ORGANOMETALLICS
Communication
Cite This: *Organometallics* XXXX, XXX, XXX−XXX
pubs.acs.org/Organometallics

Direct Installation of a Silyl Linker on Ready-Made NHC Ligands: Immobilized NHC-Pd Complex for Buchwald−Hartwig Amination

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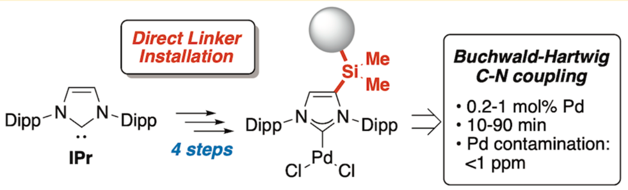
Supporting Information

ABSTRACT: An immobilized N-heterocyclic carbene (NHC)-Pd complex was prepared via direct silyl linker installation onto the imidazole backbone of commercially available 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) ligand. The IPr backbone was lithiated and treated with Me_2SiCl_2 to afford $ClMe_2Si$-IPr, which reacted with $[Pd(\pi\text{-allyl})Cl]_2$ to yield a $ClMe_2Si$-IPr-Pd complex, and this was immobilized on Wang resin. The immobilized NHC-Pd complex facilitated quantitative Buchwald−Hartwig amination of aryl chlorides within 10 min, even at a low Pd loading of 0.2 mol %. The catalyst could be removed from the reaction mixture by simple filtration, and Pd leaching into the reaction medium was suppressed to below 1 ppm.



Carbon−nitrogen bond formation is one of the most important reactions in organic synthesis because many biologically active compounds include nitrogen functionalities in their molecular structures. In addition, triarylamine is a ubiquitous structural motif that is frequently utilized in materials science.[1,2] Consequently, significant effort has been devoted to the development of efficient C−N bond formation reactions.[3] In particular, Buchwald−Hartwig amination, which involves palladium-catalyzed cross-coupling of aryl halides and amines, has emerged as a reliable method for C−N bond formation from readily accessible substrates under mild reaction conditions.[4]

N-heterocyclic carbenes (NHCs) have been widely applied as ligands in transition-metal catalysis. Strong metal−ligand binding occurs, as NHCs are strong σ donors and comparatively weak π acceptors, which contributes to enhanced catalyst stability.[5] NHCs are proven efficient ligands for Buchwald−Hartwig amination.[6,7] Commercially available 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr), which bears sterically bulky 2,6-diisopropylphenyl groups as N substituents, is one of the most frequently used ligands in Buchwald−Hartwig amination.[4a] To enhance the practical utility of NHC ligands in transition-metal-catalyzed reactions, the development of immobilized NHC-metal catalysts has received increasing attention over the past two decades.[8,9]

There are two common approaches to NHC immobilization on a supporting material such as silica or polystyrene resin, via covalent grafting: installation of a linker on an N substituent (Figure 1a)[10,11] and addition of a linker to the imidazole backbone (Figure 1b).[12−14] Although successful immobilization has been achieved with both approaches, synthesis of the reported immobilized catalysts is usually laborious and requires multiple steps. Specific synthetic routes include linker installation, imidazolium core formation, carbene formation, complexation, and immobilization, which are costly and time-consuming. Thus, direct installation of a linker on ready-made (if possible, commercially available) NHC ligands is desirable in terms of practicality.

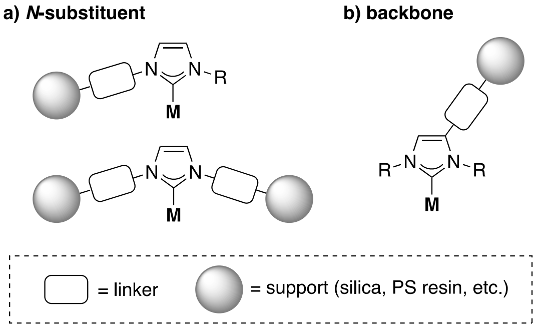


Figure 1. Immobilization by covalent grafting onto (a) an N substituent and (b) an imidazole backbone.

Robinson and colleagues recently reported the direct lithiation of the imidazole backbone of IPr with *n*-butyllithium

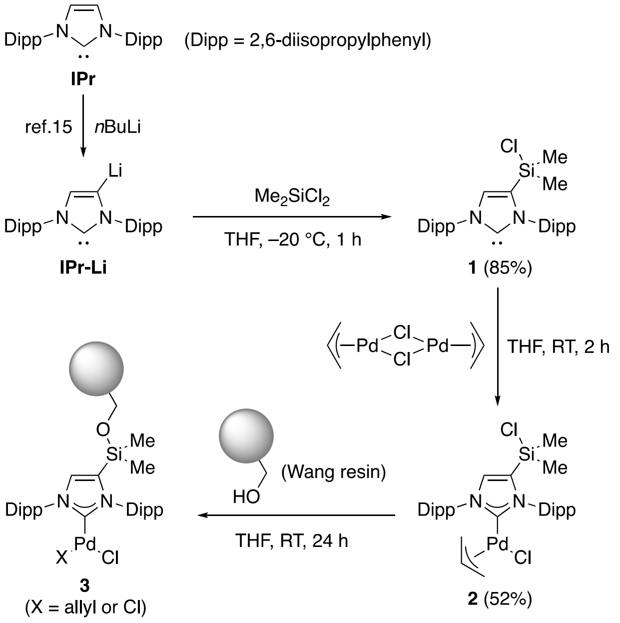
Received: March 10, 2019

DOI: 10.1021/acs.organomet.9b00159

(n-BuLi) and subsequent treatment with trimethylsilyl chloride to yield 4-Me_3Si-IPr without masking the carbene.[15,16] This report inspired us to attempt postfunctionalization of commercially available IPr. We synthesized an array of 4-silylated IPr ligands and revealed that the postfunctionalized IPr ligands bearing electron-donating silyl groups showed better catalytic performance for Buchwald–Hartwig amination than did the parent IPr ligand under homogeneous conditions.[17] In this study, we used the postfunctionalization method for the direct installation of a silyl linker onto commercially available IPr for immobilization. Herein, we report heterogeneous catalysis of an immobilized NHC-Pd complex in Buchwald–Hartwig amination of aryl chlorides with amines.

Scheme 1 illustrates the direct installation of a silyl linker onto the IPr backbone before complexation with palladium and immobilization on polystyrene resin. IPr-Li, which was generated from commercial IPr following a slightly modified Robinson protocol, was initially treated with Me_2SiCl_2 at −20 °C to produce 4-$ClMe_2Si$-IPr (**1**) with a yield of 85%. Immobilization precursor **2** was subsequently synthesized in a 52% yield by reacting **1** with $[Pd(\pi\text{-allyl})Cl]_2$. Finally, precursor **2** was immobilized on Wang resin to afford the novel immobilized NHC-Pd complex **3**. NHC-Pd complex **3** was thus obtained from IPr in four steps.

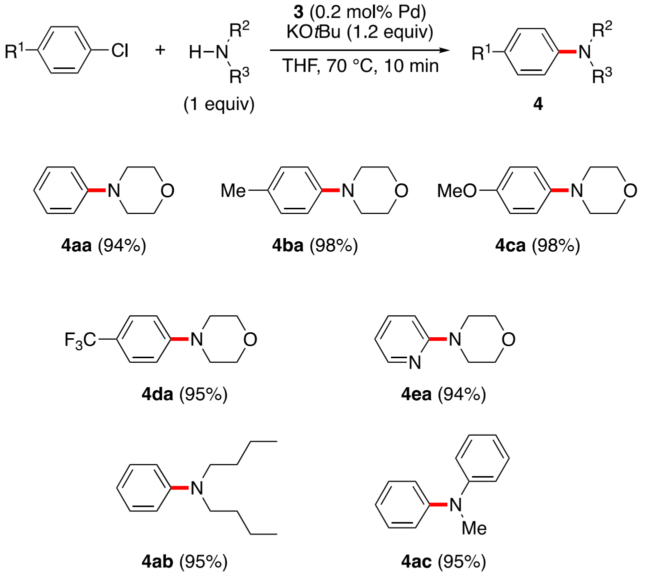
Scheme 1. Direct Installation of a Silyl Linker on IPr and Immobilization of the NHC-Pd Complex on Wang Resin



The chemical structure of the immobilized NHC-Pd complex **3** was characterized by X-ray photoelectron spectroscopy (XPS), solid-state nuclear magnetic resonance (NMR) spectroscopy, elemental analysis, and inductively coupled plasma atomic emission spectroscopy (ICP-AES). XPS analysis of **3** showed that the electronic state of the immobilized Pd species was mainly Pd(II), along with a small amount of Pd(0) (Figure S1 in the Supporting Information). Coproduction of propylene was observed during the immobilization step. Immobilization through Si–O bond formation concomitantly forms HCl, which is known to react with NHC-Pd(allyl)Cl species to generate propylene along with the corresponding NHC-$PdCl_2$ species.[7a] Thus, the immobilized NHC-Pd complex **3** would include NHC-Pd(allyl)Cl and NHC-$PdCl_2$ species, both of which can participate in the Buchwald–Hartwig amination through the formation of the same NHC-Pd^0 active species. In the $^{29}Si\{^1H\}$ cross-polarized magic angle spinning (CPMAS) NMR spectrum of immobilized NHC-Pd **3**, a peak was observed around 1.5 ppm (Figure S2a in the Supporting Information). In contrast, the $^{29}Si\{^1H\}$ NMR spectrum of the precursor **2** showed a peak at 11.8 ppm (Figure S2b in the Supporting Information). The significant peak shift (Δ = 10 ppm) indicated conversion of the Si–Cl bond to Si–O, which meant that immobilization on the resin occurred. The nitrogen and palladium contents were determined to be 0.98% (0.70 mmol N/g cat.) and 3.94% (0.37 mmol Pd/g cat.), respectively, by elemental analysis and ICP-AES. The approximate N to Pd molar ratio of 2:1 indicated that 1:1 coordination of NHC to the Pd center was maintained during immobilization.

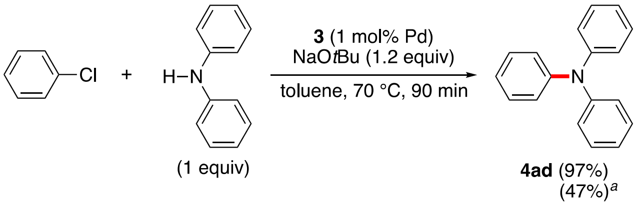
The catalytic performance of the immobilized NHC-Pd complex **3** was investigated by using it in the Buchwald–Hartwig amination of aryl chlorides and amines with 1.2 equiv of potassium *tert*-butoxide (KO*t*Bu) as the base in THF at 70 °C (Chart 1). Chlorobenzene underwent amination by morpholine to give *N*-phenylmorpholine (**4aa**) in a 96% yield. Reactions with aryl chlorides bearing electron-donating methyl and methoxy groups or an electron-withdrawing trifluoromethyl group proceeded smoothly to generate the amination products **4ba**–**4da** in excellent yields. A heterocycle, 2-chloropyridine, was also aminated by morpholine in 97% yield. Other amines, such as dibutylamine and *N*-methylaniline, were also suitable for the amination and furnished the corresponding products **4ab** (98%) and **4ac** (98%). Notably, all of the reactions proceeded to completion within 10 min even when only 0.2 mol % Pd was used.

Chart 1. Buchwald–Hartwig Amination of Aryl Chlorides Catalyzed by the Immobilized NHC-Pd Complex 3



The immobilized NHC-Pd complex **3** can be employed in the synthesis of triphenylamine, a key motif in materials science,[2] by Buchwald–Hartwig amination of chlorobenzene with diphenylamine (Scheme 2). While a very low yield of 3% was obtained with the previously described reaction con-

Scheme 2. Triphenylamine Synthesis



[a] (IPr)Pd(π-allyl)Cl in place of immobilized NHC-Pd **3**.

ditions, the desired triphenylamine **4ad** was obtained in a high yield of 97% with 1 mol % Pd when NaO*t*Bu was used as the base in toluene. It was worth noting that the parent IPr ligand produced an inferior yield of 47% under these conditions, demonstrating the accelerating effect of immobilization. Although the details are unclear at present, formation of single sites that prevented unfavorable interactions between the palladium complexes and the electron-donating effect of the silyl group may have contributed to the better catalytic performance of immobilized NHC-Pd **3**.

The immobilized catalyst **3** was recovered via filtration under a nitrogen atmosphere after the amination of chlorobenzene with diphenylamine. The catalyst **3** exhibited a drastic color change from orange to black, indicating the formation of Pd black. Analysis of the recovered **3** by scanning transmission electron microscopy (STEM) revealed that fine nanoparticles were widely dispersed on the resin (Figure S3 in the Supporting Information). Energy-dispersive X-ray (EDX) analysis confirmed that the nanoparticles consisted of Pd (Figure S4 in the Supporting Information). Since the recovered **3** exhibited no catalytic activity during amination, we concluded the Pd nanoparticles were not the active species. On the other hand, ICP-AES analysis of the filtrate following amination showed that <1 ppm Pd had leached into the reaction medium. Thus, contamination of the products by Pd and the NHC component during amination with **3** was effectively suppressed without the use of any scavengers.[18]

The practical efficiency of the immobilized NHC-Pd complex **3** was confirmed in a gram-scale synthesis of *N*,*N*-dibutylaniline **4ab**. A 3.86 g amount (94% yield) of **4ab** was isolated in high purity by a simple and facile procedure without use of standard chromatographic and distillation techniques. The reaction was complete within 10 min, following which the reaction mixture was filtered and extracted with ethyl acetate. Contamination of the products by Pd species was determined to be <1 ppm by ICP analysis.

In summary, we have developed a novel and facile method for the synthesis of immobilized NHC complexes via direct installation of a silyl linker onto the carbon backbone of commercially available NHC ligands. The immobilized NHC-Pd complex **3** shows excellent catalytic activity in the Buchwald–Hartwig amination of aryl chlorides and amines. The desired amination products can be obtained in high yields within 10 min in the presence of only 0.2 mol % Pd. Although the immobilized catalyst cannot be reused due to the formation of Pd nanoparticles, Pd contamination of the amination products can be suppressed without the use of a scavenger. The feasibility of applying the immobilized NHC-Pd catalyst in other reactions and the direct installation method for the preparation of other immobilized NHC-metal complexes are being investigated in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.9b00159.

Experimental procedures and spectral data (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Dr. Hiroshi Igarashi and Dr. Yasuhiro Seki (N. E. CHEMCAT Corporation) for helpful discussions. We also thank Dr. Toshikazu Takahashi for assistance with solid-state NMR spectroscopy.

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DOI: 10.1021/acs.organomet.9b00159
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