JOC Article

Highly Regio- and Chemoselective Palladium-Catalyzed Propargylallylation of Activated Olefins: A Novel Route to 1,7-Enyne Derivatives

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An efficient method for the synthesis of 1,7-enyne derivatives via phosphine−palladium-catalyzed three-component assembling of activated olefins, allylic chlorides, and allenylstannanes is described. Substituted arylethylidene malononitriles **1a**−**g** (RCH═C(CN)$_2$: R = C_6H_5 (**1a**), *p*-ClC_6H_4 (**1b**), *p*-$OMeC_6H_4$ (**1c**), *p*-$NO_2C_6H_4$ (**1d**), 1-naphthyl (**1e**), 2-furyl (**1f**), and 2-thienyl (**1g**)) undergo propargylallylation with allylic chlorides **2a**−**e** (allyl chloride (**2a**), methallyl chloride (**2b**), 4-chloropent-2-ene (**2c**), cinnamyl chloride (**2d**), and 3-chlorocyclohexene (**2e**)) and *n*-tributylallenylstannane (*n*-$Bu_3SnCH═C═CH_2$, **3a**) in the presence of $Pd(PPh_3)_4$ in toluene to afford the corresponding 1,7-enyne derivatives **4a**−**m** in good to excellent yields. The catalytic reaction is highly regioselective, with the propargyl group adding to the carbon where the R group is attached and the allyl group adding to the carbon connected to the CN groups of activated olefins **1a**−**g**. The present catalytic reaction is successfully extended to substituted arylethylidene-1,3-indanediones **5a**−**j** (RCH = (1,3-indanedione): R = C_6H_5 (**5a**), *p*-ClC_6H_4 (**5b**), *p*-BrC_6H_4 (**5c**), *p*-$OMeC_6H_4$ (**5d**), *p*-$NO_2C_6H_4$ (**5e**), *p*-CNC_6H_4 (**5f**), *p*-biphenyl (**5g**), 1-naphthyl (**5h**), 2-thienyl (**5i**), and 2-benzo[*b*]furane-2-yl (**5j**)) and substituted 2,2-dimethyl-5-(arylethylidene)-1,3-dioxane-4,6-diones **7a**,**b** (RCH = (1,3-dioxane-4,6-dione): R = *p*-$NO_2C_6H_4$ (**7a**), *p*-$OMeC_6H_4$ (**7b**)). The three-component assembling of these substrates with allylic chlorides (**2a**,**b**,**d**,**e**) and *n*-tributylallenylstannane (*n*-$Bu_3SnCH═C═CH_2$, **3a**) proceeds smoothly to afford the corresponding 1,7-enyne derivatives **6a**−**m** and **8a**−**d** in good to excellent yields. The catalytic propargylallylation can be further applied to the activated dienes, $C_6H_5CH═CH═CR_2$ (R_2 = $(CN)_2$ (**9a**), 1,3-indanedione (**9b**), 2,2-dimethyl-1,3-dioxane-4,6-dione (**9c**)), with allylic chlorides (**2a**,**b**,**d**) and allenylstannane **3a** to give regio- and chemoselective 1,2-addition products **10a**−**h** in good to excellent yields. A plausible mechanism based on an η^1-allenyl η^3-allyl palladium intermediate is proposed to account for the catalytic three-component reaction.

Introduction

Transition metal-catalyzed multicomponent assembling reactions provide an efficient route for the construction of complex organic molecules.[1] The palladium-catalyzed addition of an electrophile and a nucleophile to an unsaturated species is representative of this class of transformations and has been useful to construct two carbon−carbon bonds in a single step.[2] However, the control of regio- and stereoselectivity is an important consideration for the design of new three-component assembling reactions. In addition, it is necessary to suppress competing direct coupling of the nucleophile and electrophile, β-hydride elimination, and polymerization of the unsaturated species (alkenes or alkynes).

The chemistry of π-allyl palladium complexes has been the subject of intense interest in organic synthesis.[3] It is well-known that the π-allyl groups in these complexes react with a wide variety of nucleophiles such as malonates,[3] β-keto esters,[4] and amines[5] to form new carbon−carbon or carbon−heteroatom bonds. However, the charge reversal of the allyl group could be realized by reacting the π-allyl palladium complex with a low-valent metal compound such as $SnCl_2$,[6] Et_2Zn,[7] SmI_2,[8] Zn,[9] In,[10] and InI[11] to generate the corresponding nucleophilic organometallic reagents, which then react with electrophiles.

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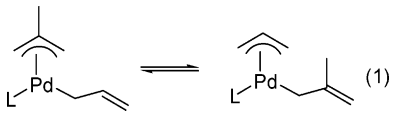
Another strategy reported by Yamamoto et al. involves the use of a nucleophilic bis-allyl palladium complex generated by the reaction of allyl chloride and allylstannane with a palladium catalyst. This bis-allyl palladium complex can act as an amphiphilic reagent (i.e. both electrophilic and nucleophilic) reacting with activated olefins[12] and arynes[13] to form the corresponding bis-allylation products. This new type of catalytic reaction proceeds via bis-allyl palladium intermediate in which the σ-allyl group acts as a nucleophile and the π-allyl group as an electrophile. However, the utility of this catalytic reaction is limited to allyl chloride and allylstannane. Subsequently, Szabó et al. reported a similar type of palladium-catalyzed reactions of activated olefins[14] or isocyanates[15] with substituted allylic chlorides and allylstannanes. In the bis-allylation of activated olefins, although the two allyl groups come from two different allyl reagents, the regioselectivity is low. This is probably due to the ready $\sigma-\pi$ exchange of the bis-allyl intermediate leading to the interchange of the nucleo- and electrophilicity (eq 1). This reversal of

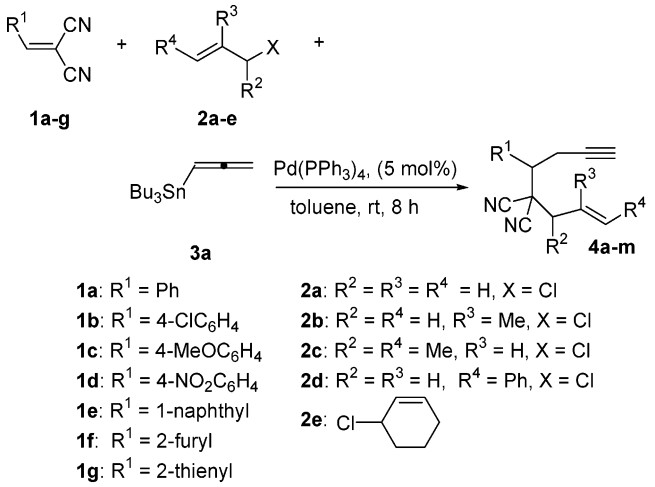


(1)

reactivity of bis-allyl palladium complexes imposes considerable synthetic limitation on the bis-allylation reaction. Thus, a challenging problem in this chemistry is whether it is possible to use new nucleophiles for the three-component reaction and control the regiochemistry of the reaction.

Allenylstannanes are mild organometallic reagents that undergo a number of useful transformations including allylation reaction with aldehydes,[16] coupling reactions,[17] and cyclization reactions,[18] but the utility of this reagent in the three-component coupling reaction has not been explored. We have been working on palladium-catalyzed three-component reactions involving allenes, leading to two carbon−carbon bond formation in one pot.[19] Our continuous interest in the allene chemistry[20] prompted us to explore the possibility of using allenylstannanes as nucleophiles for the palladium-catalyzed reaction involving activated olefins and allylic chlorides. In a preliminary communication,[21] we reported a highly regio- and chemoselective palladium-catalyzed three-component assembling reaction of arylethylidene malononitriles with allylic chlorides and allenylstannanes to give substituted 1,7 enyne derivatives. The results promoted us to extend this methodology into other activated olefins. In this paper, we wish to report the full details of this study.

SCHEME 1



Results and Discussion

Phenylethylidene malononitrile (**1a**) underwent propargylallylation with allyl chloride (**2a**) and *n*-tributylallenylstannane (**3a**) in the presence of $Pd(PPh_3)_4$ (5 mol %) in toluene at ambient temperature for 8 h to furnish 1,7-enyne derivative **4a** in 86% yield (Scheme 1). This catalytic three-component assembling reaction is completely regioselective with the propargyl and the allyl groups adding to the β and the α carbons, respectively, of **1a**. No other regioisomer was detected as evidenced by the ^{1}H NMR spectrum of the crude reaction mixture. The regiochemistry of **4a** was established by ^{1}H−^{1}H decoupling NMR experiments. Control experiments revealed that in the absence of palladium catalyst, no desired product **4a** was formed.

To optimize the present catalytic reaction, various conditions were tested for the reaction of **1a** with **2a** and

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SCHEME 2

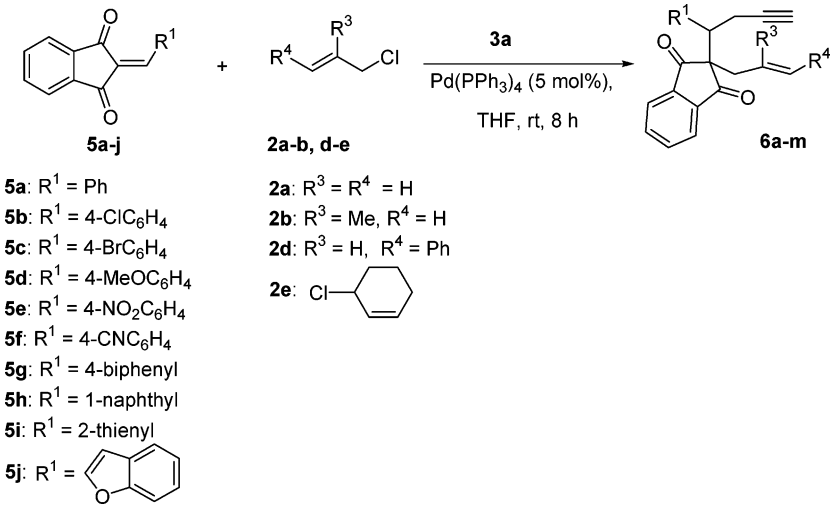


TABLE 1. Effects of Catalysts, Allyl Halides 2, and Solvents on the Propargylallylation of Malononitrile 1a with Allyl Halide 2 and Allenylstannane 3a[a]

entry	X	catalyst	solvent	yield of **4a** (%)[b]
1	−Cl	$Pd(dba)_2$	toluene	NR
2	−Cl	$Pd(OAc)_2$	toluene	NR
3	−Cl	$PdCl_2(CH_3CN)_2$	toluene	NR
4	−Cl	$Pd(PCy_3)_2Cl_2$	toluene	42
5	−Cl	$PdCl_2(PPh_3)_2$	toluene	46
6	−Cl	$Pd(PPh_3)_4$	toluene	86
7	−Br	$Pd(PPh_3)_4$	toluene	38
8	−I	$Pd(PPh_3)_4$	toluene	15
9	−OAc	$Pd(PPh_3)_4$	toluene	10
10	−OH	$Pd(PPh_3)_4$	toluene	5
11	−Cl	$Pd(PPh_3)_4$	THF	71
12	−Cl	$Pd(PPh_3)_4$	CH_3CN	41
13	−Cl	$Pd(PPh_3)_4$	DMF	26
14	−Cl	$Pd(PPh_3)_4$	ethyl acetate	42
15	−Cl	$Pd(PPh_3)_4$	CH_2Cl_2	28

[a] All reactions were carried out under the following conditions: malononitrile (**1a**, 1.00 mmol), allyl halide (**2a**, 1.20 mmol), allenylstannane (**3a**, 1.20 mmol), Pd complex (0.050 mmol), and solvent (2.0 mL). [b] Yields were determined by the ^1H NMR integration method, using mesitylene as an internal standard.

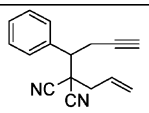
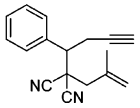
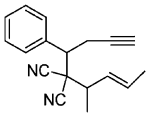
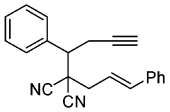
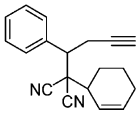
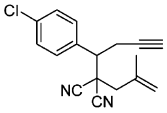
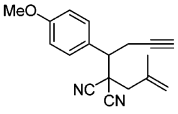
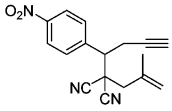
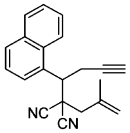
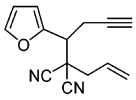
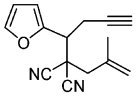
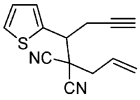
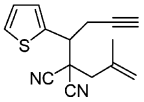
3a. The results are shown in Table 1. Palladium complexes $Pd(dba)_2$, $Pd(OAc)_2$, and $PdCl_2(CH_3CN)_2$ in toluene were totally ineffective for the reaction (entries 1−3). The reaction proceeded by using phosphine palladium complexes $PdCl_2(PCy)_2$ and $PdCl_2(PPh_3)_2$, but product **4a** was obtained in low yields of 42% and 46%, respectively (entries 4 and 5). $Pd(PPh_3)_4$ shows the highest catalytic activity, giving **4a** in 86% yield (entry 6). The nature of the leaving group on the allylic substrate has revealed great influence on the yield of the product (entries 6−10). Allyl chloride gave the highest yield of three-component assembling product (entry 6). Other substrates such as allyl bromide, allyl iodide, allyl acetate, and allyl alcohol were less effective for the reaction, affording **4a** in low yields (entries 7−10). Several solvents were examined for the reaction. The results (entries 6 and 11−15) suggested that toluene was the solvent of choice (entry 6). THF was also effective affording **4a** in 71% yield (entry 11). The other solvents CH_3CN, DMF, ethyl acetate, and CH_2Cl_2 gave **4a** in much lower yields (entries 12−15).

Under similar conditions employed for the reaction in entry 6, Table 1, several substituted allylic chlorides (**2b**−**e**) react with **1a** and **3a** effectively to afford the corresponding 1,7-enyne derivatives in good to excellent yields (Table 2). Methallyl chloride (**2b)** afforded product **4b** in 80% yield (entry 2). The regiochemistry of **4b** was established based on the characteristic coupling pattern (two doublets at δ 2.50 and 2.29) of the methylene protons of the allyl group and also the results of $^1H-^1H$ decoupling experiments. Similarly, the reactions of 4-chloropent-2-ene (**2c**), cinnamyl chloride (**2d**), and 3-chlorocyclohexene (**2e**) with **1a** and **3a** furnished the corresponding propargylallylation products **4c**−**e** in 76%, 74%, and 76% yields, respectively (entries 3−5). In the case of 3-chlorocyclohexene, the reaction gave two diastereomers in ca. 1:1 ratio in 76% combined yield (entry 5). The allylation by **2d** is highly regioselective giving exclusively the cinnamyl-substituted product **4d** (entry 4).

Various substituted arylethylidene malononitriles **1b**−**e** also undergo propargylallylation with **2b** and **3a** to give the corresponding three-component assembling products **4f**−**i** in good yields (entries 6−9). Arylethylidene malononitriles with an electron-donating group or electron-withdrawing group on the aryl ring are all effective substrates for the assembling reaction (entries 6−8). The present protocol is successfully extended to ethylidene malononitriles with a heterocyclic substituent. Thus, treatment of furylethylidene malononitrile **(1f)** and **3a** with **2a** as well as **2b** in the presence of $Pd(PPh_3)_4$ afforded the corresponding 1,7-enyne derivatives **4j** and **4k** in 75% and 76% yields, respectively (entries 10 and 11). Under similar conditions, the reaction of thienylethylidene malononitrile (**1g**) and **3a** with **2a** as well as **2b** produced the corresponding assembling products **4*l*** and **4m** in 83% and 79% yields, respectively (entries 12 and 13).

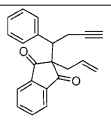
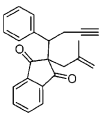
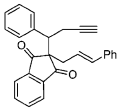
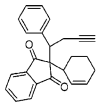
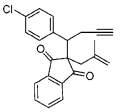
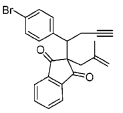
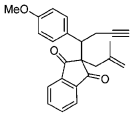
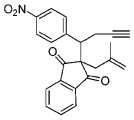
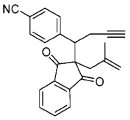
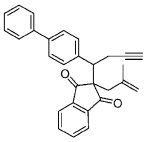
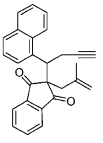
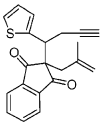
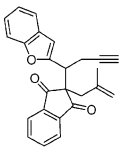
The present three-component assembling reaction can also be applied to substituted 2-(arylmethylene)-1,3-indanediones **5a**−**j** (Scheme 2). The results are listed in Table 3. Treatment of 2-(phenylmethylene)-1,3-indanedione (**5a**) with **2a** and **3a** in the presence of $Pd(PPh_3)_4$ afforded 1,7-enyne derivative **6a** in 78% yield (entry 1). No other regioisomer was detected in the ^1H NMR spectrum of the crude reaction mixture, indicating that the catalytic reaction is highly regioselective. The regio-

TABLE 2. Palladium-Catalyzed Propargylallylation of Malononitriles 1a−g with Allylic Chlorides 2a−e and Allenylstannane 3a[a]

Entry	1	2	Product	Yield (%)[b]
1	**1a**	**2a**	 **4a**	78 (86)
2	**1a**	**2b**	 **4b**	80
3	**1a**	**2c**	 **4c**	76
4	**1a**	**2d**	 **4d**	74
5	**1a**	**2e**	 **4e**[c]	76
6	**1b**	**2b**	 **4f**	77
7	**1c**	**2b**	 **4g**	78
8	**1d**	**2b**	 **4h**	76
9	**1e**	**2b**	 **4i**	75
10	**1f**	**2a**	 **4j**	75
11	**1f**	**2b**	 **4k**	76
12	**1g**	**2a**	 **4l**	83
13	**1g**	**2b**	 **4m**	79

[a] All reactions were carried out under the following conditions: malononitrile (**1**, 1.00 mmol), allylic chloride (**2**, 1.20 mmol), allenylstannane (**3a**, 1.20 mmol), $Pd(PPh_3)_4$ (0.050 mmol), and toluene (2.00 mL). [b] Isolated yields: yield in parentheses was determined by the ^1H NMR integration method, using mesitylene as an internal standerd. [c] 1:1 diastereomers (determined by ^1H NMR).

TABLE 3. Palladium-Catalyzed Propargylallylation of Indanediones 5a−j with Allylic Chlorides 2a,b,d,e and Allenylstannane 3a[a]

Entry	5	2	Product	Yield (%)[b]
1	**5a**	**2a**		**6a** 78
2	**5a**	**2b**		**6b** 79
3	**5a**	**2d**		**6c** 68
4	**5a**	**2e**		**6d**[c] 67
5	**5b**	**2b**		**6e** 78
6	**5c**	**2b**		**6f** 76
7	**5d**	**2b**		**6g** 81
8	**5e**	**2b**		**6h** 84
9	**5f**	**2b**		**6i** 75
10	**5g**	**2b**		**6j** 74
11	**5h**	**2b**		**6k** 72
12	**5i**	**2b**		**6l** 76
13	**5j**	**2b**		**6m** 71

[a] All reactions were carried out under the following conditions: indanedione (**5**, 1.00 mmol), allylic chlorides (**2**, 1.20 mmol), allenylstannane (**3a**, 1.20 mmol), $Pd(PPh_3)_4$ (0.050 mmol), and THF (3.0 mL). [b] Isolated yields. [c] 1:1 diastereomers (determined by ^1H NMR).

SCHEME 3

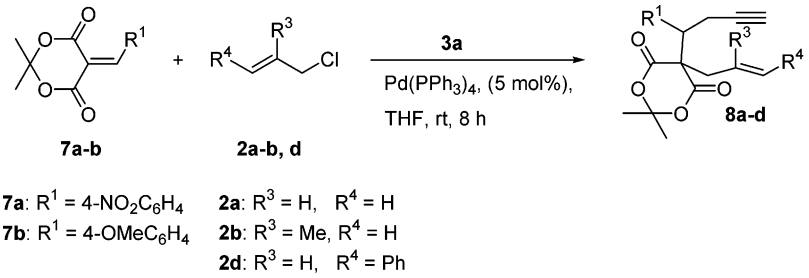
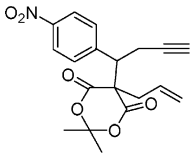
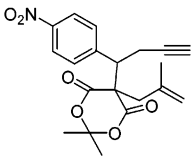
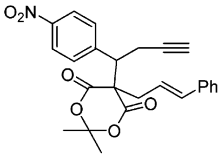
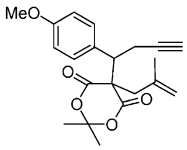


TABLE 4. Palladium-Catalyzed Propargylallylation of Substituted 2−2-Dimethyl-5-(arylmethylene)-1,3-dioxane-4,6-diones 7a,b with Allylic Chlorides 2a,b,d and Allenylstannane 3a[a]

Entry	7	2	Product	Yield (%)[b]
1	**7a**	**2a**	 **8a**	76
2	**7a**	**2b**	 **8b**	79
3	**7a**	**2d**	 **8c**	66
4	**7b**	**2b**	 **8d**	77

[a] All reactions were carried out under the following conditions: substituted 2,2-dimethyl-5-(arylmethylene)-1,3-dioxane-4,6-dione (**7**, 1.00 mmol), allylic chloride (**2**, 1.20 mmol), allenylstannane (**3a**, 1.20 mmol), $Pd(PPh_3)_4$ (0.050 mmol), and THF (3.00 mL). [b] Isolated yields.

chemistry of **6a** was established based on the results of the $^1H-^1H$ decoupling experiments. Under similar reaction conditions, various allylic chlorides **2 (2b**, **2d**, and **2e)** react smoothly with **5a** and **3a** to yield the corresponding three-component assembling products **6b**−**d** in good yields (entries 2−4). As expected, **2e** afforded product **6d** consisting of two diastereomers with a 1:1 molar ratio (entry 4).

In addition to **5a**, several substituted 2-(arylmethylene)-1,3-indanediones **5b**−**j** were also used for the three-component assembling reactions with **2b** and **3a** successfully. The reactions gave the corresponding 1,7-enyne derivatives **6e**−**m** in good to moderate yields (entries 5−13). It is noteworthy that the catalytic reaction tolerates a variety of functional groups such as chloro, bromo, methoxy, nitro, cyano, sulfur, and oxygen on the aryl ring of **5** (entries 5−9, 12, and 13).

The scope and generality of the present catalytic reaction is further extended into substituted 2,2-dimethyl-5-(arylmethylene)-1,3-dioxane-4,6-diones **7a**,**b** that contain two electron-withdrawing diesters (Scheme 3). The $Pd(PPh_3)_4$-catalyzed propargylallylation reaction of **7a** with allylic chlorides **2** (**2a**,**b**,**d**) and allenylstannane **3a** is highly regioselective, affording **8a**−**c**, respectively, in 66−79% yields (Table 4, entries 1−3). Under similar conditions, **7b** with an electron-donating methoxy group on the aryl ring reacts smoothly with **2b** and **3a** to furnish the corresponding product **8d** in 77% yield (entry 4).

To further understand the regioselectivity of this catalytic reaction, the three-component assembling of conjugated olefins was investigated (Scheme 4). Treatment of diene **9a** with **2a** and **3a** in the presence of $Pd(PPh_3)_4$ afforded 1,2-addition product **10a** in 79% yield (Table 5, entry 1). No other regioisomer or 1,4-addition product was detected in the ^1H NMR of the crude reaction mixture, indicating that the catalytic reaction is highly regio- and chemoselective. The 1,2-addition product **10a** was characterized by ^1H NMR NOE experiments. Irradiation of the H_a proton at δ 6.67 caused 2.32%

SCHEME 4

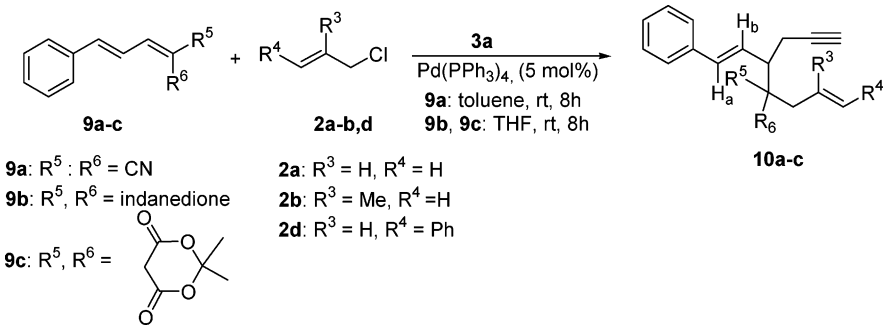


TABLE 5. Palladium-Catalyzed Propargylallylation of Dienes 9a−c with Allylic Chlorides 2a,b,d and Allenylstannane 3a[a]

Entry	9	2	Product	Yield (%)[b]
1	**9a**	**2a**	**10a**	79
2	**9a**	**2b**	**10b**	82
3	**9a**	**2d**	**10c**	73
4	**9b**	**2a**	**10d**	75
5	**9b**	**2b**	**10e**	76
6	**9c**	**2a**	**10f**	72
7	**9c**	**2b**	**10g**	74
8	**9c**	**2d**	**10h**	62

[a] All reactions were carried out under the following conditions: diene (**9**, 1.00 mmol), allylic chlorides (**2**, 1.20 mmol), allenylstannane (**3a**, 1.20 mmol), $Pd(PPh_3)_4$ (0.050 mmol), and toluene or THF (3.00 mL). [b] Isolated yields.

enhancement of the ortho proton signal of the phenyl ring at δ 7.30, while irradiation of the H_b proton at δ 6.00 caused 3.30% enhancement of the ortho proton signal at δ 7.30. These NOE data strongly support that **10a** is a

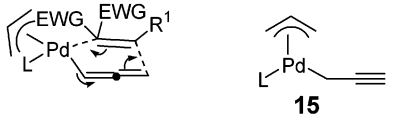
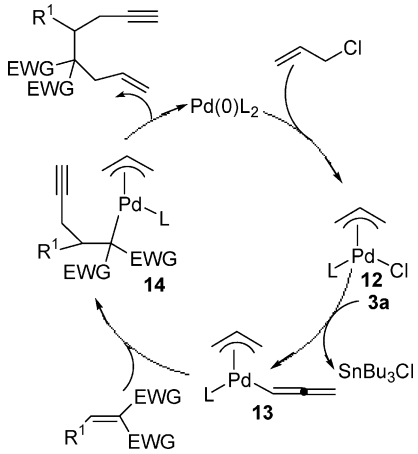


FIGURE 1.

SCHEME 5



1,2-addition product and exclude the possibility of a 1,4-addition product. In a similar fashion, the three-component reactions of **9a**, **3a**, and **2b** or **2d** afforded **10b** or **10c** in 75% and 71% yields, respectively (entries 2 and 3). The catalytic reactions can be successfully applied to 2-[(1*E*,3*E*)-4-phenyl-1,3-butadienyl]-1,3-indanedione **9b** and 2,2-dimethyl-5-[(1*E*,3*E*)-4-phenyl-1,3-butadienyl]-1,3-dioxane-4,6-dione **9c** (entries 4−8). In all cases, the three-component assembling reactions are highly regio- and chemoselective, affording only the corresponding 1,2-addition products in moderate to good yields (Table 5).

On the basis of the known palladium chemistry and the mechanisms for the catalytic reactions involving bis-allyl palladium complexes as key intermediates,[12−15,21] a mechanism is proposed to account for the present catalytic propargylallylation reaction (Scheme 5). The first step likely involves the oxidative addition of allyl chloride **2** to Pd(0) to give π-allyl palladium complex **12**. Transmetalation of allenylstannane **3a** with **12** gives σ-allenyl π-allyl palladium intermediate **13** and Bu_3SnCl.[17,21] Reaction of activated olefin **1** with **13** gives **14**. Subsequent reductive elimination of **14** affords the final product and regenerates the Pd(0) catalyst.

Transmetalation of allenylstannane with palladium(II) complex to give the η^1-allenyl palladium intermediate was evidenced by the palladium-catalyzed coupling of aryl iodides or aryl triflates with allenylstannane to afford arylallene.[17] The accompanying formation of Bu_3SnCl was supported by the observation of Bu_3SnCl signals in the ^1H NMR spectra of the crude reaction mixture of the reaction of **1** with **2** and **3a**. While the exact reason for the high product yield obtained for the allyl chloride compared to other allylic substrates is not known, a possible driving force is the great stability of the Sn−Cl bond and the facile formation of Bu_3SnCl in the transmetalation step.

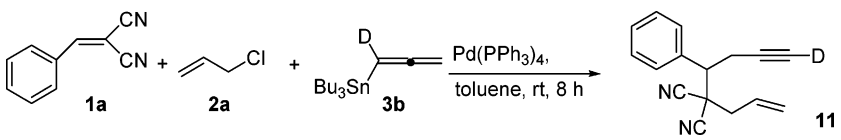
The formation of intermediate **14** occurs likely via an S_E2' pathway that involves the attack of γ-carbon of the allenyl group of **13** at activated olefin **1**. A six-membered cyclic transition state (Figure 1) formed by alkene **1**, palladium metal, and the allenyl group in **13** can account for the facile transformation of **13** to **14**. Such a six-membered transition state has been used to explain the propargylation of aldehydes by allenylstannanes.[22] The six-membered cyclic transition state is further supported by the result of the following deuterium studies (Scheme 6). The reaction of deuterated allenylstannane **3b** with **1a** and **2a** in the presence of $Pd(PPh_3)_4$ in toluene at room temperature for 8 h gave **11** in 78% yield. The deuterium is incorporated in the terminal carbon of the propargyl group of **11** with 79% deuterium purity. No deuterium label was observed in the methylene carbon, indicating that the γ-carbon of the allenyl group undergoes propargylation with the electrophilic carbon of activated olefins.

Another possible mechanism involves a σ-propargyl π-allyl palladium intermediate **15** from the reaction of **12** with the γ-carbon of the allenyl group in **3a**. Migratory insertion of alkene **1** to the propargylpalladium in **15** gives **14**. This pathway cannot to be ruled out, but it is less likely on the basis of the following observation. The reaction of alkene **1a** with propargyl chloride and allylstannane under our standard conditions did not afford three-component assembling product **4a**.

The high regioselectivity of the present catalytic reaction can be attributed to the ready formation of a σ-allenyl π-allyl palladium complex **13**. This intermediate regioselectively transfers the σ-allenyl group to the β-carbon and the π-allyl group to the α-carbon of the activated alkenes to give the final product. It should be noted that in the bis-allylation reaction reported by Szabó, a mixture of regioisomers was observed for the reaction of methallyl chloride, allylstannane, and activated alkene due to $\sigma-\pi$ exchange of the allyl groups in the resulting palladium intermediate.[14,15] However, in the present three-component reaction of methallyl chloride, activated olefins (**1**, **5**, and **7**), and **3a**, only a single regioisomer was obtained (Tables 2−4).

Several interesting features emerge from the present catalytic reaction. First, the catalytic reaction is highly regio- and chemoselective. In all cases, a single regioisomer was observed in which the propargyl group added to the carbon-containing R group and the allyl group added to the carbon-containing EWG group of the activated olefins. Second, no trace of the competitive direct coupling reaction of allenylstannanes with allylic chlorides was detected under our standard conditions. Keinan and Peretz [23] reported that a palladium-catalyzed reaction of allenylstannanes with allylic acetates afforded

SCHEME 6



allylic progargylation product. In the present case, the η^1-allenyl η^3-allyl palladium intermediates react with the activated olefins faster than the coupling of the allenyl and allyl groups in the intermediate. Third, variation is allowed in each of the three component leading to a wide range of 1,7-enyne derivatives in good to excellent yields. It is noteworthy that the 1,7-enyne derivatives are versatile substrates for various reactions including the Pauson-Khand reaction,[24] the metal-catalyzed cycloisomerization,[25] and the cycloreduction reaction.[26]

Attempts to use *trans*-styryl(tributyl)stannane or (2-phenylethynyl)(tributyl)stannane as the nucleophile to replace allenylstannane **3a** in the three-component assembling reaction failed probably due to the fact that no six-membered cyclic transition state can be formed. On the basis of the results of Yamamoto's type bis-allylation and our present catalytic reaction, it appears that an allyl or allenyl group with a γ-addition ability is necessary to act as the nucleophile in this type of catalytic three-component reaction.

Conclusion

In conclusion, we have developed a new palladium-catalyzed highly regioselective three-component assembling reaction of activated olefins with allylic chlorides and allenylstannanes. This method allows an efficient synthesis of various 1,7-enyne derivatives in good to excellent yields. The present catalytic reaction proceeds with various substituted activated olefins. Furthermore, the reaction was successfully extended to activated dienes.

Experimental Section

General. All reactions were conducted under nitrogen atmosphere on a dual-manifold Schlenk line unless otherwise mentioned and in oven-dried glasswares. All solvents were dried according to known methods and distilled prior to use.[27] The starting materials substituted arylethylidene malononitriles **1a**−**g** and **9a**,[28] substituted arylethylidene-1,3-indanediones[29] **5a**−**j** and **9b**, substituted 2,2-dimethyl-5-(arylethylidene)-1,3-dioxane-4,6-diones **7a**,**b** and **9c**,[30] and allenylstannanes **3a** and **3b**[31] were synthesized according to the literature procedures. $Pd(PPh_3)_4$,[32] $PdCl_2(PPh_3)_2$,[33] and $Pd(dba)_2$[34] were prepared by reported procedures. Other reagents were commercially available and used as purchased.

2-(1-Phenyl-3-butynyl)-2-(2-propenyl)propanedinitrile (4a): pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.36 (m, 5H), 5.89−5.83 (m, 1H), 5.39 (d, J = 10.5 Hz, 1H), 5.31 (d, J = 17.0 Hz, 1H), 3.26 (dd, J = 10.5, 4.5 Hz, 1H), 3.05−3.01 (m, 2H), 2.53 (dd, J = 14.0, 7.5 Hz, 1H), 2.42 (dd, J = 14.0, 7.5 Hz, 1H), 1.90 (t, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.6, 129.3, 129.1, 128.8, 128.4, 123.5, 114.7, 113.9, 79.3, 71.7, 50.0, 42.7, 40.6, 22.4; HRMS calcd for $C_{16}H_{14}N_2$ 234.1157, found 234.1156.

2-(2-Methyl-2-propenyl)-2-(1-phenyl-3-butynyl)propanedinitrile (4b): pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.37 (m, 5H), 5.12 (s, 1H), 5.10 (s, 1H), 3.28 (dd, J = 10.5, 4.5 Hz, 1H), 3.10−3.01 (m, 2H), 2.50 (d, J = 14.0 Hz, 1H), 2.29 (d, J = 14.0 Hz, 1H), 1.90 (t, J = 2.5 Hz, 1H), 1.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 134.6, 129.3, 129.1, 128.8, 118.6, 115.1, 114.2, 79.3, 71.6, 51.5, 44.2, 41.8, 23.0, 22.3; HRMS calcd for $C_{17}H_{16}N_2$ 248.1313, found 248.1303.

2-(1-Methyl-2-butenyl)-2-(1-phenyl-3-butynyl)propanedinitrile (4c): pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.38 (m, 5H), 5.74−5.69 (m, 1H), 5.47−5.41 (m, 1H), 3.29 (dd, J = 10.4, 4.4 Hz, 1H), 2.93−2.91 (m, 2H), 2.57−2.53 (m, 1H), 1.89 (t, J = 3.0 Hz, 1H), 1.75 (d, J = 6.8 Hz, 3H), 1.31 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 132.6, 129.4, 129.1, 128.9, 127.9, 114.6, 113.7, 79.8, 71.8, 48.1, 42.4, 42.2, 22.2, 18.3, 17.2; HRMS calcd for $C_{18}H_{18}N_2$ 262.1470, found 262.1472.

2-Allyl-2-(1-phenyl-3-butynyl)-1,3-indanedione (6a): pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79−7.63 (m, 4H), 7.05−6.99 (m, 5H), 5.38−5.31 (m, 1H), 5.01 (d, J = 18.6 Hz, 1H), 4.82 (d, J = 9.6 Hz, 1H), 3.45 (t, J = 7.8, 1H), 2.89 (dd, J = 7.8, 2.4 Hz, 2H), 2.72 (dd, J = 13.2, 7.2 Hz, 1H), 2.55 (dd, J = 13.2, 7.2 Hz, 1H), 1.72 (t, J = 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.5, 202.5, 142.6, 142.4, 138.1, 135.4, 135.4, 131.2, 129.1, 127.9, 127.2, 122.7, 122.5, 119.8, 82.2, 70.2, 61.0, 49.5, 37.9, 19.8; HRMS calcd for $C_{22}H_{18}0_2$ 314.1307, found 314.1307.

2-(2-Methylallyl)-2-(1-phenyl-3-butynyl)-1,3-indanedione (6b): pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 7.2 Hz, 1H), 7.66−7.59 (m, 3H), 7.06−6.98 (m, 5H), 4.53 (d, J = 4.5 Hz, 2H), 3.43 (dd, J = 8.5, 7.5 Hz, 1H), 2.89−2.87 (m, 2H), 2.81 (d, J = 13.0 Hz, 1H), 2.53 (d, J = 13.0 Hz, 1H), 1.71 (t, J = 3 Hz, 1H), 1.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7, 202.6, 142.9, 142.7, 139.7, 138.1, 135.3, 135.3, 129.1, 127.9, 127.2, 122.6, 122.3, 116.7, 82.2, 70.1, 61.2, 50.6, 41.8, 24.0, 19.9; HRMS calcd for $C_{23}H_{20}O_2$ 328.1463, found 328.1462.

2-(1-Phenyl-3-butynyl)-2-[(*E*)-3-phenyl-2-propenyl]-1,3-indanedione (6c): pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85−7.58 (m, 4H), 7.13−7.01 (m, 10H), 6.33 (d, J = 15.6 Hz, 1H), 5.76−5.70 (m, 1H), 3.53 (dd, J = 9.0, 6.6 Hz, 1H), 2.96−2.93 (m, 2H), 2.89 (dd, J = 7.8, 1.2, 1H), 2.73 (dd, J = 7.8, 1.2, 1H), 1.75 (t, J = 2.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.5, 202.5, 142.6, 142.4, 138.1, 135.4, 134.6, 129.1, 128.3, 127.9, 127.3, 127.2, 126.1, 122.7, 122.5, 122.5, 82.2, 70.3, 61.0, 49.5, 37.1, 19.9; HRMS calcd for $C_{28}H_{22}O_2$ 390.1620, found 390.1617.

5-Allyl-2,2-dimethyl-5-[1-(4-nitrophenyl)-3-butynyl]-1,3-dioxane-4,6-dione (8a): pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 5.56−5.58 (m, 1H), 5.20 (dd, J = 17.4, 10.4, 2H), 3.73 (dd, J = 10.4, 5.4 Hz, 1H), 3.05−2.99 (m, 2H), 2.95 (dd, J = 12.6, 7.8, 1H), 2.73 (dd, J = 12.6, 7.2 Hz, 1H), 1.74 (t, J = 2.4 Hz, 1H), 1.49 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.3, 166.7, 147.7, 144.9, 130.4, 130.3, 123.7, 122.6, 106.4, 80.5, 71.1, 58.9, 51.5, 40.7, 30.4, 28.4, 19.3; HRMS calcd for $C_{19}H_{19}NO_6$ 357.1212, found 357.1215.

2,2-Dimethyl-5-(2-methylallyl)-5-[1-(4-nitrophenyl)-3-butynyl]-1,3-dioxane-4,6-dione (8b): pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 4.93 (s, 2H), 4.85 (s, 1H), 3.73 (t, J = 10.6, 5.4 Hz, 1H), 3.10−3.00 (m, 2H), 2.98 (d, J = 12.6 Hz, 1H), 2.70 (d, J = 12.6 Hz, 1H), 1.73 (t, J = 2.4 Hz, 1H), 1.67 (s, 3H), 1.47

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(s, 3H), 0.77 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.4, 166.9, 147.7, 145.0, 138.9, 130.6, 123.8, 119.2, 106.4, 80.6, 71.1, 58.9, 52.1, 44.0, 30.0, 28.7, 23.9, 19.5; HRMS calcd for $C_{20}H_{21}NO_6$ 371.1369, found 371.1374.

2-(1-((*E*)-2-Phenyl-1-ethenyl)-3-butynyl)-2-(2-propenyl)-propanedinitrile (10a): pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 7.5 Hz, 2H), 7.28−7.25 (m, 3H), 6.67 (d, J = 15.5 Hz, 1H), 6.00 (dd, J = 15.5, 9.5 Hz, 1H), 5.88 (m, 1H), 5.43 (d, J = 10.5 Hz, 1H), 5.38 (d, J = 17.0 Hz, 1H), 2.84−2.63 (m, 5H), 2.07 (t, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 135.3, 128.8, 128.3, 126.8, 123.5, 121.9, 114.3, 113.7, 78.9, 72.3, 48.0, 41.5, 40.4, 22.3; HRMS calcd for $C_{18}H_{16}N_2$ 260.1313, found 260.1315.

2-Allyl-2-(1-((*E*)-2-phenyl-1-ethenyl)-3-butynyl)-1,3-indanedione (10d): pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87−7.84 (m, 2H), 7.73−7.72 (m, 2H), 7.25−7.12 (m, 5H), 6.43 (d, J = 15.6 Hz, 1H), 6.12 (dd, J = 10 Hz, 1H m,1H), 5.89−5.87 (m, 1H), 5.38 (dd, J = 17.0, 10.5 Hz, 2H), 2.91−2.87 (m, 2H), 2.64 (d, J = 13.2 Hz, 1H), 2.55 (d, J = 13.2 Hz, 1H), 2.28−2.17 (m, 2H), 1.75 (t, J = 2.4 Hz, 1H), 1.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.6, 202.8, 143.1, 142.9, 139.8, 136.7, 135.8, 135.6, 134.3, 128.4, 127.5, 126.7, 126.5, 122.6, 122.8, 116.6, 81.4, 71.0, 60.5, 48.7, 42.5, 24.1, 20.8; HRMS calcd for $C_{25}H_{22}O_2$ 354.1620, found 354.1625.

5-Allyl-2,2-dimethyl-5-(1-((*E*)-2-phenyl-1-ethenyl)-3-butynyl)-1,3-dioxane-4,6-dione (10f): pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, J = 9.6 Hz, 2H), 7.26−7.18 (m, 3H), 6.48 (d, J = 15.6 Hz, 1H), 6.01 (dd, J = 15.6, 10.2 Hz, 2H), 5.63−5.58 (m,1H), 5.18−5.11 (m, 2H), 3.09−3.05 (m, 1H), 2.72 (d, J = 7.2, 2H), 2.61−2.57 (m, 2H), 2.44−2.40 (m, 1H), 1.92 (t, J = 2.4 Hz, 1H), 1.59 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 167.3, 136.1, 135.5, 131.1, 130.8, 128.4, 128.0, 126.6, 125.5, 121.9, 106.3, 80.6, 71.3, 57.9, 50.8, 40.4, 30.8, 28.8, 29.9; HRMS calcd for $C_{21}H_{22}O_4$ 338.1518, found 338.1516.

2-(3-Deuterio-1-phenylbut-3-ynyl)-2-(2-propenyl)propanedinitrile (11): pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.36 (m, 5H), 5.89−5.83 (m, 1H), 5.39 (d, J = 10.0 Hz, 1H), 5.31 (d, J = 17.0 Hz, 1H), 3.26 (dd, J = 10.5, 4.5 Hz, 1H), 3.08−2.96 (m, 2H), 2.52 (dd, J = 14.0, 7.5 Hz, 1H), 2.43 (dd, J = 14.0, 7.5 Hz, 1H); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 134.8, 129.6, 129.4, 129.0, 128.7, 123.7, 115.0, 114.1, 79.1 (t), 71.9, 50.2, 42.9, 40.8, 22.6; HRMS calcd for $C_{16}H_{13}DN_2$ 235.1219, found 235.1221.

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Supporting Information Available: General experimental procedure and spectral data for compounds **4d**−**m**, **6d**−**m**, **8c**,**d**, and **10b**,**c**,**e**,**g**,**h**; ^{1}H NMR spectra of **4e**,**j**,**l**, **6a**−**m**, **8a**−**d**, **10d**−**h**, ^{1}H− H NMR decoupling data for **4a**,**b**, **6b**, and **8a** and NOE data for compounds **10a**,**b**,**e**,**g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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