# Palladium-catalyzed Arylative Cyclizations of Allenylmalonates with Aryl Halides

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Palladium-catalyzed arylative cyclizations of allenylmalonates with various aryl halides gave the carbocycles with good chemoselectivity and efficiency.

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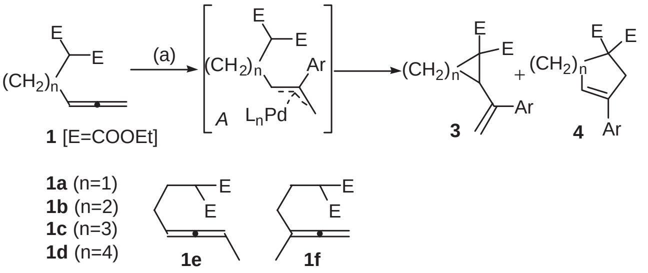
Because of the interesting reactivity of allenes originated mainly from their unique strained structure spreading over three contiguous carbons, continuous efforts have been made to explore allene-based new, more efficient and selective synthetic methodologies for organic synthesis.[1] Especially, palladium-catalyzed reactions of allenes have been most extensively investigated to achieve numerous transformations.[2] For example, a Pd-catalyzed arylative cyclization of $\beta$-allenylmalonate with an aryl halide or an alkenyl halide is known to form the $\pi$-allylpalladium intermediate, which was cyclized by the pendant malonate anion to give either cyclopropyl or cyclopentene derivative.[3,4] Therefore, the control of regioselectivity is an important issue of the cyclization process.[5] Ma and co-workers reported the regioselective Pd(0)-catalyzed coupling-cyclization of 2-(2′,3′-allenyl)-malonates with organic halides, where they obtained cyclopropyl derivatives by using two ways: one was conducted in the presence of phase transfer catalysts in acetonitrile and the other was conducted in THF without using phase transfer catalyst.[6] Here we wish to report our recent findings on Pd-catalyzed arylative cyclizations of a variety of allenylmalonate esters.

When a mixture of the allenylmalonate **1a** and iodobenzene (**2l**) was stirred in the presence of 1.5 equivalent of potassium carbonate and 3 mol% of Pd(PPh$_3$)$_4$ in DMF at 100 °C for 8 h, the product **3al** was formed as an exclusive product by analyzing $^1$H NMR spectrum of the crude product, while Ma obtained a mixture of two regioisomers under the similar conditions. Purification on silica gel chromatography gave the pure product **3al** in 89% yield. This excellent regioselectivity prompted us to investigate a scope of this reaction of allenylmalonate **1a** with aryl halides **2** (Scheme 1 and Table 1).

Thus, the arylative cyclizations of allenylmalonate **1a** with 4-iodoanisole (**2m**), 4-iodonitrobenzene (**2n**), 4-iodotoluene (**2o**), and 1-naphthyl iodide (**2p**) under the same conditions gave the expected products (entries 2–5). In general, these arylative cyclizations occurred with aryl iodides and less efficiently with aryl bromides. Sterically hindered 2-bromotoluene (**2q**) under the standard conditions afforded an 1 : 1 mixture of the two products **3aq** and **4aq** (entry 6) and bromobenzene (**2r**) also gave the product **3al** in only 73% yield (entry 7). Not surprisingly, chlorobenzene did not react at all due to its poor reactivity (entry 8).

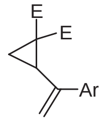


(a) 1.1 eq ArX (**2**), 3 mol% Pd(PPh$_3$)$_4$, 1.5 eq K$_2$CO$_3$, DMF, heat

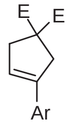
**Scheme 1.**

**Table 1.** Palladium-catalyzed arylative cyclizations of 4-allenylmalonate (**1a**) with aryl halides (2) in DMF

| | ArX | Temp (°C) /Time (h) | % Yield (products, ratio) |
|---|---|---|---|
| 1 | C$_6$H$_5$-I (**2l**) | 100/8 | 89 (**3al**) |
| 2 | (4-MeO)C$_6$H$_4$-I (**2m**) | 60/8 | 80 (**3am**) |
| 3 | (4-NO$_2$)C$_6$H$_4$-I (**2n**) | 100/5 | 23 (**3an**) |
| 4 | (4-Me)C$_6$H$_4$-I (**2o**) | 70/5 | 73 (**3ao**) |
| 5 | 1-C$_{10}$H$_7$-I (**2p**) | 80/4 | 85 (**3ap**) |
| 6 | (2-Me)C$_6$H$_4$-Br (**2q**) | 100/10 | 55 (**3aq** : **4aq** = 1 : 1) |
| 7 | C$_6$H$_5$-Br (**2r**) | 80/6 | 73 (**3al**) |
| 8 | C$_6$H$_5$-Cl (**2s**) | 80/6 | nr |



**3al-aq**



**4aq**

With these preliminary results, we extended this reaction to allenylmalonates **1b–1f** to obtain the carbocycles (Table 2). The reactions of allenylmalonates **1b–d**, a homolog of **1a**, reacted with aryl iodides and aryl bromides **2l–r** formed the arylated carbocycles in high yields.

The regioselectivities of these reactions are interesting. The substrates **1a** (Table 1), **1c**, and **1d** gave the products **3a**, **3c**, and **3d**, respectively, except the reaction of **1a** with **2q**. Although the substrate **1b** gave the 4-membered carbocycles **3b** as major products under these conditions, the thermodynamically more stable 6-membered carbocycles **4b** were also formed as minor products. As structurally hindered homologs of **1b**, substrates **1e** and **1f** were prepared for comparison on regioselectivity. Both substrates **1e** and **1f** underwent arylative cyclizations very well with both aryl iodides and aryl bromides, but their regioselectivities were quite different. Both **1e** and **1f** gave the corresponding 6-membered carbocycles as the major products.

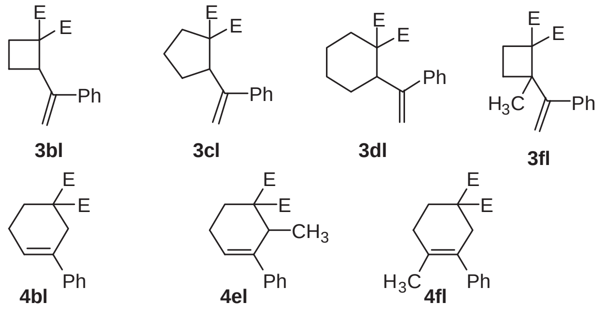
While **1e** formed 6-membered rings **4e** exclusively, **1f** formed a mixture of 4- and 6-membered rings with 6-membered carbocycles **4f** as the major products. The presence of a hindered group (methyl group) seemed to favor the formation of 6-membered rings, especially in the substrate **1e** bearing an external methyl group.

Mechanistically, aryl halides **2** were first reacted with Pd(PPh$_3$)$_4$ to form arylpalladium halides which would be coupled with the central carbon of the allenes **1** to form $\pi$-allylpalladium

**Table 2.** Palladium-catalyzed arylative cyclizations of allenylmalonate (**1b–f**) with aryl halides (2) in DMF

| Substrates | Ar-X | Temp (°C) /Time (h) | % Yield (products, ratio) |
|---|---|---|---|
| **1b** | **2l** | 100/10 | 74 (**3bl** : **4bl** = 2 : 1) |
| (n = 2) | **2m** | 80/4 | 70 (**3bm** : **4bm** = 3 : 1) |
| | **2n** | 80/4 | 97 (**3bn** : **4bn** = 9 : 1) |
| | **2o** | 70/4 | 85 (**3bo**) |
| | **2p** | 80/15 | 75 (**3bp** : **4bp** = 9 : 1) |
| | **2q** | 100/16 | 89 (**3bq** : **4bq** = 1 : 1) |
| **1c** | **2l** | 100/10 | 95 (**3cl**) |
| (n = 3) | **2r** | 80/7 | 73 (**3cl**) |
| | **2m** | 80/22 | 76 (**3cm**) |
| | **2n** | 80/6 | 98 (**3cn**) |
| | **2o** | 80/4 | 88 (**3co**) |
| | **2p** | 90/12 | 52 (**3cp**) |
| | **2q** | 90/15 | 74 (**3cq**) |
| **1d** | **2l** | 70/14 | 64 (**3dl**) |
| (n = 4) | **2m** | 70/4 | 85 (**3dm**) |
| | **2n** | 70/7 | 50 (**3dn**) |
| **1e** | **2l** | 80/9 | 82 (**3el**) |
| | **2m** | 80/4 | 63 (**3em**) |
| | **2n** | 80/4 | 87 (**3en**) |
| **1f** | **2l** | 80/6 | 91 (**3fl** : **4fl** = 1 : 2) |
| | **2m** | 80/8 | 52 (**3fm** : **4fm** = 1 : 4) |
| | **2n** | 80/9 | 79 (**3fn** : **4fn** = 1 : 20) |

**Phenyl-group (l) incorporated structures**



intermediates $\boldsymbol{A}$ as shown in Scheme 1. The $\pi$-allylpalladium intermediates then were attacked by the carbon nucleophiles to form the carbocycles **3** and their regioisomers **4**.

In summary, this study demonstrated an extended version of Ma's arylative cyclization, where allenylmalonates under the Pd(0) catalyst were arylated with aryl halides and then subsequently cyclized with the pendant carbon nucleophiles to give the carbocycles.

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