Silver-Triggered Activity of a Heterogeneous Palladium Catalyst in Oxidative Carbonylation Reactions

Man-Bo Li,*† Ying Yang†, Abdolrahim A. Rafi, Michael Oschmann, Erik Svensson Grape, A. Ken Inge, Armando Córdova,* and Jan-E. Bäckvall*

Abstract: A silver-triggered heterogeneous Pd-catalyzed oxidative carbonylation has been developed. This heterogeneous process exhibits high efficiency and good recyclability, and was utilized for the one-pot construction of polycyclic compounds with multiple chiral centers. AgOTf was used to remove chloride ions in the heterogeneous catalyst Pd-AmP-CNC, thereby generating highly active PdII, which results in high efficiency of the heterogeneous catalytic system.

Palladium-catalyzed oxidative carbonylations have been widely used for the introduction of carbonyl groups into organic molecules, which provides a basis for the streamlined construction of valuable products from various feedstocks.[1] As a powerful approach towards direct oxidative carbonylations of aliphatic hydrocarbons, these reactions are attractive for applications in industry. A central challenge in palladium-catalyzed oxidative carbonylation reactions is achieving high palladium efficiency, and at the same time, realizing well-controlled selectivity and recovery of the metal in the transformations.[2]

Over the past six years, our group has developed efficient oxidative carbonylation reactions of enallenes catalyzed by Pd(OAc)2 or Pd(TFA)2.[1j,3] As shown in Scheme 1a, the olefin group of enallene A coordinates to PdII (Int-A), triggering allenic C(sp3)–H cleavage to give Int-B. After a carbon monoxide insertion and a subsequent olefin insertion, this reaction allows the construction of a cyclopentenone intermediate (Int-C), which can be transformed into different useful products. In these transformations, coordination of the olefin to PdII (Int-A) is essential for the allenic C(sp3)–H cleavage to afford Int-B. Replacement of the olefin group by an alkyl or aryl group completely shuts down the reactivity of the allene.[4] Inspired by these previous studies, we were interested in investigating the oxidative carbonylation of allenes bearing a nitrogen-containing functionality (NHR, Scheme 1b). In this approach the NHR group would trigger attack by the allene (Int-1 to Int-2) and subsequent carbonylation would give pyrrolidone 2. In a very recent work, we observed that an amide group can trigger allene attack on PdII.[5]

We initiated our proposal by using allene 1f (R = Ph) as the starting material in the presence of Pd(TFA)2, BQ, CHCl3, and 1 atm of CO at room temperature (Scheme 2). 1f was very reactive and it was consumed completely under the reaction conditions. However, dihydropyrrole 3 was observed as the sole product, which was generated from Pd-catalyzed intramolecular aminopalladation (Int-D). In contrast, treatment of allene 1f (R = Ts) under the same reaction conditions resulted in recovery of the starting material. At 60 °C, a similar aminopalladation product 3 was isolated in 89% yield, while, to our delight, the desired product 2 was observed in 8% yield. These results demonstrated that 1) allene amine (1f) and allene amide (1f) are reactive with Pd for cyclization...
through intramolecular aminopalladation;[6] and 2) the reactivity of allene amide (1f) can be partially switched to undergo Pd-catalyzed oxidative carbonylation, giving desired pyrrolidone product 2.[7]

Based on the initial results, we tried to improve the selectivity of the reaction by using allene amide 1a as the starting material at room temperature to produce pyrrolidone 2a. Different variants of homogeneous palladium catalysts, solvents or oxidants did not give any desired product. Instead allene 1a was recovered in these cases (for details on optimization of reaction conditions, see the Supporting Information, p. S9). Very recently, our group has developed an efficient heterogeneous palladium catalyst immobilized on amino-functionalized siliceous mesocellular foam (Pd-AmP-MCF) for oxidative cyclizations of enallenol.[8] In these transformations, Pd-AmP-MCF showed higher catalytic activity and stability compared to the corresponding homogeneous palladium catalysts such as Pd(OAc)2 or Pd(TFA)2. By using eco-friendly nanocellulose as the support, we also prepared a heterogeneous palladium catalyst immobilized on renewable amino-functionalized crystalline nanocellulose foam (Pd-AmP-CNC).[9] To improve the activity and selectivity of the Pd-catalyzed oxidative carbonylation of allene 1a, we turned our attention to heterogeneous catalysts. Initially, nothing of the desired product could be isolated when using 5 mol% of Pd-AmP-CNC as the catalyst (Figure 1A). However, surprisingly, when we added catalytic amounts of AgOTf (10 mol%) to the heterogeneous system, highly improved activity and selectivity by Pd-AmP-CNC were observed, and pyrrolidone 2a was obtained in 95% yield at room temperature in 30 minutes (Figure 1E). In contrast, the homogeneous catalytic system did not give satisfactory results (Figure 1B,C,D).[10] Notably, the heterogeneous system is highly efficient: the catalyst and AgOTf loading can be reduced to 0.5 mol% and 1 mol%, respectively, producing pyrrolidone 2a in greater than 90% yields within 30 minutes (Figure 1F).

Under the optimized reaction conditions (Figure 1F), we explored the substrate scope for the oxidative carbonylation of allenes 1 at room temperature (Scheme 3). Substituents including various aryl and alkyl groups (cyclic or acyclic) on R1, R2, R3, and the terminal positions of allenes 1 worked well to give pyrrolidones 2 in excellent yields. Different functional groups such as EtO2C, TsO, Ns, and Ms were tolerated in the oxidative carbonylation reactions. Notably, the catalytic system is highly efficient. For all of the substrates, only 0.5 mol% of Pd-AmP-CNC and 1 mol% of AgOTf were used, and the reactions were completed within 30 minutes.

Figure 1. Comparison of different catalyst variants.

Figure 2. A) Molar ratios of Cl/Pd in Pd-AmP-CNC with and without AgOTf treatment. B) Pd3d XPS spectra of Pd-AmP-CNC with and without AgOTf treatment. C) An illustration of Ag+–triggered generation of catalytic active cationic palladium in Pd-AmP-CNC.

Figure 2. A) Molar ratios of Cl/Pd in Pd-AmP-CNC with and without AgOTf treatment. B) Pd3d XPS spectra of Pd-AmP-CNC with and without AgOTf treatment. C) An illustration of Ag+–triggered generation of catalytic active cationic palladium in Pd-AmP-CNC.
Based on the 1,3-diene moiety in the oxidative carbonylation products 2, an efficient one-pot-two-step reaction was developed for the construction of polycyclic compounds 4 with multiple chiral centers (Scheme 4a). This strategy provides an atom- and step-economic procedure for the construction of cyclohexenyl-γ-lactam based polycyclic compounds[12] in high yield and stereoselectivity, which will be beneficial in synthetic chemistry. An enantiodivergent synthesis of pyrrolidones (R)-2i and (S)-2i with high yields and enantioselectivity was realized starting from allenic alcohol 1i-ol (Scheme 4b), followed by an enzymatic kinetic resolution, Mitsunobu reaction, and the standard reaction conditions of Pd-AmP-CNC-catalyzed oxidative carbonylation.

To further verify the efficiency of the heterogeneous Pd catalyst in oxidative carbonylations, we conducted catalyst-recycling experiments and a hot-filtration test. The recycling experiments revealed that the efficiency of Pd-AmP-CNC was maintained from the first to the ninth run (Figure 3A). Pd3d XPS spectra and TEM images of Pd-AmP-CNC after the first and ninth run showed no detectable change in the catalyst (Figure 3B,C and D). TEM images of both samples (Figure 3) show a nanoparticle size of 1–2 nm, and the deconvoluted XPS (see the Supporting Information, p. S24) had a ratio Pd0/PdII of about 20/80 after the first and ninth run.[13] These results demonstrate that the heterogeneous palladium catalyst is robust, recoverable, and recyclable during the oxidative carbonylation. Notably, the addition of 1 mol% of AgOTf is necessary in each cycle for triggering the activity of the homogeneous Pd catalyst.[14] Pd leaching was not observed based on a hot-filtration test (for details, see the Supporting Information, p. S25), which excludes the possibil-
ity that the reaction proceeds through a homogeneous pathway.

To gain a deeper insight into the mechanism of the Pd-AmP-CNC-catalyzed oxidative carbonylation, we performed deuterium kinetic isotope effect (KIE) studies (for details, see the Supporting Information, p. S26–S28). An intermolecular competitive experiment was conducted by using a 1:1 mixture of 1a and 1a-d6 at 0 °C. The product ratio 2a:2a-d6 measured at 8% conversion was 5:1. From this ratio and the conversion, the competitive KIE value was determined to be $k_D/k_H = 5.4$. Furthermore, the parallel KIE experiments afforded $k_D/k_H = 3.9$. These results indicate that in the heterogeneous process, the simultaneous coordination of the sulfonamide group (NHTs) and the allene unit to the PdII center does trigger the activity that the reaction proceeds through a homogeneous pathway.

Based on the experimental results, we propose a mechanism for Pd-AmP-CNC-catalyzed oxidative carbonylation triggered by the silver salt (Scheme 5). Initially, Ag+ would activate Pd-AmP-CNC to generate highly active PdII. Simultaneous coordination of the sulfonamide group (NHTs) and the allene unit to the PdII center (Int-1) would promote allenic C(sp3)–H bond cleavage to form Int-2. Coordination of CO to palladium leads to Int-3, which would undergo a nucleophilic attack by NHTs on the coordinated CO to afford Int-4. Reductive elimination of Int-4 would give the final carbonylative product 2 and the released Pd0 is reoxidized to PdII by BQ.

**Scheme 5. Proposed mechanism.**

In conclusion, we have developed a highly efficient heterogeneous catalytic system for oxidative carbonylation reactions. The heterogeneous Pd (Pd-AmP-CNC), which is activated by Ag+, catalyzes the transformation of allene amide to pyrrolidone 2 in 30 minutes at room temperature. This heterogeneous process can be applied for a one-pot-two-step construction of polycyclic systems with multiple chiral centers. The high efficiency of the heterogeneous catalytic system originates from the removal of Cl from Pd-AmP-CNC by the silver salt, thereby generating highly active PdII. The heterogeneous catalyst is robust in oxidative carbonylation reactions, and can be recycled for at least nine runs without loss of activity. This heterogeneous catalytic system may open up new opportunities in oxidative carbonylation reactions, and stimulate more research on the development of heterogeneous transition-metal catalysts with high activity and selectivity.

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**Conflict of interest**

The authors declare no conflict of interest.

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Recently, we reported a Pd-catalyzed oxidative alkynylation of allenic amide. In that case, Pd(OAc)₂ or Pd(TFA)₂ worked well to give the oxidative products: M.-B. Li, E. S. Grape, J.-E. Bäckvall, Angew. Chem. Int. Ed. 2018, 57, 16842 – 16846; Angew. Chem. 2018, 130, 17084 – 17088.


These are not the final page numbers!
Silver bullet: A silver-triggered heterogeneous palladium-catalyzed oxidative carbonylation of allene amides was developed for the one-pot construction of pyrrolidones and polycyclic compounds with multiple chiral centers. The heterogeneous catalyst (Pd-AmP-CNC) can be recycled at least nine times without loss of activity. The Ag salt removes Cl from Pd-AmP-CNC to generate highly active PdII, which results in high efficiency of the heterogeneous catalytic system.