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# Palladium-Catalyzed Regioselective Cyclopropanating Allenylation of (2,3-Butadienyl)malonates with Propargylic Carbonates and Their Application to Synthesize Cyclopentenones

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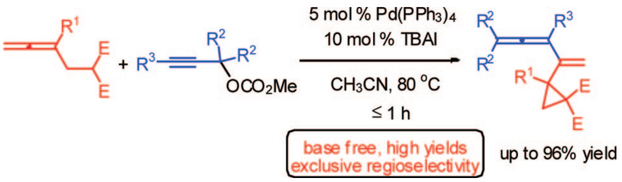
## ABSTRACT



**An efficient and highly regioselective route to synthesize polysubstituted 1,3,4-alkatrien-2-yl cyclopropane derivatives via Pd(0)-catalyzed highly regioselective coupling cyclization of (2,3-butadienyl)malonate or bis(phenylsulfonyl)methane with propargylic carbonates was reported. The reaction proceeded smoothly under neutral conditions to afford the products in 73−96% yields. The products may be efficiently converted to cyclopentenone derivatives via a catalytic Pauson−Khand reaction under ambient conditions.**

During the last 10−15 years, allenes have been demonstrated as a class of very powerful starting materials in organic synthesis.[1,2] In the next stage, the development of efficient methods for the synthesis of allenes with a unique structural feature from readily available starting materials will dictate the future of allene chemistry.[3,4] In this area, as is known, the Pd(0)-catalyzed reactions of alkynes with an appropriate leaving group[5] at the propargylic position usually afforded

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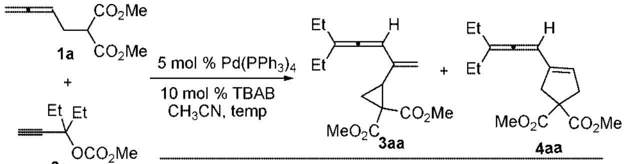
**Scheme 1.** Optimization of the Reaction Temperature

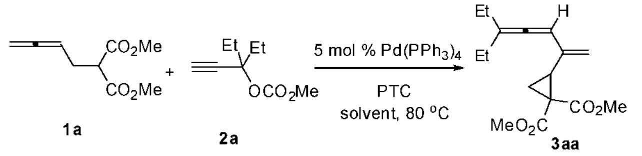


| temp (°C)/time (h) | yield of **3aa** (%) | yield of **4aa** (%) |
|---|---|---|
| 40/22 | 65 | - |
| 60/5 | 77 | - |
| 80/1 | 94 | - |

allenylic/propargylic palladium intermediates, which may further react with alkenes, terminal or internal alkynes, and CO to afford 1,2,4-trienes,[6,7] 4,5-allenyl aldehydes/ketones,[7] 2,3-allenoic acids,[8] esters,[8a,9] and amides,[10] respectively. To the best of our knowledge, the insertion of the above $\sigma$-allenylpalladium species into an allene has not yet been explored.[11] As part of our program investigating the transition-metal-catalyzed coupling cyclization of functionalized allenes[12] we report here an efficient and exclusive route to synthesize cyclopropylvinyl allene via the Pd(0)-catalyzed regioselective coupling cyclization of (2,3-butadienyl)malonates or bis(phenylsulfonyl)methane with propargylic carbonates.

Our initial investigation was based on the reaction of dimethyl (2,3-butadienyl)malonate **1a** with pentyn-3-yl carbonate **2a** in the presence of 5 mol % of Pd(PPh$_3$)$_4$ and 10 mol % of TBAB in CH$_3$CN at 40 °C. Interestingly, we observed the exclusive formation of 1,3,4-alkatrien-2-yl cyclopropane derivative **3aa** as the only product in 65% yield. The formation of the 5-membered product **4aa** was not observed. After some screening, best results were obtained when the reaction was conducted at 80 °C, affording **3aa** in 94% yield (Scheme 1).

**Table 1.** Solvent and PTC Effects on Pd(0)-Catalyzed Coupling Cyclization of **1a** in the Presence of Pentyn-3-yl Carbonate **2a**[a]



| entry | solvent | PTC | time (h) | yield of **3aa**[b] (%) |
|---|---|---|---|---|
| 1 | CH$_3$CN | 10 mol % TBAB | 1 | 94 |
| 2 | DMF | 10 mol % TBAB | 1 | 65 |
| 3 | toluene | 10 mol % TBAB | 1 | 91 |
| 4 | DCE | 10 mol % TBAB | 1 | 87 |
| 5 | THF | 10 mol % TBAB | 1 | 92 |
| 6 | CH$_3$NO$_2$ | 10 mol % TBAB | 1 | 88 |
| 7[c] | CH$_3$CN | no PTC | 48 | 39[d] |
| 8 | CH$_3$CN | 30 mol % TBAB | 1 | (80)[e] |
| 9 | CH$_3$CN | 10 mol % TBAI | 1 | 96 |
| 10 | CH$_3$CN | 10 mol % TBAC | 1 | 54 |

[a] The reaction was carried out using 0.2 mmol of **1a**, 0.3 mmol of **2a**, 5 mol % Pd(PPh$_3$)$_4$, and 10 mol % TBAB in 2 mL of solvent at 80 °C in a Schlenk tube. TBAB = tetrabutylammonium bromide. TBAI = tetrabutylammonium iodide. TBAC = tetrabutylammonium chloride. [b] Isolated yield; the yield in parentheses is the NMR yield using mesitylene as the interal standard. [c] The reaction was conducted at 40 °C. [d] 15% of the starting material was recovered. [e] 8% of the starting material was recovered.

Next, the solvent effect on the reaction was examined (entries 1−6, Table 1). To our delight, this reaction was very general for the solvents tested except for DMF (entry 2, Table 1). Among the solvents tested, CH$_3$CN afforded the product **3aa** in the highest yield (entry 1, Table 1). A survey of phase-transfer catalysts (PTC) indicated that the presence of a phase-transfer catalyst is essential to the reaction (entries 7−10, Table 1): the reaction is very sluggish in the absence of PTC (entry 7, Table 1). However, increasing the amount of TBAB did not favor the reaction (entry 8, Table 1). In the presence of 10 mol % of TBAI, the yield of the desired 1,3,4-alkatrien-2-yl cyclopropane derivative **3aa** can be further improved to 96% (entry 9, Table 1). TBAC is also effective, albeit with a much lower yield of **3aa** (entry 10, Table 1).

To demonstrate the efficiency and scope of the present method, we applied the above optimized reaction conditions to a variety of (2,3-butadienyl)malonates **1** and propargylic carbonates **2**. The results are summarized in Table 2. To our delight, besides the simple methyl (2,3-butadienyl)malonate, ethyl- and benzyl-substituted methyl (2,3-butadienyl)malonates at the 2′ position afforded the corresponding 1,3,4-alkatrien-2-ylcyclopropane derivatives with a quaternary carbon center in good yields (entries 1−4, Table 2). It is noted that the formation of all-carbon quaternary centers is not easy since the process requires the creation of a new

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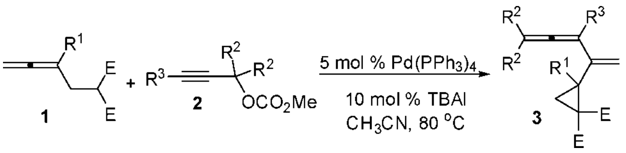
**Table 2.** Pd(0)-Catalyzed Coupling Cyclization of **1** with Propargylic Carbonates **2**[a]



| | **1** | | **2** | | |
|---|---|---|---|---|---|
| entry | $R^1$ | E | $R^2$ | $R^3$ | isolated yield of **3** (%) |
| 1 | H | $CO_2Me$ (**1a**) | Et | H (**2a**) | 96 (**3aa**) |
| 2 | Bn | $CO_2Me$ (**1b**) | Et | H (**2a**) | 78 (**3ba**) |
| 3 | Bn | $CO_2Me$ (**1b**) | -($CH_2$)$_5$- | H (**2b**) | 92 (**3bb**) |
| 4 | Et | $CO_2Me$ (**1c**) | Et | H (**2a**) | 92 (**3ca**) |
| 5 | H | $SO_2Ph$ (**1d**) | Et | H (**2a**) | 92 (**3da**) |
| 6 | H | $CO_2Me$ (**1a**) | −($CH_2$)$_5$− | H (**2b**) | 73 (**3ab**) |
| 7 | H | $CO_2Me$ (**1a**) | −($CH_2$)$_4$− | H (**2c**) | 75 (**3ac**) |
| 8 | H | $CO_2Me$ (**1a**) | Me | H (**2d**) | 85 (**3ad**) |
| 9 | H | $CO_2Me$ (**1a**) | Me | Ph (**2f**) | 89 (**3af**) |
| 10 | H | $CO_2Me$ (**1a**) | Me | *n*-Bu (**2g**) | 79 (**3ag**) |
| 11 | H | $CO_2Me$ (**1a**) | Me | *c*-$C_3H_5$ (**2h**) | 91 (**3ah**) |
| 12 | H | $CO_2Me$ (**1a**) | Me | $CO_2Me$ (**2i**) | 96 (**3ai**) |
| 13 | H | $CO_2Me$ (**1a**) | Me | $CH_2OMe$ (**2j**) | 90 (**3aj**) |

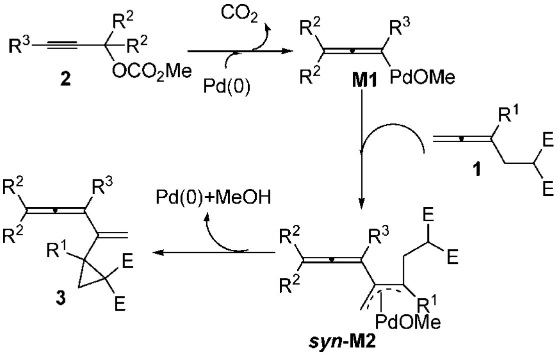
[a] The reaction was carried out using 0.1−0.2 mmol of **1**, 1.5 equiv of **2**, 5 mol % $Pd(PPh_3)_4$, and 10 mol % TBAI in 2 mL of $CH_3CN$ at 80 °C in a Schlenk tube.

C−C bond at a sterically hindered carbon center.[13] Moreover, (2,3-butadienyl)bis(phenylsulfonyl)methane may also be used in this reaction, affording the product in 92% yield (entry 5, Table 2). As to the propargylic carbonates, not only terminal propargylic carbonates are suitable substrates (entries 1−8, Table 2) but also internal propargylic carbonates with phenyl, alkyl, cycloalkyl, methoxycarbonyl, and methoxymethyl substitution on the C−C triple bond have been successfully employed in this reaction (entries 9−13, Table 2). Propargylic carbonates possessing alkyl and cycloalkyl groups at the propargylic position worked equally well under the present conditions (Table 2).

A rationale of this reaction is shown in Scheme 2. Oxidative addition of **2** with Pd(0) would afford allenyl palladium intermediate **M1**, which underwent intermolecular carbopalladation with the allene moiety of **1** to generate $\pi$-allyl palladium intermediate *syn*-**M2**. The malonate moiety in *syn*-**M2** was deprotonated by the methoxy anion, which was followed by regioselective intramolecular attacking at the $\pi$-allyl palladium moiety to afford the final product **3**. Disubstituted propargylic carbonates at the α-position may stablize the allenyl palladium species **M1**.

When these 2-cyclopropyl-1,3,4-trienes **3** were exposed to the catalytic [4 + 1] cycloaddition reaction conditions[14] (catalyzed by $[RhCl(CO)_2]_2$ (2.5 mol %) under 1 atm of CO at room temperature),[15] various polysubstituted cyclopentenone derivatives **5** were obtained in good yields (Table 3). Cyclopentenones are core structural units extensively existing in natural products and bioactive molecules.[16]

**Scheme 2.** Plausible Mechanism of the Reaction



In summary, we have demonstrated a new method for the synthesis of allenes with a cyclopropylvinyl substituent. This reaction proceeded smoothly under neutral conditions, and the regioselectivity is exclusive for the formation of 1,3,4-alkatrien-2-yl cyclopropane derivatives. These compounds

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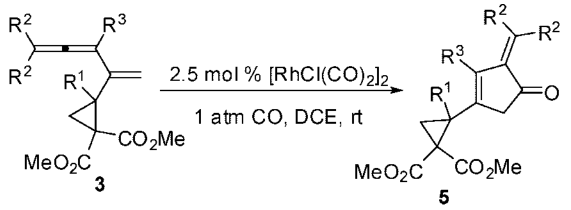
**Table 3.** [4 + 1] Cycloaddition Reaction of **3** with CO[a]



| entry | $R^1$ | $R^2$ | $R^3$ | time (h) | yield of **5**[b] (%) |
|---|---|---|---|---|---|
| 1 | H | Et | H (**3aa**) | 7 | 72(**5a**) |
| 2 | H | Me | H (**3ad**) | 7 | 80(**5b**) |
| 3 | Et | Et | H (**3ca**) | 12 | 86(**5c**) |
| 4 | H | Me | Ph (**3af**) | 36 | 89(**5d**) |
| 5 | H | $-(CH_2)_4-$ | H (**3ac**) | 3 | 82(**5e**) |
| 6 | H | Me | *n*-Bu (**3ag**) | 60 | 69 (**5f**) |

[a] The reaction was carried out using 0.1−0.2 mmol of **3** in 2 mL of DCE. [b] Isolated yields.

may be successfully applied to the synthesis of polysubstituted cyclopentenones via a catalytic [4 + 1] cycloaddition reaction under ambient conditions. Due to diverse reactivity of allenes and cyclopropanes,[17,18] this method will be of interest to synthetic organic chemists. Further studies on the scope of the reaction and synthetic applications of the products are being pursued in our laboratory.

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**Supporting Information Available:** Experimental procedures and analytical data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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