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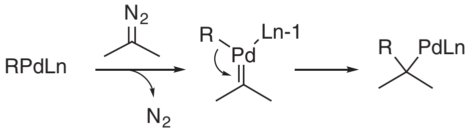
Palladium-catalyzed Cross-coupling of Aryl Iodides with β-Trimethylsiloxy-α-diazoesters: A Novel Approach toward β-Keto-α-arylesters

Zhibin Shu,[1,2] Ji Zhang,[1,2] Yan Zhang,[1,2] and Jianbo Wang*[1,2]
[1]*Beijing National Laboratory for Molecular Sciences (BNLMS), Peking University, Beijing 100871, P. R. China*
[2]*Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education,*
College of Chemistry, Peking University, Beijing 100871, P. R. China

(Received June 15, 2011; CL-110499; E-mail: wangjb@pku.edu.cn)

Palladium-catalyzed cross-coupling of β-trimethylsiloxy-α-diazoesters with aryl iodides provides a new approach to β-keto-α-arylesters. It is shown that the β-trimethylsiloxy group can significantly suppress the direct 1,2-hydride shift from palladium carbene.

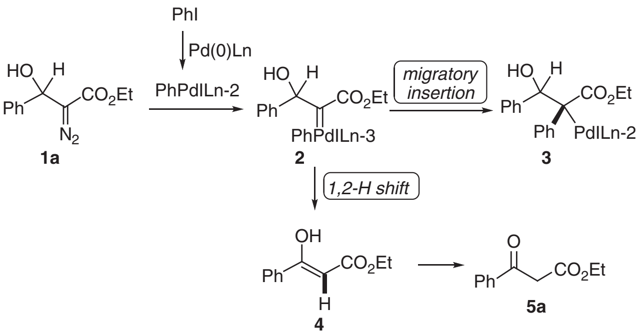
Palladium-catalyzed cross-coupling reaction has been developed into one of the most powerful methods for C–C bond formation.[1] In the Pd-catalyzed cross-coupling reactions, the nucleophiles are in general organometallic compounds, such as Grignard reagents, boron reagents, zinc reagents, tin reagents, and silicon reagents. The corresponding electrophiles are usually halides or pseudo-halides. Recently, a new type of Pd-catalyzed cross-coupling has emerged, in which diazo compounds serve as cross-coupling partner.[2–9] In this type of cross-coupling reaction, the key steps are believed to involve the formation of Pd–carbene species, which is followed by migratory insertion of the carbon ligand (eq 1).[2] This type of cross-coupling is general, and the migratory groups include aryl,[3] benzyl,[4] vinyl,[5] allyl,[6] acyl,[7] alkynyl,[8] and allenyl[9] groups. As a continuation of our interest in this area, we report in this paper the Pd-catalyzed cross-coupling of aryl iodides with β-trimethylsiloxy-α-diazoesters. The reaction provides a new approach toward β-keto-α-arylesters.



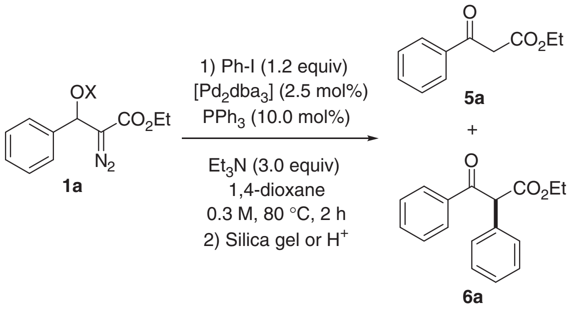
(1)

In the beginning, our interest is the Pd-catalyzed cross-coupling of aryl iodide and β-hydroxy-α-diazoester. We had expected that migratory insertion will occur from Pd species **2**, affording the palladium species **3** (Scheme 1). However, a competing process from Pd carbene species **2** is 1,2-hydride shift, which will lead to the formation of **4** and eventually 1,3-dicarbonyl compound **5a**, without new C–C bond formation. Previous studies have indicated that the existence of the β-hydroxy group significantly enhances the 1,2-hydride shift of a metal carbene species.[10]

The initial experiments indicated that this was indeed the case. When phenyl iodide and diazo compound **1a** was catalyzed by $[Pd_2(dba)_3]$ (dba: dibenzylideneacetone), a mixture of **5a** and **6a** was obtained in approximately 1:1 ratio (Scheme 2). Changing the reaction conditions, including the Pd catalyst, ligand, and the reaction temperature seems not significantly to affect the ratio. We then conceived that the 1,2-hydride shift of Pd carbene might be affected by modifying the β-hydroxy group. Our previous studies have demonstrated that β-siloxy groups significantly retard the 1,2-hydride shift of metal carbene.[10a,11] To our delight, we found that this was also the case in the current Pd-catalyzed reaction. When the β-hydroxy was replaced by a trimethylsiloxy group, the ratio of **5a**:**6a** was increased to 20:80. Further modifying the hydroxy group by converting to triisopropylsiloxy (TIPSO), *tert*-butyldimethylsiloxy (TBDMSO), or *tert*-butyldiphenylsiloxy (TBDPSO) did not improve the ratio. In contrast, in all these cases the ratios were actually diminished compared with β-trimethylsiloxy-α-diazoesters. It is noteworthy that the initially produced enol ester is converted into the corresponding β-keto-α-arylester **6a** by treatment with silica gel or protonic acid.



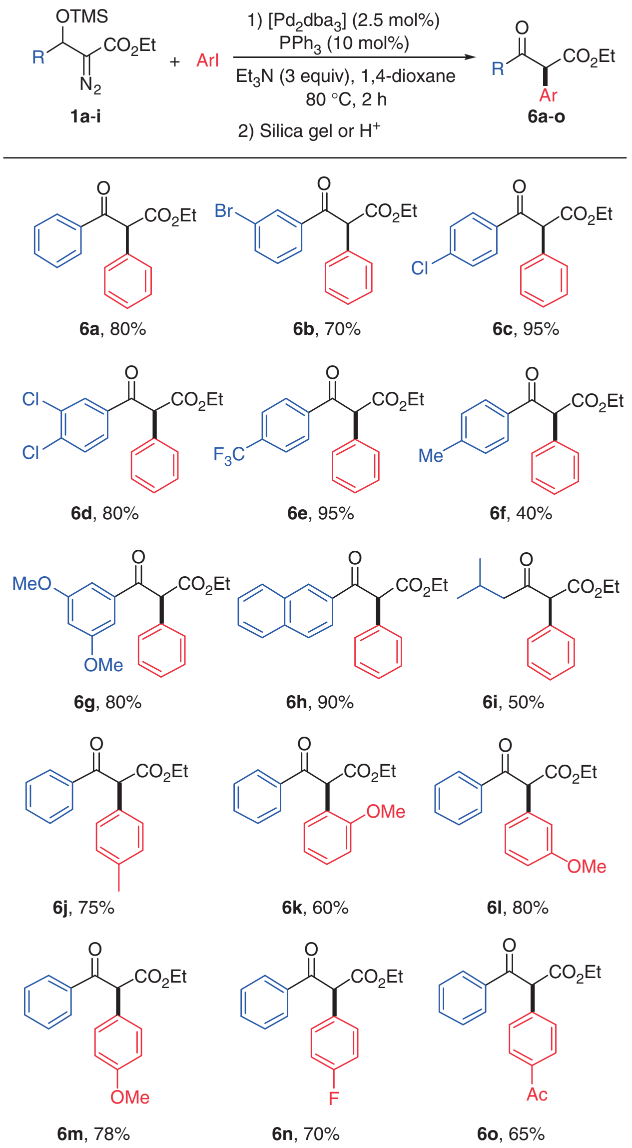
Scheme 1. Migratory insertion vs. 1,2-H shift.



X =	H	$SiMe_3$	$Si(i\text{-}Pr)_3$	$SiMe_2t\text{-}Bu$	$SiPh_2t\text{-}Bu$
5a:**6a** =	50:50[a]	20:80	31:69	33:67	34:66
	97%[b]	98%[b]	85%[c]	90%[c]	91%[c]

Scheme 2. Migratory insertion vs. 1,2-H shift. [a]All the ratios were determined by GC. [b]Isolated yield of **5a** and **6a** combined. [c]The combined yields were determined by GC.

Palladium-catalyzed cross-coupling of 1,3-dicarbonyl compounds with aryl halide has been reported previously.[12] Therefore, the possibility exists that **6a** is formed by Pd-catalyzed



6a, 80% **6b**, 70% **6c**, 95%

6d, 80% **6e**, 95% **6f**, 40%

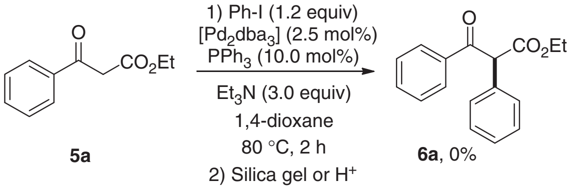
6g, 80% **6h**, 90% **6i**, 50%

6j, 75% **6k**, 60% **6l**, 80%

6m, 78% **6n**, 70% **6o**, 65%

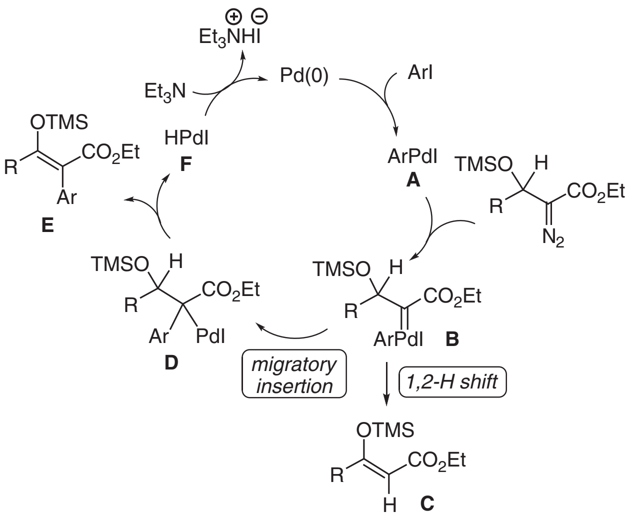
Figure 1. Palladium-catalyzed cross-coupling of **1a–1i** with aryl iodides. Reaction conditions: **1** (0.3 mmol), ArI (0.36 mmol, 1.2 equiv), 1,4-dioxane (1.0 mL). Isolated yields are described.

coupling of **5a** with phenyl iodide. To confirm such possible pathway, **5a** and phenyl iodide were reacted under the identical-conditions (eq 2). No β-keto-α-arylester could be detected in the ^{1}H NMR spectrum of the crude product. Consequently, this pathway can be excluded.



5a **6a**, 0% (2)

Next, we studied the scope of this coupling reaction by employing a series of β-trimethylsiloxy-α-diazoesters **1a–1i** to couple with aryl iodides (Figure 1).[13] The reaction provides the coupling products in good yields in general for the diazo substrates bearing various β-aryl groups. The reaction also works with the diazo substrates bearing β-alkyl group, although the yields are slightly diminished (**6i**). The scope of aryl iodide was investigated by employing diazo compound **1a** (R = Ph). For a series of aryl iodide substrates, the reaction worked well to provide the corresponding β-keto-α-arylesters **6j–6o** in good yields.



Scheme 3. Mechanistic rationale.

This coupling reaction can be rationalized by the mechanism depicted in Scheme 3. First, oxidative addition of aryl iodide to Pd(0) catalyst generates arylpalladium(II) species **A**. Palladium carbene **B** is then generated by reaction of **A** with diazo substrate. From palladium carbene **B**, one possible reaction pathway is direct 1,2-H shift, providing non-cross-coupling product **C**. Alternatively, aryl group migratory insertion occurs to generate Pd intermediate **D**, which is followed by β-H elimination to afford cross-coupling product **E**. Finally, Pd(0) catalyst is regenerated with the assistance of triethylamine.

In summary, we have demonstrated that Pd-catalyzed cross-coupling of β-trimethylsiloxy-α-diazoesters with aryl iodides is efficient.[14] The coupling reaction provides a new approach to β-keto-α-arylesters. The study demonstrates that the β-trimethylsiloxy group can significantly suppress the direct 1,2-hydride shift from palladium carbene. This observation is consistent with our previous report on the bystander group effect of metal carbene 1,2-hydride shift.[10,11]

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13 β-Trimethylsiloxy-α-diazoesters **1a**–**1i** were prepared in two steps from the corresponding aromatic aldehydes and ethyl diazoacetate. See Refs. 10a and 11, and Supporting Information.

14 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.