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Palladium-Catalyzed Intermolecular Three-Component Coupling of Organic Halides with Alkynes and Alkenes: Efficient Synthesis of Oligoene Compounds

Kana Shibata,[a] Tetsuya Satoh,[a,*] and Masahiro Miura[a,*]

[a] Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan
Fax: (+81)-6-6879-7362; e-mail: satoh@chem.eng.osaka-u.ac.jp or miura@chem.eng.osaka-u.ac.jp

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Abstract: The intermolecular three-component coupling of aryl or vinyl halides, diarylacetylenes, and monosubstituted alkenes effectively proceeds in the presence of palladium acetate, lithium chloride, and sodium bicarbonate as catalyst, promoter, and base, respectively, in aqueous DMF or DMSO to produce the corresponding 1,3-butadiene or 1,3,5-hexatriene derivatives. Use of dienyl bromides allows the coupling to afford 1,3,5,7-octatetraenes. Under the present catalytic conditions, fulvene derivatives are also formed efficiently by the 1:2 coupling of vinyl bromides and diarylacetylenes without adding the alkenes.

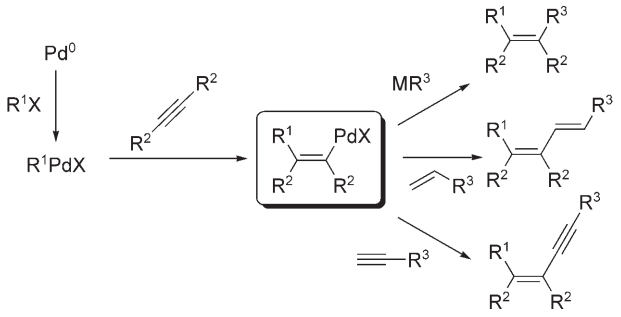
Keywords: alkynes; C–C coupling; Heck reaction; multicomponent reactions; oligoenes; palladium

Introduction

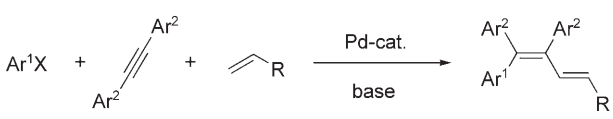
The palladium-catalyzed arylation and vinylation of internal alkynes by the corresponding halides or their synthetic equivalents *via* carbometalation are powerful tools for the construction of π-conjugated molecules.[1] Such reactions are often carried out with the addition of various terminators including organometallic reagents, alkenes, and terminal alkynes to give rise to three-component coupling products (Scheme 1).

While the reactions *via* intramolecular cyclization with alkynylhaloarenes followed by intermolecular termination or the reverse with substrates such as alkenylhaloarenes and alkynes have been studied extensively,[1,2] the fully intermolecular versions to afford π-conjugated acyclic compounds have been less explored.[3,4] As one of the rare but efficient examples, Larock and co-workers recently reported the 1:1:1 coupling of aryl or vinyl iodides, internal alkynes, and organoboron reagents involving the Suzuki–Miyaura coupling in the termination step.[3b–d] We also demonstrated that two molecules of alkynes can be inserted between aryl halides and arylboronic acids to produce the corresponding 1:2:1 coupling products, 1,4-diaryl-1,3-butadienes, when a suitable base such as silver carbonate is used.[5]

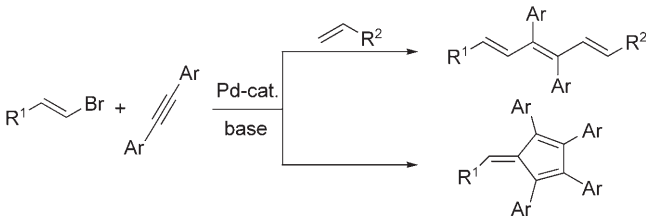
During the course of our study of the catalytic processes involving carbometalation of alkynes,[5–7] we observed that the 1:1:1 coupling of aryl halides, diarylacetylenes, and monosubstituted alkenes can take place selectively under palladium catalysis by employing appropriate conditions to give the corresponding 1,3-butadiene derivatives (Scheme 2).[7] This represents a rare example for the above *intermolecular* three-component coupling involving the Mizoroki–



Scheme 1. Palladium-catalyzed three-component coupling of organic halides, alkynes, and terminators.



Scheme 2. Palladium-catalyzed three-component coupling of aryl halides, alkynes, and alkenes.



Scheme 3. Palladium-catalyzed coupling of vinyl bromides with alkynes in the presence or absence of alkenes.

Heck reaction with alkenes in the termination step.[8] The reaction employing various β-bromostyrenes in place of aryl halides also proceeds to afford 1,3,5-hexatriene derivatives (Scheme 3). In the absence of the alkenes, the bromides couple with two molecules of the alkynes to produce fulvene derivatives efficiently.[9] The details of the results obtained with respect to the scope and limitations for these reactions are described herein.

Results and Discussion

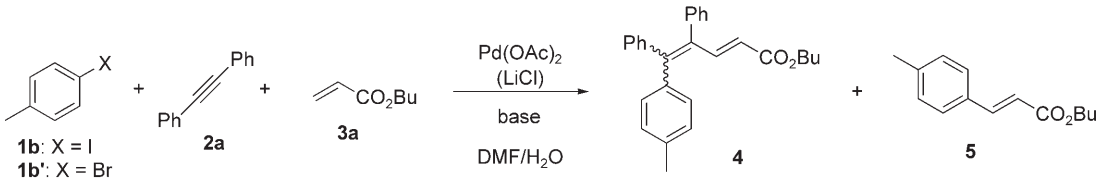
First, 4-iodotoluene (**1b**) was reacted with diphenylacetylene (**2a**) (1 equiv.) and butyl acrylate (**3a**) (1 equiv.) under conditions similar to those employed for the reaction of **1b** with **2a** and arylboronic acids.[5] In the presence of $Pd(OAc)_2$ (5 mol%) and Ag_2CO_3 (1 equiv.) in 1-propanol/H_2O (9:1) at 120 °C for 20 h, butyl 5-(4-methylphenyl)-4,5-diphenyl-2,4-pentadienoate (**4**) was formed in 16% yield along with a normal Mizoroki–Heck-type product, butyl 3-(4-methylphenyl)-2-propenoate (**5**), in 25% yield (Table 1, entry 1). In this case, a trace amount of 1:2 coupling product, methyl(tetraphenyl)naphthalene, was also detected by GC-MS.[6d] The reaction rate was found to be enhanced significantly by using DMF/H_2O as solvent (entry 2). Various bases could be used in place of Ag_2CO_3 (entries 3–7), and among those examined relatively weak and less expensive $NaHCO_3$ gave the best result (entry 7). The use of excess **2a** (4 equivs.) improved the selectivity for the desired three-component coupling product **4** (entry 4 *vs.* 3). When the reaction was conducted with the addition of LiCl (0.7 equivs.) as promoter at 130 °C, **4** was obtained in a further improved yield of 72% with a suppressed amount of **5** (entry 10). The NMR spectra of **4** isolated in entry 10 indicated that it consists of two geometrical isomers [(2*E*,4*E*):(2*E*,4*Z*) = 1.2:1]. Either decreasing or increasing the amount of LiCl resulted in a reduction in the yield of **4** (entries 11 and 12). 4-Bromotoluene (**1b′**) could be used in place of **1b** with the addition of P(*p*-tolyl)$_3$ (20 mol%) as ligand (entry 14).

Table 2 summarizes the results for the reactions of various aryl iodides **1a–d** with diarylacetylenes **2a–d** and alkenes **3a–g**. As expected, the reaction using the substrate combination of an aryl iodide and a diarylacetylene, in which same aryl groups are contained, with **3a** gave the corresponding butyl 4,5,5-triaryl-2,4-pentadienoate as the predominant product. Thus, dienes **6a–d** were obtained from **1a–d** and **2a–d** (entries 1–4). The alkenes with an electron-withdrawing group such as ethyl acrylate (**3b**), *N*,*N*-dimethylacrylamide (**3c**), and acrylonitrile (**3d**) smoothly reacted with **1a** and **2a** to produce the corresponding dienes **6e–g** (entries 5–7). Styrene (**3e**) also underwent the three-component coupling to afford 1,1,2,4-tetraphenyl-1,3-butadiene (**6h**). In this case, the addition of PPh_3 (10 mol%) was found to improve the yield of **6h** (entry 9 *vs.* 8) The use of 4-methyl- and 4-chlorostyrenes, **3f** and **3g**, afforded the corresponding dienes **6i** and **6j** (entries 10 and 11).

A plausible mechanism for the reaction of aryl halides **1** with diarylacetylenes **2** and alknens **3** is illustrated in Scheme 4. The formation of an arylpalladium intermediate **A** *via* oxidative addition of **1** toward Pd(0) species generated *in situ* followed by insertion of **2** forms a vinylpalladium intermediate **B**. Then, successive insertion of **3**, β-hydrogen elimination, and release of HX to regenerate Pd(0) may occur to allow the catalytic production of dienes **4** and **6**. The competitive insertions of **2** and **3** into **A** may be the principal selectivity-determinating steps that lead to diene **4** or **6** and Mizoroki–Heck-type product **5**. The results of the reaction of **1b** with **2a** and **3a** in Table 1 imply that *E*/*Z* isomerization takes place in the next intermediate **B**.[10] The lack of double insertion of **2** suggests that the reaction of **B** with **3** is significantly faster than that with **2**, while the reasonn is not clear at the present stage.

The synthesis of 1,3,5-hexatrienes by the reaction of β-bromostyrenes with alkynes and alkenes was next examined. Treatment of β-bromostyrene (**7a**) [(*E*):(*Z*) = 6.5:1] with **2a** (4 equivs.) and **3a** (1 equiv.) in the presence of $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%), LiCl (0.7 equivs.), and $NaHCO_3$ (2 equivs.) in DMF/H_2O (9:1) at 120 °C for 2 h gave the 1:1:1 coupling product, butyl (*2E*,*4E*,*6E*)-4,5,7-triphenyl-2,4,6-heptatrienoate (**8a**) in 44% yield, along with the Mizoroki–Heck-type coupling product of **7a** and **3a**, butyl 5-phenyl-2,4-pentadienoate (**9**) (9%) and the 1:2 coupling-cyclization product of **7a** and **3a**, 1,2,3,4,6-pentaphenylfulvene (**10a**) (14%) (Table 3, entry 1). It should be noted that all the double bonds of the hexatriene had exclusively (*E*)-configurations, no other geometrical isomers being detected by GC-MS and NMR. This contrasts with the fact that the three-component product **4** in Table 1 was a mixture of two geometrical isomers. The Mizoroki–Heck-type product **9** was, however, formed as a mixture of at least three geometrical isomers. In the absence of LiCl, the yield of undesired **9** significantly increased (entry 2). Under

Table 1. Reaction of 4-halotoluene (**1b** or **1b′**) with diphenylacetylene (**2a**) and butyl acrylate (**3a**).[a]



Entry	X	Base [mmol]	LiCl [mmol]	Temp [°C]	Time [h]	% Yield[b]	
						4	**5**
1[c,d]	I	Ag_2CO_3 (1)		120	20	16	25
2[c]	I	Ag_2CO_3 (1)		120	2	20	36
3[c]	I	Cs_2CO_3 (2)		120	0.5	29	58
4	I	Cs_2CO_3 (2)		120	0.5	53	40
5	I	Na_2CO_3 (2)		120	2	53	28
6	I	NaOAc (2)		120	0.5	51	35
7	I	$NaHCO_3$ (2)		120	2.5	60	31
8	I	$NaHCO_3$ (2)	0.7	120	1.5	64	28
9[e]	I	$NaHCO_3$ (2)	0.7	120	0.5	53	22
10	I	$NaHCO_3$ (2)	0.7	130	1	72 (50)[f]	12
11	I	$NaHCO_3$ (2)	0.5	130	1	53	15
12	I	$NaHCO_3$ (2)	1.0	130	2	63	12
13[g]	I	$NaHCO_3$ (2)	0.7	130	0.5	70	14
14[g]	Br	$NaHCO_3$ (2)	0.7	130	4	58	24

[a] *Reaction conditions:* [**1b** or **1b′**]:[**2a**]:[**3a**]:[$Pd(OAc)_2$] = 1:4:1:0.05 (in mmol), in DMF/H_2O (9:1, 5 mL) under N_2.
[b] GC yield based on the amount of **1** used. Value in parentheses indicates yield after purification.
[c] **2a** (1 mmol) was used.
[d] In 1-propanol/H_2O (9:1, 5 mL).
[e] In DMSO/H_2O (9:1, 5 mL).
[f] (2*E*,4*E*):(2*E*,4*Z*) = 1.2:1.
[g] With P(*p*-tolyl)$_3$ (0.2 mmol).

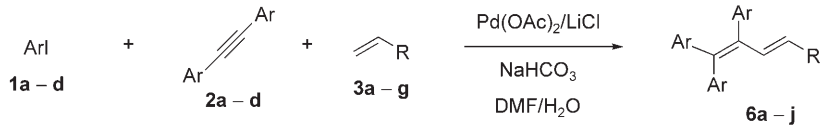
such conditions, Cs_2CO_3 and NEt_3 were less effective than $NaHCO_3$ (entries 3 and 4). When the reaction was conducted in DMSO/H_2O, the yield of **8a** was enhanced up to 53% (entry 5). In other solvents such as DMAc/H_2O, NMP/H_2O, and 1-propanol/H_2O, the reaction was less efficient (entries 6–8). Eliminating PPh_3 and decreasing or increasing the reaction temperature resulted in slightly lower yields of **8a** (entries 9–11).

A number of hydroxy- and/or methoxy-substituted cinnamic acids such as coumaric- and sinapinic acids occur in common agricultural residues and are readily available. Such acids, as well as related other ones, smoothly underwent decarboxylative bromination under the reported conditions[11] to give the corresponding β-bromostyrenes. Using the bromides thus prepared, the three-component coupling with **2a** and **3a** was examined. As shown in Table 4, a number of substituted β-bromostyrenes **7b**–**e** and 2-(2-thienyl)-ethenyl bromide (**7f**) underwent the reaction to afford the corresponding 7-aryl-4,5-diphenyl-2,4,6-heptanoates **8b**–**f**. While the triene **8b** consisted of the single isomer having all (*E*)-configuration (entry 1), contamination of each (*2E*,*4Z*,*6E*)-isomer was observed in the case of **8c**–**f** (entries 2–5). 1-Bromo-4-phenyl-1,3-butadiene (**7g**) also reacted with **2a** and **3a** to give butyl (*2E*,*4E*,*6E*,*8E*)-4,5,9-triphenyl-2,4,6,8-nonatetraenoate (**8g**) in 42% yield (entry 6).

The reactions of **7a** with bis(4-methoxyphenyl)- and bis(4-chlorophenyl)acetylenes, (**2e**) and (**2c**), in the presence of **3a** took place to afford the corresponding trienes **8h** and **8i**, respectively (entries 7 and 8). Ethyl acrylate (**3b**) and *N*,*N*-dimethylacrylamide (**3c**) also reacted with **7a** and **2a** effectively to afford trienes **8j** and **8k** (entries 9 and 10).

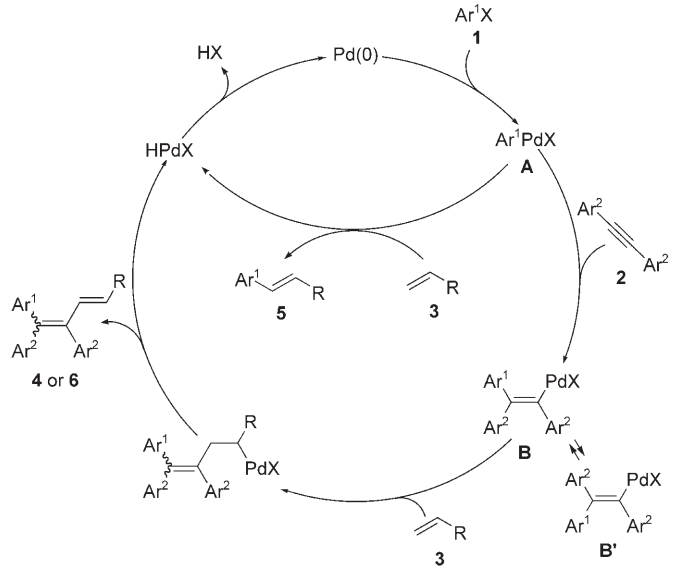
As expected, the fulvene **10a** was formed as the single major product, when the reaction of **7a** with **2a** was conducted in the absence of any alkenes. The reaction was found to proceed efficiently without any additives such as LiCl and PPh_3. Thus, a series of

Table 2. Reaction of aryl iodides **1** with diarylacetylenes **2** and alkenes **3**.[a]



Entry	Substrates				Time [h]	Product, % Yield[b,c]
	1, 2	Ar	3	R		
1	**1a**, **2a**	Ph	**3a**	CO_2Bu	1.5	**6a**, 65 (47)
2	**1b**, **2b**	4-MeC_6H_4	**3a**	CO_2Bu	0.5	**6b**, 55 (42)
3	**1c**, **2c**	4-ClC_6H_4	**3a**	CO_2Bu	1	**6c**, 60 (35)
4	**1d**, **2d**	2-thienyl	**3a**	CO_2Bu	1.5	**6d**, 30 (18)
5	**1a**, **2a**	Ph	**3b**	CO_2Et	1.5	**6e**, 62 (46)
6	**1a**, **2a**	Ph	**3c**	$CONMe_2$	3.5	**6f**, 55 (50)
7	**1a**, **2a**	Ph	**3d**	CN	1	**6g**, 60 (53)
8	**1a**, **2a**	Ph	**3e**	Ph	2.5	**6h**, 44
9[d]	**1a**, **2a**	Ph	**3e**	Ph	2	**6h**, 63 (45)
10[d]	**1a**, **2a**	Ph	**3f**	4-MeC_6H_4	5	**6i**, 55 (50)
11[d]	**1a**, **2a**	Ph	**3g**	4-ClC_6H_4	4	**6j**, 69 (52)

[a] *Reaction conditions:* [**1**]:[**2**]:[**3**]:[$Pd(OAc)_2$]:[LiCl]:[$NaHCO_3$] = 1:4:1:0.05:0.7:2 (in mmol), in DMF/H_2O (9:1, 5 mL) at 130 °C under N_2.
[b] GC yield based on the amount of **1** used. Value in parentheses indicates yield after purification.
[c] In each run, a minor amount of Mizoroki–Heck type product (ArCH=CHR) was also formed (3–26 %).
[d] With PPh_3 (0.1 mmol).

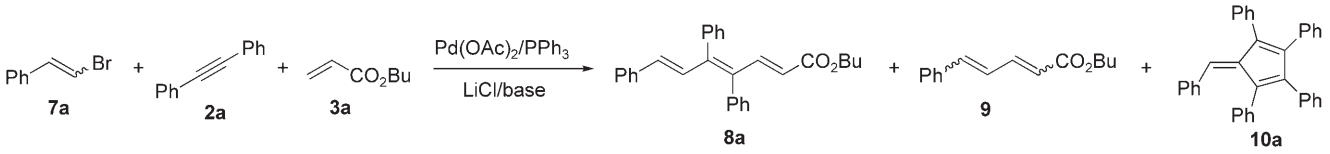


Scheme 4. A plausible mechanism for the reaction of **1** with **2** and **3**.

vinyl bromides **7** was treated with **2** (2 equivs.) in the presence of $Pd(OAc)_2$ (5 mol %) and $NaHCO_3$ (2 mmol) in DMF at 120 °C and the corresponding fulvenes **10a–j** were obtained selectively (Table 5).

The application of 1,2,3,4,6-pentaarylfulvenes as the luminescent organic material of organic EL devices[12] as well as organic glasses[13] has recently been disclosed. Although some palladium-catalyzed reactions

Table 3. Reaction of β-bromostyrene (**7a**) with diphenylacetylene (**2a**) and butyl acrylate (**3a**).[a]



Entry	Base	Solvent [9/1]	Time [h]	% Yield[b]		
				8a	**9**	**10a**
1	$NaHCO_3$	DMF/H_2O	2	44	9	14
2[c]	$NaHCO_3$	DMF/H_2O	5	41	19	8
3[c]	Cs_2CO_3	DMF/H_2O	2	30	20	6
4[c]	NEt_3	DMF/H_2O	5	31	17	8
5	$NaHCO_3$	DMSO/H_2O	2	53 (47)	5	22 (19)
6	$NaHCO_3$	DMAc/H_2O	2	34	11	7
7	$NaHCO_3$	NMP/H_2O	2	26	7	4
8	$NaHCO_3$	1-propanol/H_2O	2	23	6	13
9[d]	$NaHCO_3$	DMSO/H_2O	2	45	12	21
10[e]	$NaHCO_3$	DMSO/H_2O	5	40	10	10
11[f]	$NaHCO_3$	DMSO/H_2O	2	41	5	19

[a] *Reaction conditions:* [**7a**]:[**2a**]:[**3a**]:[$Pd(OAc)_2$]:[PPh_3]:[LiCl]:[base] = 1:4:1:0.05:0.1:0.7:2 (in mmol), in solvent (5 mL) under N_2 at 120 °C.
[b] GLC yield based on the amount of **7a** used. Value in parentheses indicates yield after purification.
[c] Without LiCl.
[d] Without PPh_3.
[e] At 100 °C.
[f] At 130 °C.

of vinyl halides with alkynes to form fulvenes were reported previously, the efficiencies were moderate.[9a–d] Recently, Takahashi and co-workers reported that pentasubstituted fulvenes can be produced effectively by the reaction of vinyl iodides with alkynes using Ag_2CO_3 as a base.[9e] The present reaction appears to be synthetically useful, since readily available vinyl bromides reacted smoothly even when using the common, inexpensive base, $NaHCO_3$.

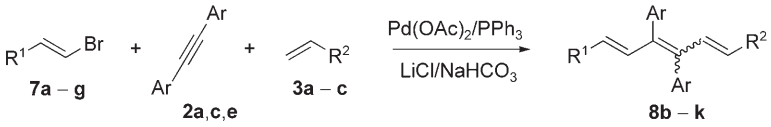
A plausible mechanism for the reaction of vinyl bromides **7** with diarylacetylenes **2** in the presence or absence of alkenes **3** is illustrated in Scheme 5. The three-component coupling appears to proceed *via* fundamental steps as in the reaction of aryl halides **1** (Scheme 4). Thus, triene **8** may be constructed *via* oxidative addition, successive alkyne-alkene insertion, and β-hydrogen elimination steps. The fact that the (*2E*,*4E*,*6E*)-isomers of **8** were formed predominantly, or even exclusively in some cases, suggests that the dienylpalladium intermediate **C** appears to tend to more preferably isomerize to **C′**, compared to the vinylpalladium species **B** in Scheme 4. On the other hand, in the absence of **3**, **C** may undergo the second insertion of **2** followed by cyclization to lead to fulvene **10**.

It was found that pentadienoate **6a**, obtained by the three-component coupling of **1a** with **2a** and **3a**, can be converted to the corresponding nonatetraenoate (homologation). Thus, as depicted in Scheme 6, dienyl bromide **11** was prepared *via* hydrolysis and decarboxylative bromination[11] of **6a**. As expected, **11** underwent the second three-component coupling with **2a** and **3a** to give butyl 4,5,8,9,9-pentaphenyl-2,4,6,8-nonatetraenoate **12**, that has exclusively (*E*)-configuration. As a whole, the 1:2:2 couping of **1a**, **2a**, and **3a** was achieved forming four C–C bonds. On the other hand, treatment of **11** with **2a** in the absence of **3a** efficiently afforded fulvene **13** by 1:2 coupling.

Conclusion

We have demonstrated that the three-component coupling reaction of aryl or vinyl halides with diarylacetylenes and monosubstituted alkenes can be performed under palladium catalysis to selectively give the corre-

Table 4. Reaction of vinyl bromides **7** with diarylacetylenes **2** and alkenes **3**.[a]

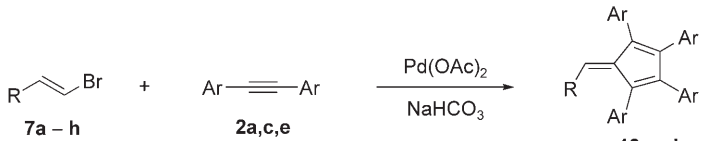


7a – g 2a,c,e 3a – c 8b – k

Entry	Substrates						Product, % Yield,[b,c] (*4E*):(*4Z*)[d]
	7	R^1	**2**	Ar	**3**	R^2	
1	**7b**	4-MeC_6H_4	**2a**	Ph	**3a**	CO_2Bu	**8b**, 64 (44), >99:1
2	**7c**	4-$MeOC_6H_4$	**2a**	Ph	**3a**	CO_2Bu	**8c**, 65 (55), 19:1
3	**7d**	2-$MeOC_6H_4$	**2a**	Ph	**3a**	CO_2Bu	**8d**, 51 (41), 10:1
4	**7e**	3,4,5-$(MeO)_3C_6H_2$	**2a**	Ph	**3a**	CO_2Bu	**8e**, (56), 13:1
5	**7f**	2-thienyl	**2a**	Ph	**3a**	CO_2Bu	**8f**, (43), 12:1
6	**7g**	PhCH=CH	**2a**	Ph	**3a**	CO_2Bu	**8g**, (42), >99:1
7	**7a**	Ph	**2e**	4-$MeOC_6H_4$	**3a**	CO_2Bu	**8h**, 50 (40), 13:1
8	**7a**	Ph	**2c**	4-ClC_6H_4	**3a**	CO_2Bu	**8i**, 38 (32), 12:1
9	**7a**	Ph	**2a**	Ph	**3b**	CO_2Et	**8j**, (46), >99:1
10	**7a**	Ph	**2a**	Ph	**3c**	$CONMe_2$	**8k**, (47), >99:1

[a] *Reaction conditions:* [**7**]:[**2**]:[**3**]:[$Pd(OAc)_2$]:[PPh_3]:[LiCl]:[$NaHCO_3$] = 1:4:1:0.05:0.1:0.7:2 (in mmol), in DMSO/H_2O (9:1, 5 mL) at 120 °C under N_2 for 2 h.
[b] GC yield based on the amount of **7** used. Value in parentheses indicates yield after purification.
[c] In each run, minor amounts of Mizoroki–Heck-type product and fulvene derivative were also formed, but their exact yields were not determined.
[d] Determined by ^1H NMR.

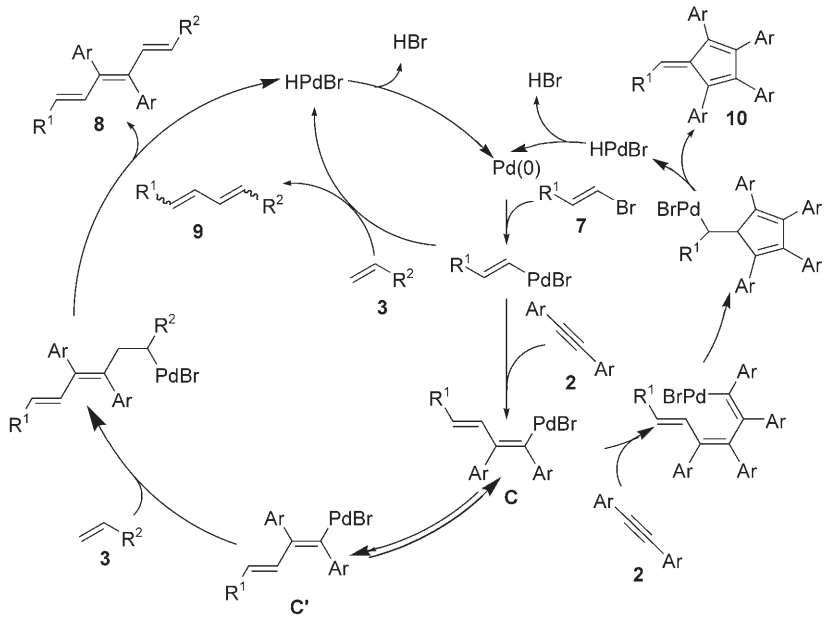
Table 5. Reaction of vinyl bromides **7** with diarylacetylenes **2**.[a]



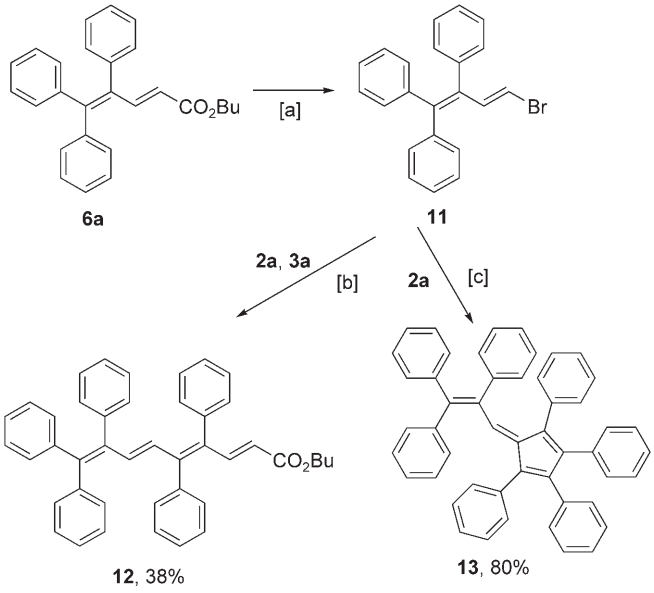
7a – h 2a,c,e 10a – j

Entry	Substrates				Time [h]	Product, % Yield[b]
	7	R	**2**	Ar		
1	**7a**	Ph	**2a**	Ph	2	**10a**, 90 (80)
2	**7b**	4-MeC_6H_4	**2a**	Ph	2	**10b**, (80)
3	**7c**	4-$MeOC_6H_4$	**2a**	Ph	5	**10c**, (63)
4	**7d**	2-$MeOC_6H_4$	**2a**	Ph	2	**10d**, (56)
5	**7e**	3,4,5-$(MeO)_3C_6H_2$	**2a**	Ph	5	**10e**, (84)
6	**7f**	2-thienyl	**2a**	Ph	5	**10f**, (57)
7	**7g**	PhCH=CH	**2a**	Ph	2	**10g**, (67)
8	**7h**	1-naphthyl	**2a**	Ph	5	**10h**, (78)
9	**7a**	Ph	**2e**	4-$MeOC_6H_4$	2	**10i**, (57)
10	**7a**	Ph	**2c**	4-ClC_6H_4	2	**10j**, (57)

[a] *Reaction conditions:* [**7**]:[**2**]:[$Pd(OAc)_2$]:[$NaHCO_3$] = 1:2:0.05:2 (in mmol), in DMF (5 mL) under N_2 at 120 °C.
[b] GC yield based on the amount of **7** used. Value in parentheses indicates yield after purification.



Scheme 5. A plausible mechanism for the reaction of **7** with **2** in the presence or absence of **3**.



Scheme 6. Syntheses of **12** and **13** from **6a**. *Reaction conditions:* [a] i) NaOH (4 equivs.), MeOH, 80 °C, 6 h; ii) NBS (1.2 equivs.), NEt_3 (20 mol%), $MeCN/H_2O$ (99:1), room temperature, 5 min. [b] See footnote[a] in Table 4. [c] See footnote[a] in Table 5.

sponding 1:1:1 coupling products. The reaction provides a straightforward route to arylated oligoenes, which are of interest for their photo- and electrochemical and biological properties.[14] A further homologation method of the oligoene chain of the three-component products by a simple procedure has also been presented. The present catalytic system has appeared to be useful for the 1:2 coupling of vinyl bromides with diarylacetylenes to produce pentaarylfulvenes.

Experimental Section

General Remarks

The ^1H and ^{13}C NMR spectra were recorded at 400 or 270 MHz and 100 or 68 MHz, respectively, for $CDCl_3$ solutions. MS data were obtained by EI, unless noted. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm × 1.5 m) or a CBP-1 capillary column (i. d. 0.5 mm × 25 m). GC-MS analysis was carried out using a CBP-1 capillary column (i. d. 0.25 mm × 25 m).

Bromides **7b–h** and **11**[11b] and diarylacetylenes **2b–d**[15] and **2e**[16] were prepared by the methods reported previously. Other starting materials were commercially available. Characterization data of all the products are reported in the Supporting Information.

The following experimental procedures may be regarded as typical in methodology and scale.

Palladium-Catalyzed Reaction of 4-Iodotoluene (1b) with Diphenylacetylene (2a) and Butyl Acrylate (3a) (entry 10 in Table 1)

A mixture of 4-iodotoluene (**1b**) (1 mmol, 218 mg), diphenylacetylene (**2a**) (4 mmol, 712 mg), butyl acrylate (**3a**) (1 mmol, 128 mg), $Pd(OAc)_2$ (0.05 mmol, 11 mg), LiCl (0.7 mmol, 30 mg), $NaHCO_3$ (2 mmol, 168 mg), and 1-methylnaphthalene (*ca.* 60 mg) as internal standard was stirred in DMF/H_2O (5 mL, 9:1) under nitrogen at 130 °C. After 1 h,

the reaction mixture was poured into ether (70 mL), washed by water (100 mL, three times), and dried over sodium sulfate. GC and GC-MS analyses confirmed the formation of **4** and **5** in 72 and 12% yields, respectively. The product **4** (197 mg, 50%) was isolated by column chromatography on silica gel using hexane-ethyl acetate (99.5:0.5, v/v) as eluant. Although the NMR spectra of **4** indicated that it consists of two geometrical isomers [(2*E*,4*E*):(2*E*,4*Z*)=1.2:1], the minor isomer could be isolated by recrystallization from hexane after the column chromatographic separation and was determined to possess (2*E*,4*Z*)-geometry by NOE experiments (see the Supporting Information).

Compound **4** [(2*E*,4*E*):(2*E*,4*Z*)=1.2:1]:[7a] oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.87–0.91 (m, 3H), 1.25–1.36 (m, 2H), 1.53–1.58 (m, 2H), 2.20 (s, 3H, 4*Z*), 2.39 (s, 3H, 4*E*), 4.04–4.09 (m, 2H), 5.59 (d, J=15.4 Hz, 1H, 4*Z*), 5.61 (d, J=15.4 Hz, 1H, 4*E*), 6.76 (d, J=8.1 Hz, 2H, 4*Z*), 6.83 (d, J=8.1 Hz, 2H, 4*Z*), 6.88–6.90 (m, 2H, 4*E*), 7.01–7.04 (m, 2H, 4*E*), 7.08–7.37 (m, 10H), 7.70 (d, J=15.4 Hz, 1H, 4*Z*), 7.76 (d, J=15.4 Hz, 1H, 4*E*);^{13}C NMR (100 MHz, $CDCl_3$): δ= 13.7 (overlapped), 19.1 (4*Z*), 19.2 (4*E*), 21.2 (4*Z*), 21.3 (4*E*), 30.68 (4*Z*), 30.71 (4*E*), 64.0 (overlapped), 121.3 (4*Z*), 121.4 (4*E*), 126.9 (4*Z*), 127.0 (4*E*), 127.4 (4*E*), 128.0 (4*Z*), 128.10 (4*E*), 128.12 (4*Z*), 128.15 (4*Z*), 128.18(4*Z*), 128.8 (4*E*), 130.98 (4*Z*), 131.03 (overlapped), 131.08 (overlapped), 131.14 (4*E*), 136.6 (4*Z*), 136.7 (4*E*), 137.0 (4*Z*), 138.2 (4*E*), 138.5 (4*E*), 139.0 (4*Z*), 139.51 (4*E*), 139.54 (4*Z*), 141.6 (4*Z*), 142.1 (4*E*), 146.4 (4*Z*), 146.5 (4*E*), 149.6 (4*Z*), 149.7 (4*E*), 167.6 (4*Z*), 167.7 (4*E*); MS: m/z=396 (M^+); anal. calcd. for $C_{28}H_{28}O_2$: C 84.81, H 7.12; found: C 84.67, H 7.16.

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