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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Pd-Catalyzed Ring-Opening Cross-Coupling of Cyclopropenes with Aryl Iodides

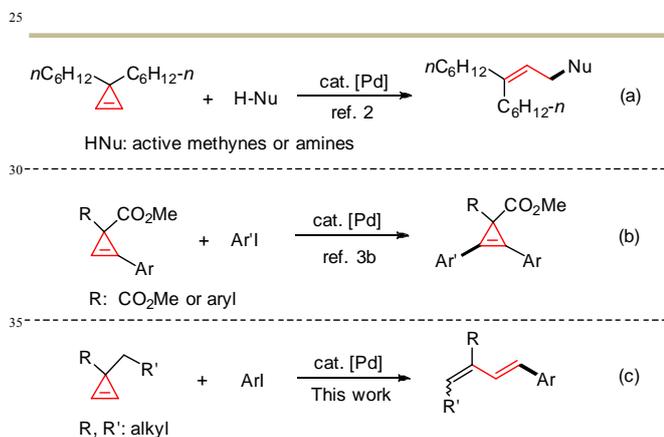
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Received (in XXX, XXX) Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXX 20XX

DOI: 10.1039/b000000x

Transition metal-catalyzed cross-coupling reaction of cyclopropenes with aryl iodides proceeds with the opening of cyclopropene ring, affording 1,3-butadienes as the products.

Cyclopropenes display diverse reaction patterns, largely due to their enormous ring strain.¹ The strained double bond of cyclopropene can interact with transition metals and undergoes various highly efficient transformations under catalytic conditions. Yamamoto and co-workers reported a ring-opening Pd-catalyzed reaction of 3,3-dihexylcyclopropene with pronucleophiles, giving allylated nucleophiles (Scheme 1, a).² On the contrary, Gevorgyan and co-workers have shown that cyclopropenes undergo direct arylation without ring-opening in Pd-catalyzed coupling reactions with aryl iodide (Scheme 1, b).³ We have speculated that the intriguing differences of these two reactions might be attributed to the substituents on the cyclopropene ring, rather than the coupling partners. In connection to our interest in transition-metal-catalyzed reaction of cyclopropenes,⁴ we report herein the Pd-catalyzed ring-opening cross-coupling of cyclopropenes with aryl iodides, which affords 1,3-butadiene



Scheme 1 Pd-Catalyzed coupling reactions with cyclopropenes.

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Electronic Supplementary Information (ESI) available: Experimental procedures, reaction conditions optimization, characterization data, and ¹H and ¹³C NMR spectra for products. See DOI: 10.1039/b000000x/

derivatives as the products (Scheme 1, c).

At the outset, we have investigated the Pd-catalyzed cross-coupling of cyclopropene **1a** with phenyl iodide **2a**. The cyclopropene **1a**,⁵ which bears an adamantyl substituent, was chosen as the carbene precursor mainly because of the simplicity in the product isolation and identification. Initially, we found that in the presence of 5 mol % Pd(PPh₃)₄, 10 mol % dppf, and 2 equiv of Cs₂CO₃, the expected 1,3-diene **3a** was obtained in 30% yield. Through optimization of the reaction conditions,⁶ **3a** could be obtained in good yield by using Pd(OAc)₂ as the catalyst, dppf

Table 1. Pd-Catalyzed ring-opening cross-coupling of cyclopropene **1a** and aryl iodides^a

entry	temp (°C)	2, Ar	yield of 3, % ^b
1	60	2a , C ₆ H ₅	3a , 79
2	60	2b , <i>p</i> -CH ₃ C ₆ H ₄	3b , 81
3	60	2c , <i>p</i> -CH ₃ OC ₆ H ₄	3c , 85
4	60	2d , <i>p</i> -C ₆ H ₅ C ₆ H ₄	3d , 78
5	60	2e , <i>m</i> -CH ₃ OC ₆ H ₄	3e , 86
6	60	2f , <i>o</i> -CH ₃ OC ₆ H ₄	3f , 81
7	70	2g , <i>p</i> -CF ₃ C ₆ H ₄	3g , 63
8	70	2h , <i>p</i> -CH ₃ O ₂ CC ₆ H ₄	3h , 73
9	90	2i , <i>p</i> -O ₂ NC ₆ H ₄	3i , 59
10	80	2j , <i>p</i> -CH ₃ (O)CC ₆ H ₄	3j , 52
11	80	2k , <i>p</i> -NCC ₆ H ₄	3k , 66
12	80	2l , <i>p</i> -BrC ₆ H ₄	3l , 69
13	80	2m , <i>p</i> -ClC ₆ H ₄	3m , 80
14	80	2n , <i>p</i> -FC ₆ H ₄	3n , 75
15	60	2o , 1-naphthyl	3o , 76
16	60	2p , 3-pyridinyl	3p , 72

^aIf not otherwise noted, the reaction conditions are as following: a solution of **1a** (0.1 mmol), **2a** (0.1 mmol), Pd(OAc)₂ (5 mol% or 8 mol%), dppf (10 mol% or 16 mol%), Cs₂CO₃ (0.2 mmol) in solvent (0.3 mL) was stirred for 12h. ^bIsolated yield. ^c**1a** (0.15 mmol) was used.

as the ligand and Cs₂CO₃ as the base in MeCN (Table 1, entry 1).

Under these conditions, a series of aryl iodides **2b-p** were investigated, as shown in Table 1. Various substituents on the aromatic ring could be tolerated, and moderate to good yields of the coupling products were obtained. The reaction was found marginally affected by electronic effects of the substituents of aryl iodides. For the electron-withdrawing group substituted substrates, the reaction needed higher temperature and the yield was slightly diminished as compared with electron-donating groups (entries 7-11). It is noteworthy that bromo and chloro substituents are tolerated in the reaction conditions, which may be advantageous for further transformations (entries 12, 13). Naphthyl and pyridinyl iodide also gave good yields (entries 15, 16).

It is noteworthy that in all the cases only one stereoisomer was observed. The configuration of the formed double bond was confirmed to be *E* through ¹H NMR spectra of the products. For one of the products (**3d**), the *E* configuration was unambiguously confirmed by X-ray diffraction (Figure 1).⁷ We assume that all the products have the same *E* configuration based on the comparison of their NMR spectra.

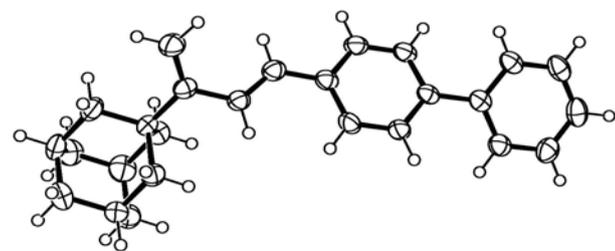


Figure 1. X-Ray structure of **3d**.

Next, we examined the scope of cyclopropenes. A series of 3,3-disubstituted cyclopropenes **1c-j** were examined (Table 2). For cyclopropenes **1c-e** the reaction all gave the corresponding cross-coupling products as single stereoisomer in good yields (entries 1-3). On the other hand, the reaction of various aryl iodides with cyclopropene **1f**, which bears two aliphatic chain substituents, produced the mixture of *E*- and *Z*-isomeric products in essentially non-selective manner (entries 4-10). Spiro cyclopropene **1g** bearing 12-membered ring also lead to a mixture of *Z/E* isomers with low selectivity (entry 11). Cyclopropene **1h-j** and aryl iodide **2d** produced regio-isomers because of the existence of two different substituents which can undergo β -H elimination (entries 12-14).

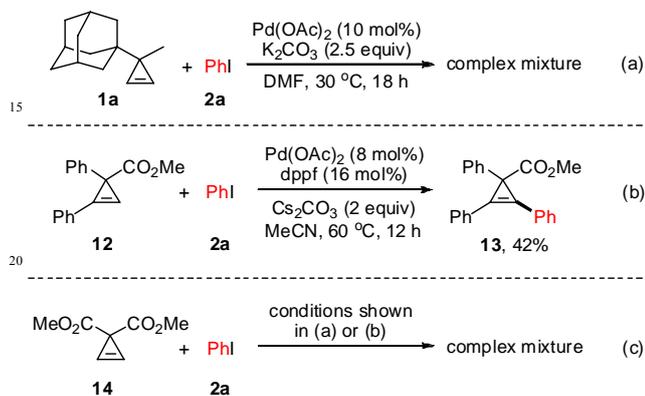
In order to gain insight into the reaction, control experiments have been carried out as shown in Scheme 2. First, using cyclopropene **1a**, the coupling reaction with phenyl iodide **2a** was carried out under Gevorgyan's conditions (Scheme 2, a).^{3b} The reaction resulted in a complex mixture without the formation of the expected 1,3-diene product. Next, cyclopropene **12**, which was one of the substrate used in Gevorgyan's Heck-type coupling reaction, was submitted to the coupling with **2a** under the current reaction conditions (Scheme 2, b). The reaction gave the Heck-type coupling product **13** in 42% yield without the formation of diene product. Finally, cyclopropene **14**, which has two 3,3-ester

Table 2. Substrate scope of cyclopropenes^a

entry	cyclopropene	temp	yield ^b
1		80 °C	67%
2		80 °C	91%
3		80 °C	84%
4-10		70 °C, 80 °C, 90 °C, 70 °C, 80 °C, 80 °C, 90 °C	93 (1:1.2), 90 (1:1.1), 73 (1:1.2), 87 (1:1.2), 86 (1:1.6), 85 (1:1.3), 62 (1:1.2)
11		80 °C	78 (1:2.5)
12		80 °C	91% (>19:1)
13		80 °C	56% (6.7:1:1)
14		80 °C	81% (6.2:1:1:1)

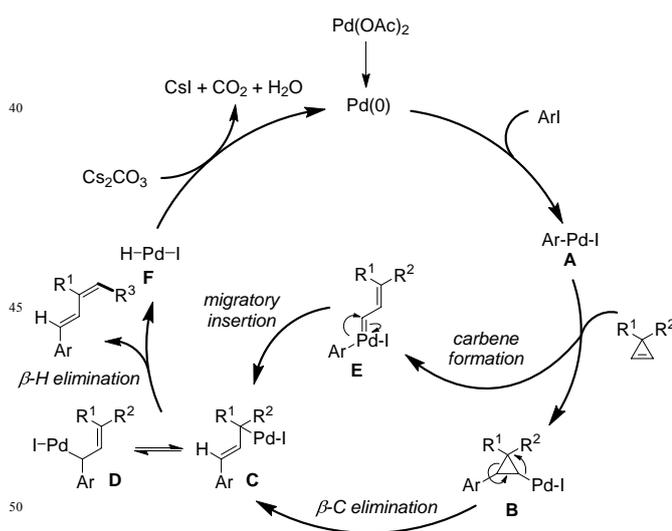
^aReactions were carried out with **1** (0.45 mmol), **2** (0.3 mmol), Pd(OAc)₂ (8 mol%), dppf (16 mol%) and Cs₂CO₃ (0.6 mmol) in MeCN (1.0 mL). ^bIsolated yield. ^c**1d** was added as a solution in pentane (0.3 M).

substituents but without substitution on double bond, has been submitted to both Gevorgyan's conditions and our conditions. In both cases, the reaction gave complex mixture (Scheme 2, c). These experiments support the speculation that the different reaction path shown in Scheme 1 (a) and (b) is attributed to the substituents on the cyclopropene ring. As suggested in Gevorgyan's report, the carbonyl group of the ester substituent may play an important role in stabilizing the Heck-type coupling intermediate through coordination with palladium, while the 1-phenyl substituent stabilizes the generated carbon cation.^{3b}



Scheme 2 Control experiments.

Putative reaction mechanisms to account for the 1,3-diene formation in the current reaction have been proposed as shown in Scheme 3. The reaction is initiated by the reduction of Pd(OAc)₂ to generate Pd(0). The first step of the catalytic cycle is oxidative addition of Pd(0) to the aryl iodide, affording the Pd(II) intermediate **A**. Cyclopropene is then activated by **A**, from which there are two possible pathways. Migratory insertion of cyclopropene affords cyclopropylpalladium species **B**, from which β -carbon elimination occurs to generate η^3 -allylpalladium



Scheme 3. Proposed reaction mechanism

intermediate **C** (in equilibrium with **D**).^{1d,8} Subsequently, β -H elimination from **C** gives the 1,3-diene product. At last, Pd(0) is regenerated through reductive elimination.

Since rearrangement of cyclopropene to vinyl carbene through ring opening under transition-metal-catalyzed conditions has been well-documented in the literature,^{4a,9} an alternative pathway involving Pd carbene species cannot be strictly ruled out. Thus, Pd carbene intermediate **E** is formed through the reaction of **A** with cyclopropene, which is subsequently followed by aryl group migration to afford intermediate **C**.^{10,11} However, rigorous study is needed to unambiguously confirm the proposed reaction mechanisms.

In summary, we have reported the Pd-catalyzed ring-opening cross-coupling reaction of cyclopropenes with aryl iodides. The results shown in this study indicate that the outcome of Pd-catalyzed coupling reaction with cyclopropene is markedly affected by the substituents on the cyclopropene substrates. In addition, this reaction represents a new synthetic method to synthesize 1,3-dienes,¹² which may find application in organic synthesis.

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