and 100 mL of methanol were mixed. To this solution, 0.100 g of 2,2':6',2''-terpyridine-4'-benzoic acid and 0.067 g of NiCl<sub>2</sub>·6H<sub>2</sub>O were dissolved. The solution was allowed to settle overnight. The solid was then vacuum filtered, rinsed with hexanes, and dried before characterization or catalytic reactions.

One-step method: 0.100 g of (2,2':6',2''-terpyridine-4'-benzoic acid)NiCl<sub>2</sub> (**COOH-Ni**) was dissolved in 100 mL of deionized water. To this solution, NaBF<sub>4</sub> was added, resulting in green colored solid to precipitate out of solution. NaBF<sub>4</sub> was added until no additional precipitate formation was observed. The solid was filtered from the solution and dried. A 0.1 mmol solution of the resulting (2,2':6',2'')-terpyridine-4'-benzoic acid)Ni(BF<sub>4</sub>)<sub>2</sub> complex was generated in methanol, and 1.00 g of Aerosil A300 was added to the solution

and allowed to sit overnight. The solid was then vacuum filtered, rinsed with hexanes, and dried before catalytic reactions.

Preparation of Reduced Nickel Nanoparticles on SiO<sub>2</sub>. The silica (Aerosil 300, Evonik) supported Ni nanoparticle catalyst was synthesized using the method of charge enhanced dry impregnation (CEDI),<sup>52</sup> using parameters for strong electrostatic adsorption (SEA) of hexaamminenickel(II) complex on a silica surface.<sup>5</sup> impregnating solution was prepared by dissolving Ni(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O in 14 N NH<sub>4</sub>OH solvent. The amount of solvent required was based on pore filling of the support to incipient wetness (3.0 mL/g), and the amount of salt added was determined from the desired Ni loading of 0.5% by weight for the final catalyst. The solution was added dropwise to the silica powder with intense agitation to ensure distribution into the pores. The resulting cake was dried in an oven (120 °C, 12 h) and subsequently ground up. The powder was subjected to reduction in a horizontal tubular furnace, under 250 sccm flow of 20% H<sub>2</sub>, with He comprising the remaining balance, ramping the temperature at 5  $^{\circ}C/$ min to 500 °C and holding the temperature for 1 h, before being cooled.

**General Catalytic Reaction Scheme.** In a round-bottom flask, 0.100 g of **COOH-NilSiO**<sub>2</sub>, 0.68 mmol of aryl halide, 0.82 mmol of boronic acid, and 1.7 mmol of  $K_3PO_4$  were added to 20 mL of dioxane. This solution was heated to 115 °C and kept at reflux for 24 h. The resulting solution was concentrated, and the product was isolated by preparative scale TLC.

For recycle experiments, the solid catalyst was collected post reaction via suction filtration, rinsed with hexanes, and dried. The collected catalyst was then placed in a new reaction following the general procedure described above.

#### ASSOCIATED CONTENT

#### **S** Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organo-met.9b00082.

X-ray crystallography details, <sup>1</sup>H and <sup>13</sup>C NMR data, and references to previously reported products (PDF)

#### **Accession Codes**

CCDC 1896060 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data\_request/cif, or by emailing data\_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

#### AUTHOR INFORMATION

#### Corresponding Author

\*E-mail: vannucci@mailbox.sc.edu.

#### ORCID 💿

Aaron K. Vannucci: 0000-0003-0401-7208

#### Notes

The authors declare no competing financial interest.

#### ACKNOWLEDGMENTS

The authors gratefully acknowledge support for this work by the University of South Carolina.

#### REFERENCES

(1) Serna, P.; Gates, B. C. Molecular Metal Catalysts on Supports: Organometallic Chemistry Meets Surface Science. *Acc. Chem. Res.* **2014**, *47*, 2612–2620.

(2) Al-Hashimi, M.; Qazi, A.; Sullivan, A. C.; Wilson, J. R. H. Dithio palladium modified silicas—New heterogeneous catalysts for Suzuki cross-coupling reactions. *J. Mol. Catal. A: Chem.* **2007**, *278*, 160–164.

(3) Phan, N. T. S.; Van Der Sluys, M.; Jones, C. W. On the Nature of the Active Species in Palladium Catalyzed Mizoroki–Heck and Suzuki–Miyaura Couplings – Homogeneous or Heterogeneous Catalysis, A Critical Review. *Adv. Synth. Catal.* **2006**, *348*, 609–679. (4) Jana, R.; Pathak, T. P.; Sigman, M. S. Advances in Transition Metal (Pd,Ni,Fe)-Catalyzed Cross-Coupling Reactions Using Alkylorganometallics as Reaction Partners. *Chem. Rev.* **2011**, *111*, 1417–1492.

(5) Gildner, P. G.; Colacot, T. J. Reactions of the 21st Century: Two Decades of Innovative Catalyst Design for Palladium-Catalyzed Cross-Couplings. *Organometallics* **2015**, *34*, 5497–5508.

(6) Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457–2483.

(7) Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize. *Angew. Chem., Int. Ed.* **2012**, *51*, 5062–5085.

(8) Martin, R.; Buchwald, S. L. Palladium-Catalyzed Suzuki– Miyaura Cross-Coupling Reactions Employing Dialkylbiaryl Phosphine Ligands. *Acc. Chem. Res.* **2008**, *41*, 1461–1473.

(9) Negishi, E. Handbook of Organopalladium Chemistry for Organic Synthesis; John Wiley & Sons Inc.: New York, 2002.

(10) Netherton, M. R.; Fu, G. G. Nickel-Catalyzed Cross-Couplings of Unactivated Alkyl Halides and Pseudohalides with Organometallic Compounds. *Adv. Synth. Catal.* **2004**, 346, 1525–1532.

(11) Crockett, M. P.; Tyrol, C. C.; Wong, A. S.; Li, B.; Byers, J. A. Iron-Catalyzed Suzuki–Miyaura Cross-Coupling Reactions between Alkyl Halides and Unactivated Arylboronic Esters. *Org. Lett.* **2018**, *20*, 5233–5237.

(12) Anderson, T. J.; Jones, G. D.; Vicic, D. A. Evidence for a NiI Active Species in the Catalytic Cross-Coupling of Alkyl Electrophiles. *J. Am. Chem. Soc.* **2004**, *126*, 8100–8101.

(13) Sherry, B. D.; Fürstner, A. The Promise and Challenge of Iron-Catalyzed Cross Coupling. Acc. Chem. Res. 2008, 41, 1500–1511.

(14) Ananikov, V. P. Nickel: The "Spirited Horse" of Transition Metal Catalysis. ACS Catal. 2015, 5, 1964–1971.

(15) Bryan, M. C.; Dunn, P. J.; Entwistle, D.; Gallou, F.; Koenig, S. G.; Hayler, J. D.; Hickey, M. R.; Hughes, S.; Kopach, M. E.; Moine, G.; Richardson, P.; Roschangar, F.; Steven, A.; Weiberth, F. J. Key Green Chemistry research areas from a pharmaceutical manufacturers' perspective revisited. *Green Chem.* **2018**, *20*, 5082–5103.

(16) Liu, N.; Wang, L.; Wang, Z.-X. Room-temperature nickelcatalysed cross-couplings of aryl chlorides with arylzincs. *Chem. Commun.* **2011**, 47, 1598–1600.

(17) Jones, K. D.; Power, D. J.; Bierer, D.; Gericke, K. M.; Stewart, S. G. Nickel Phosphite/Phosphine-Catalyzed C–S Cross-Coupling of Aryl Chlorides and Thiols. *Org. Lett.* **2018**, *20*, 208–211.

(18) Gatien, A. V.; Lavoie, C. M.; Bennett, R. N.; Ferguson, M. J.; McDonald, R.; Johnson, E. R.; Speed, A. W. H.; Stradiotto, M. Application of Diazaphospholidine/Diazaphospholene-Based Bisphosphines in Room-Temperature Nickel-Catalyzed C(sp2)–N Cross-Couplings of Primary Alkylamines with (Hetero)aryl Chlorides and Bromides. ACS Catal. 2018, 8, 5328–5339.

(19) Xi, Z.; Liu, B.; Chen, W. Room-Temperature Kumada Cross-Coupling of Unactivated Aryl Chlorides Catalyzed by N-Heterocylic Carbene-Based Nickel(II) Complexes. J. Org. Chem. **2008**, 73, 3954– 3957.

(20) Paul, A.; Smith, M. D.; Vannucci, A. K. Photoredox-Assisted Reductive Cross-Coupling: Mechanistic Insight into Catalytic Aryl– Alkyl Cross-Couplings. J. Org. Chem. **201**7, 82, 1996–2003.

(21) Zultanski, S. L.; Fu, G. C. Nickel-catalyzed carbon-carbon bond-forming reactions of unactivated tertiary alkyl halides: Suzuki arylations. J. Am. Chem. Soc. 2013, 135, 624–627.

(22) Serrano, E.; Martin, R. Nickel-Catalyzed Reductive Amidation of Unactivated Alkyl Bromides. *Angew. Chem., Int. Ed.* **2016**, *55*, 11207–11211.

(23) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. Nickel-Catalyzed CrossCouplings Involving Carbon-Oxygen Bonds. Chem. Rev. 2011, 111, 1346-1416.

(24) Cornella, J.; Zarate, C.; Martin, R. Metal-catalyzed activation of ethers via C–O bond cleavage: a new strategy for molecular diversity. *Chem. Soc. Rev.* **2014**, *43*, 8081–8097.

(25) Tobisu, M.; Chatani, N. Cross-Couplings Using Aryl Ethers via C–O Bond Activation Enabled by Nickel Catalysts. *Acc. Chem. Res.* **2015**, *48*, 1717–1726.

(26) Wisniewska, H. M.; Swift, E. C.; Jarvo, E. R. Functional-grouptolerant, nickel-catalyzed cross-coupling reaction for enantioselective construction of tertiary methyl-bearing stereocenters. *J. Am. Chem. Soc.* **2013**, *135*, 9083–9090.

(27) Zhang, S.-Q.; Taylor, B. L. H.; Ji, C.-L.; Gao, Y.; Harris, M. R.; Hanna, L. E.; Jarvo, E. R.; Houk, K. N.; Hong, X. Mechanism and Origins of Ligand-Controlled Stereoselectivity of Ni-Catalyzed Suzuki–Miyaura Coupling with Benzylic Esters: A Computational Study. J. Am. Chem. Soc. **2017**, *139*, 12994–13005.

(28) 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, 16105-16111.

(29) Camasso, N. M.; Sanford, M. S. Design, synthesis, and carbonheteroatom coupling reactions of organometallic nickel(IV) complexes. *Science* **2015**, *347*, 1218.

(30) Camasso, N. M.; Canty, A. J.; Ariafard, A.; Sanford, M. S. Experimental and Computational Studies of High-Valent Nickel and Palladium Complexes. *Organometallics* **2017**, *36*, 4382–4393.

(31) Payard, P.-A.; Perego, L. A.; Ciofini, I.; Grimaud, L. Taming Nickel-Catalyzed Suzuki-Miyaura Coupling: A Mechanistic Focus on Boron-to-Nickel Transmetalation. *ACS Catal.* **2018**, *8*, 4812–4823.

(32) Lipschutz, M. I.; Tilley, T. D. Carbon–Carbon Cross-Coupling Reactions Catalyzed by a Two-Coordinate Nickel(II)–Bis(amido) Complex via Observable NiI, NiII, and NiIII Intermediates. *Angew. Chem., Int. Ed.* **2014**, *53*, 7290–7294.

(33) Amatore, C.; Jutand, A. Rates and mechanism of biphenyl synthesis catalyzed by electrogenerated coordinatively unsaturated nickel complexes. *Organometallics* **1988**, *7*, 2203–2214.

(34) Biswas, S.; Weix, D. J. Mechanism and Selectivity in Nickel-Catalyzed Cross-Electrophile Coupling of Aryl Halides with Alkyl Halides. J. Am. Chem. Soc. **2013**, 135, 16192–16197.

(35) Everson, D. A.; Weix, D. J. Cross-Electrophile Coupling: Principles of Reactivity and Selectivity. *J. Org. Chem.* **2014**, *79*, 4793–4798.

(36) Shields, B. J.; Kudisch, B.; Scholes, G. D.; Doyle, A. G. Long-Lived Charge-Transfer States of Nickel(II) Aryl Halide Complexes Facilitate Bimolecular Photoinduced Electron Transfer. *J. Am. Chem. Soc.* **2018**, *140*, 3035–3039.

(37) Zuo, Z.; Ahneman, D. T.; Chu, L.; Terrett, J. A.; Doyle, A. G.; MacMillan, D. W. C. Merging photoredox with nickel catalysis: Coupling of a-carboxyl sp3-carbons with aryl halides. *Science* **2014**, 345, 437–440.

(38) Tellis, J. C.; Primer, D. N.; Molander, G. A. Single-electron transmetalation in organoboron cross-coupling by photoredox/nickel dual catalysis. *Science* **2014**, *345*, 433–436.

(39) Lim, C.-H.; Kudisch, M.; Liu, B.; Miyake, G. M. C–N Cross-Coupling via Photoexcitation of Nickel–Amine Complexes. J. Am. Chem. Soc. 2018, 140, 7667–7673.

(40) Ge, S.; Hartwig, J. F. Highly Reactive, Single-Component Nickel Catalyst Precursor for Suzuki–Miyuara Cross-Coupling of Heteroaryl Boronic Acids with Heteroaryl Halides. *Angew. Chem., Int. Ed.* **2012**, *51*, 12837–12841.

(41) Jo, J.; Tu, Q.; Xiang, R.; Li, G.; Zou, L.; Maloney, K. M.; Ren, H.; Newman, J. A.; Gong, X.; Bu, X. Metal Speciation in Pharmaceutical Process Development: Case Studies and Process/ Analytical Challenges for a Palladium-Catalyzed Cross-Coupling Reaction. *Organometallics* **2019**, *38*, 185–193.

(42) Oertel, A. M.; Ritleng, V.; Chetcuti, M. J. Synthesis and Catalytic Activity in Suzuki Coupling of Nickel Complexes Bearingn-Butyl- and Triethoxysilylpropyl-Substituted NHC Ligands: Toward Article

(43) Iwai, T.; Harada, T.; Shimada, H.; Asano, K.; Sawamura, M. A Polystyrene-Cross-Linking Bisphosphine: Controlled Metal Monochelation and Ligand-Enabled First-Row Transition Metal Catalysis. *ACS Catal.* **2017**, *7*, 1681–1692.

(44) Zhou, Y.-B.; Liu, Z.-K.; Fan, X.-Y.; Li, R.-H.; Zhang, G.-L.; Chen, L.; Pan, Y.-M.; Tang, H.-T.; Zeng, J.-H.; Zhan, Z.-P. Porous Organic Polymer as a Heterogeneous Ligand for Highly Regio- and Stereoselective Nickel-Catalyzed Hydrosilylation of Alkyne. *Org. Lett.* **2018**, *20*, 7748–7752.

(45) Ge, S.; Green, R. A.; Hartwig, J. F. Controlling First-Row Catalysts: Amination of Aryl and Heteroaryl Chlorides and Bromides with Primary Aliphatic Amines Catalyzed by a BINAP-Ligated Single-Component Ni(0) Complex. J. Am. Chem. Soc. **2014**, 136, 1617–1627.

(46) Key, R. J.; Vannucci, A. K. Nickel Dual Photoredox Catalysis for the Synthesis of Aryl Amines. *Organometallics* **2018**, *37*, 1468–1472.

(47) Materna, K. L.; Crabtree, R. H.; Brudvig, G. W. Anchoring groups for photocatalytic water oxidation on metal oxide surfaces. *Chem. Soc. Rev.* **2017**, *46*, 6099–6110.

(48) Vannucci, A. K.; Chen, Z.; Concepcion, J. J.; Meyer, T. J. Nonaqueous Electrocatalytic Oxidation of the Alkylaromatic Ethylbenzene by a Surface Bound RuV(O) Catalyst. ACS Catal. 2012, 2, 716–719.

(49) O'Connell, K.; Regalbuto, J. R. High Sensitivity Silicon Slit Detectors for 1 nm Powder XRD Size Detection Limit. *Catal. Lett.* **2015**, *145*, 777–783.

(50) Liu, Q.; Samad, J.; Copple, J. E.; Eskandari, S.; Satterwhite, C.; Regalbuto, J. R. A pinch of salt to control supported Pt nanoparticle size. *Catal. Today* **201**7, 280, 246–252.

(51) Miyaura, M.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, 95, 2457– 2483.

(52) Zhu, X.; Cho, H.-r.; Pasupong, M.; Regalbuto, J. R. Charge-Enhanced Dry Impregnation: A Simple Way to Improve the Preparation of Supported Metal Catalysts. *ACS Catal.* **2013**, *3*, 625–630.

(53) Campbell, K. C.; Hislop, J. S. Mercury adsorption, catalyst poisoning, and reactivation phenomena on metal catalysts. *J. Catal.* **1969**, *13*, 12–19.

(54) Tafazolian, H.; Culver, D. B.; Conley, M. P. A Well-Defined Ni(II)  $\alpha$ -Diimine Catalyst Supported on Sulfated Zirconia for Polymerization Catalysis. *Organometallics* **2017**, *36*, 2385–2388.

(55) Vannucci, A. K.; Alibabaei, L.; Losego, M. D.; Concepcion, J. J.; Kalanyan, B.; Parsons, G. N.; Meyer, T. J. Crossing the divide between homogeneous and heterogeneous catalysis in water oxidation. *Proc. Natl. Acad. Sci. U. S. A.* **2013**, *110*, 20918–20922.

(56) Kuehnel, M. F.; Orchard, K. L.; Dalle, K. E.; Reisner, E. Selective Photocatalytic CO2 Reduction in Water through Anchoring of a Molecular Ni Catalyst on CdS Nanocrystals. *J. Am. Chem. Soc.* **2017**, *139*, 7217–7223.

(57) Jiao, L.; Regalbuto, J. R. The synthesis of highly dispersed noble and base metals on silica via strong electrostatic adsorption: I. Amorphous silica. *J. Catal.* **2008**, *260*, 329–341.