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Rhodium-Catalyzed Arylzincation of Terminal Allenes Providing Allylzinc Reagents and Its Application to Versatile Three-component Coupling Reaction

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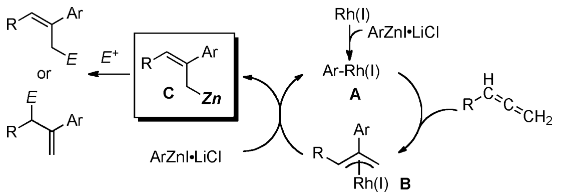
Multicomponent reactions of allenes have been attracting increasing attention owing to their inherent efficiency.[1] Among them, transition-metal-catalyzed three-component couplings involving allenes, organometallics, and carbonyls provide diversity-oriented synthesis of useful homoallylic alcohols.[2-4] In most cases, the couplings consist of (1) transmetalation from an organometallic reagent to a transition metal, (2) carbometalation of allene, and (3) nucleophilic attack of the resulting allylic transition metal to carbonyl. However, the couplings still remain unsatisfactory despite its importance: the electrophiles are limited to aldehydes and imines because of the low reactivity of the allylic transition metal intermediates.

Here we report rhodium-catalyzed arylzincation[5] of terminal allenes (Scheme 1).[6-9] The reaction represents a rare example of carbometalation of allenes accompanying accumulation of allylic metals in a reaction flask. The key is smooth transmetalation between allylrhodium **B** and arylzinc species. The resulting allylzinc reagents **C** are reactive enough to allylate a wider variety of electrophiles, realizing a more versatile three-component coupling reaction.

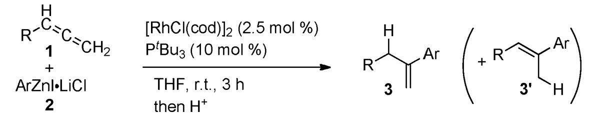
Scheme 1. Proposed Mechanism for Arylzincation of Allenes



Treatment of 1,2-tridecadiene (**1a**) with a phenylzinc iodide·LiCl complex in THF[10] in the presence of $[RhCl(cod)]_2$ and P^tBu_3 at room temperature for 3 h gave the corresponding arylated product **3a** in high yields (Table 1, entries 1 and 2). The reaction with 4-bromophenylzinc reagent **2b** also proceeded smoothly, leaving the bromo group untouched (entry 3). Arylzinc reagents bearing an electron-withdrawing or an electron-donating group were also applicable (entries 4 and 5). However, bulky 2-methylphenylzinc reagents **2e** failed to react (entry 6). Phenylzincation of allene **1b**−**1d** proceeded smoothly without loss of the siloxy, tosylamide, and additional olefinic moieties (entries 7−9). The reaction of 1-phenyl-1,2-propadiene (**1e**) afforded the phenylated product **3i** in 84% yield (entry 10).

When acetonitrile was added to the allylzinc reagent **C** (1.7 equiv) derived from **1a** and **2a**, the corresponding ketone **4a** was obtained in 62% yield. Instead, a Barbier-type reaction by mixing **1a**, **2a**, and acetonitrile together under the rhodium catalysis

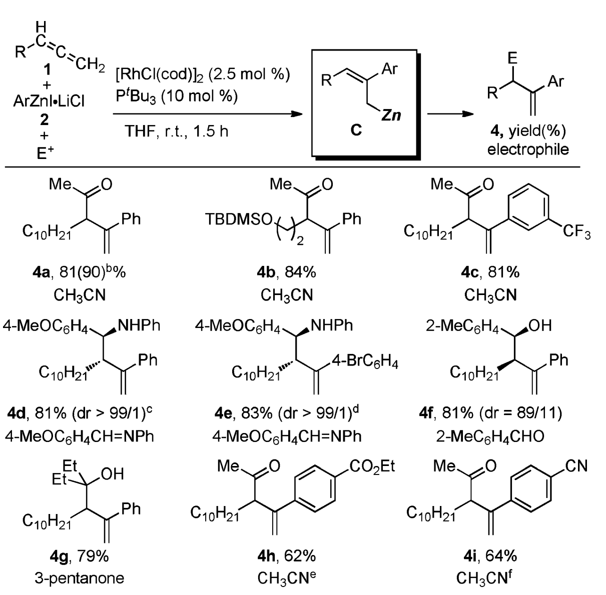
Table 1. Scope of Allenes and Arylzinc Reagents[a]



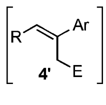
Entry	**1**, R	**2**, Ar	**3**, Yield (%)[b]
1	**1a**, $C_{10}H_{21}$	**2a**, Ph	**3a**, 80
2	**1a**, $C_{10}H_{21}$	**2a**, Ph	**3a**, 84[c]
3	**1a**, $C_{10}H_{21}$	**2b**, 4-BrC_6H_4	**3b**, 77
4	**1a**, $C_{10}H_{21}$	**2c**, 3-$CF_3C_6H_4$	**3c**, 74
5	**1a**, $C_{10}H_{21}$	**2d**, 3-$MeOC_6H_4$	**3d**, 77
6	**1a**, $C_{10}H_{21}$	**2e**, 2-MeC_6H_4	**3e**, Trace
7	**1b**, $TBDMSO(CH_2)_2$	**2a**, Ph	**3f**, 81
8	**1c**, $Ts(Bn)N(CH_2)_9$	**2a**, Ph	**3g**, 78
9	**1d**, $CH_2{=}CH(CH_2)_8$	**2a**, Ph	**3h**, 67
10[d]	**1e**, Ph	**2a**, Ph	**3i**, 84[e]

[a] The reaction was performed on a 0.3 mmol scale. [b] A small amount of product **3′** was also obtained. The ratio of **3**/**3′** was 9/1 unless otherwise noted. [c] The reaction was performed on a 3 mmol scale. [d] Performed at 66 °C for 1.5 h. [e] The ratio of **3i**/**3i′** was 97/3.

Table 2. Reaction of Allylzinc Intermediates with Various Electrophiles[a]



[a] Reaction conditions: **1** (0.5 mmol), **2** (0.5 mmol), electrophile (0.3 mmol). [b] The reaction was performed on a 3 mmol scale. [c] 9% of isomer **4d′** was contained. [d] 10% of isomer **4e′** was contained. [e] Reaction conditions: **1** (0.3 mmol), **2** (0.45 mmol), CH_3CN (0.9 mmol). [f] Reaction conditions: **1** (0.3 mmol), **2** (0.45 mmol), CH_3CN (1 mL, 18 mmol).



4′

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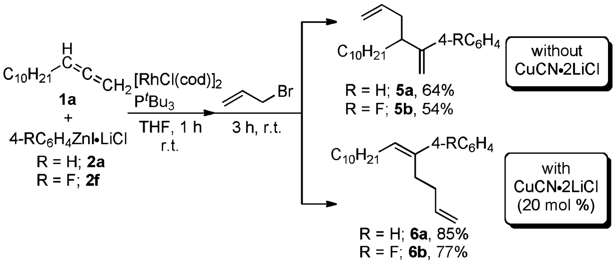
improved the yield of **4a** up to 81% (Table 2). Barbier-type reactions of **C** with imines proceeded diastereoselectively to yield homoallylamines **4d** and **4e**. Aldehyde and ketone also participated in the reaction, and homoallyl alcohols **4f** and **4g** were obtained in good yields. Arylzinc reagents bearing an ester or a nitrile group were also applicable to the reaction without the loss of the functional groups by using excess amounts of acetonitrile.

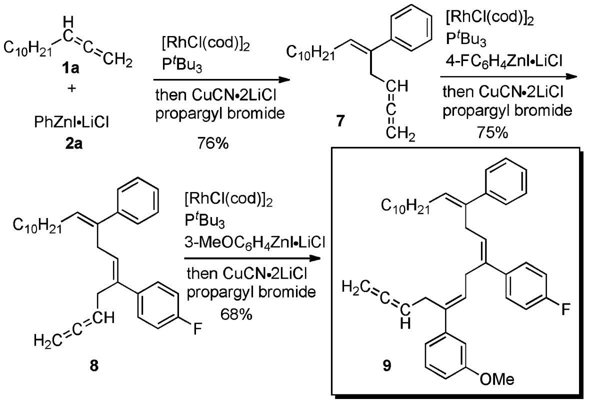
The high yield and isomer ratio of **4f** suggest that the allylzinc **C**, not allylrhodium **B**, is responsible for the allylation reaction. An allylzinc reagent was prepared from 1-chloro-2-phenyl-2-tridecene, zinc powder, and lithium chloride.[11] Treatment of 2-methylbenzaldehyde with the allylzinc reagent afforded **4f** quantitatively in a diastereomeric ratio of 86:14. The ratio is very similar to that in Table 2. In contrast, the reaction with an allylrhodium reagent, derived from the allylzinc reagent and [RhCl(P^{t}Bu$_3$)], gave a rather complex mixture which includes the major isomer of **4f** exclusively in 42% yield.

Allylzinc intermediates reacted with not only carbonyl compounds but also allyl bromide (Scheme 2). Treatment of allylzinc intermediates with allyl bromide afforded **5a** and **5b** in good yields. Interestingly, the sense of the regioselectivity was opposite when a copper catalyst was used (**6a** and **6b**).[12]

Scheme 2. Regioselective Reaction with Allyl Bromide Controlled by the Addition of a Catalytic Amount of CuCN·2LiCl



Scheme 3. Synthesis of Stereodefined Skipped Polyene via Iterative Arylzincation Reaction



Finally, we applied the reaction to the synthesis of stereodefined skipped polyene[13] via iterative arylzincation reactions (Scheme 3). Treatment of allene **1a** with phenylzinc reagent **2a** and subsequent reaction with propargyl bromide afforded the corresponding product **7** that has a terminal allene moiety in 76% yield. Iterative arylzincation reactions gave stereodefined (5*E*,8*E*,11*E*)-11-phenyl-8-(4-fluorophenyl)-5-(3-methoxyphenyl)-1,2,5,8,11-docosapentaene (**9**). It is noteworthy that no isomerization of the olefinic moiety of **9** was observed despite the basic reaction conditions.

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Supporting Information Available: Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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