Pd(II)-Catalyzed Direct Olefination of Arenes with Allylic Esters and Ethers

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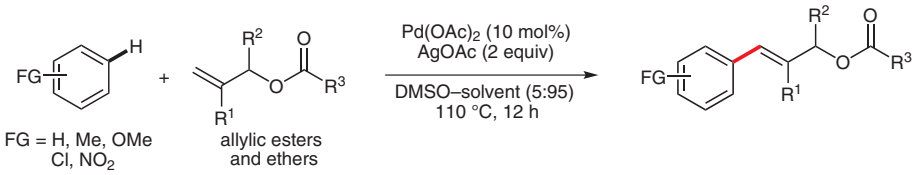
Abstract: A convenient Pd(II)-catalyzed direct olefination of unactivated arenes with allylic esters and ethers via C–H activation was demonstrated. Under the typical conditions, various aryl-substituted allylic esters and ethers can be prepared.

Key words: palladium catalysis, olefination, C–C bond formation, C–H bond activation, allylic ester

The direct carbon–carbon bond formation via C–H bond activation and functionalization remains a critical challenge for modern synthetic organic chemists.[1] Recently, direct olefination of unactivated arenes draws much attention.[2] Although several efficient protocols to construct a C–C bond via the direct alkenylation of arenes have been explored since the pioneering work developed by Fujiwara,[3] most of them suffer from limited substrate scope, such as electron-rich arenes, electron-deficient olefins, and acidic conditions.[4] Recently, Yu[5] and Zhang[6] reported two efficient methods to olefinate electron-deficient arenes. In addition, some useful *ortho* olefination of arenes using a directing group has also been developed.[7] However, most of them use electron-deficient alkenes as the olefinating reagents except for few examples using aliphatic olefins and styrenes.[8] The allylic carboxylic ester moiety has rarely been employed in the direct alkenylation of arenes via C–H activation since it readily undergoes β-acetate elimination to provide the terminal alkene.[9] Very recently, Jiao developed some efficient olefination reactions using allyl esters with aromatic halides and arenes to prepare aryl-substituted allylic esters which are even difficult to synthesize by the traditional Heck reaction.[10] However, there are still some drawbacks in the direct olefination reactions such as acidic conditions and relatively long reaction time.[10c] Herein, we wish to report an efficient Pd(II)-catalyzed olefination of unactivated arenes using allylic esters and ethers (Scheme 1).

Initially, we chose toluene and allylic acetate as the model substrates to optimize suitable conditions for this reaction (Table 1). It was found that the oxidants, catalysts, and solvent affected the reaction efficiency critically. The oxidant AgOAc was better than others such as Ag_2CO_3, Ag_2O, Ag_2SO_4, benzoquinone (BQ), and O_2 (Table 1, entries 1–10). The desired product was obtained in good yield by using a mixed solvent of 5% DMSO in toluene (Table 1, entry 11). Other solvents such as AcOH, DMF, 1,4-dioxane, *t*-BuOH, and DCE were not effective (Table 1, entries 12–16). As for the catalyst, $Pd(OAc)_2$ was more efficient than $Pd(O_2CCF_3)_2$, $PdCl_2$, $Pd(acac)_2$, $PdCl_2(Cy_3P)_2$, and $Pd(Ph_3P)_4$ (Table 1, entries 17–21). Although $PdCl_2(Ph_3P)_2$ gave a slightly higher yield than $Pd(OAc)_2$, the formation of cinnamyl acetate as byproduct, which was believed to be generated directly from the catalyst and allylic acetate, caused problems in product isolation (Table 1, entry 22).[11] The product was obtained in low yields when the reaction was carried out at lower temperature such as 80 °C and 50 °C (Table 1, entries 23 and 24).

Under the typical reaction conditions,[12] various electron-rich and electron-deficient arenes were effective substrates in the direct olefination reaction (Table 2). Electron-rich arenes gave moderate to good yields of the *E*-aryl-substituted allylic acetates (Table 2, entries 1–8). The moderate electron-deficient arene such as chlorobenzene also gave moderate yield of the corresponding product (Table 2, entry 9). The highly electron-deficient arenes such as nitrobenzene gave very low yield of the desired products (Table 2, entry 10). The scope of the allylic esters and ether has been investigated (Table 2, entries 11–15). Allylic benzoate gave 35% yield of the desired product (Table 2, entry 11). It is interesting that the aryl-substituted allylic cinnamate and methacrylate are obtained in 34% and 30% yields, respectively (Table 2, entries 12 and 13). It indicates that another C=C bond could be tolerated



Scheme 1 Pd(II)-catalyzed direct olefination of arenes with allylic esters and ethers

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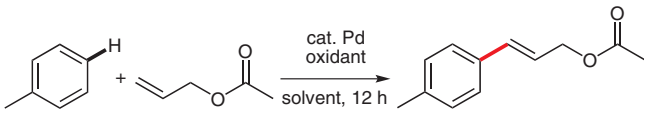
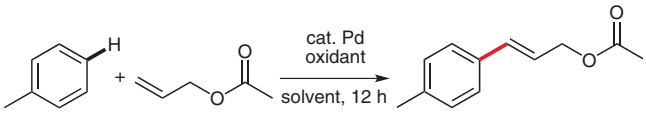
in the allylic substrates. But-3-en-2-yl acetate was effective substrate (Table 2, entry 14). It is noteworthy that allylic ether is also used successfully as the olefination partner (Table 2, entry 15).

Table 1 Optimization of the Typical Reaction Conditions[a]



Entry	Catalyst (mol%)	Solvent	Additive (equiv)	Yield (%)[b]
1	$Pd(OAc)_2$ (5)	toluene	Ag_2CO_3 (2)	16
2	$Pd(OAc)_2$ (10)	toluene	Ag_2CO_3 (2)	43
3	$Pd(OAc)_2$ (20)	toluene	Ag_2CO_3 (2)	49
4	$Pd(OAc)_2$ (10)	toluene	Ag_2CO_3 (1)	31
5	$Pd(OAc)_2$ (10)	toluene	Ag_2CO_3 (3)	41
6	$Pd(OAc)_2$ (10)	toluene	AgOAc (2)	53
7	$Pd(OAc)_2$ (10)	toluene	Ag_2O (2)	trace
8	$Pd(OAc)_2$ (10)	toluene	Ag_2SO_4 (2)	8
9	$Pd(OAc)_2$ (10)	toluene	BQ (1)	trace
10	$Pd(OAc)_2$ (10)	toluene	O_2 (1 atm)	trace
11	$Pd(OAc)_2$ (10)	toluene (5% DMSO)	AgOAc (2)	70
12	$Pd(OAc)_2$ (10)	AcOH	AgOAc (2)	trace
13	$Pd(OAc)_2$ (10)	DMF (5% DMSO)	AgOAc (2)	2
14	$Pd(OAc)_2$ (10)	1,4-dioxane (5% DMSO)	AgOAc (2)	10
15	$Pd(OAc)_2$ (10)	*t*-BuOH (5% DMSO)	AgOAc (2)	3
16	$Pd(OAc)_2$ (10)	DCE (5% DMSO)	AgOAc (2)	11
17	$Pd(TFA)_2$ (10)	toluene (5% DMSO)	AgOAc (2)	18
18	$PdCl_2$ (10)	toluene (5% DMSO)	AgOAc (2)	10
19	$Pd(PPh_3)_4$ (10)	toluene (5% DMSO)	AgOAc (2)	60
20	$Pd(acac)_2$ (10)	toluene (5% DMSO)	AgOAc (2)	23
21	$PdCl_2(PCy_3)_2$ (10)	toluene (5% DMSO)	AgOAc (2)	trace
22	$PdCl_2(PPh_3)_2$ (10)	toluene (5% DMSO)	AgOAc (2)	72

Table 1 Optimization of the Typical Reaction Conditions[a] (continued)



Entry	Catalyst (mol%)	Solvent	Additive (equiv)	Yield (%)[b]
23[c]	$Pd(OAc)_2$ (10)	toluene (5% DMSO)	AgOAc (2)	49
24[d]	$Pd(OAc)_2$ (10)	toluene (5% DMSO)	AgOAc (2)	trace

[a] Reaction conditions: toluene (1.2 equiv; 1–2 mL when used as solvent), DMSO–solvent (5:95, v/v), allylic acetate (0.6 mmol), 110 °C, 12 h, unless otherwise noted.
[b] Yields determined by ^1H NMR spectroscopy of the crude products.
[c] The reaction was carried out at 80 °C.
[d] The reaction was carried out at 50 °C.

Table 2 Olefination of Arenes with Allyl Esters and Ethers[a]

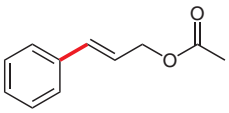
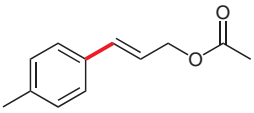
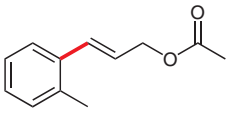
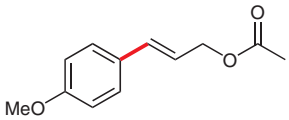
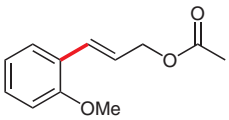
Entry	Product	Yield of *E*-isomer (%)[b]
1	 **2a**	43
2	 **2b**  **2b′**	65 (**2b**/**2b′** = 2:1)
3	 **2c**  **2c′**	64 (**2c**/**2c′** = 5:4)

Table 2 Olefination of Arenes with Allyl Esters and Ethers[a] (continued)

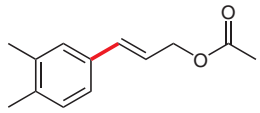
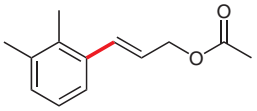
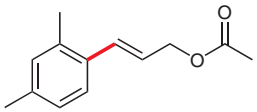
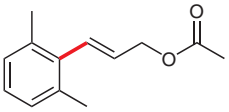
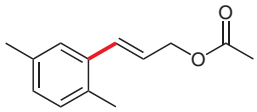
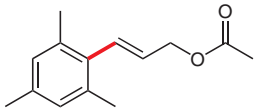
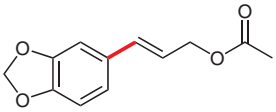
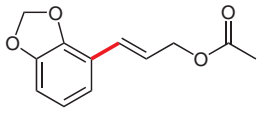
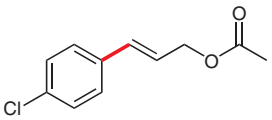
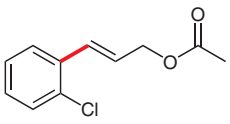
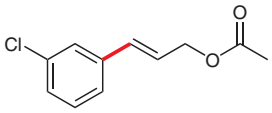
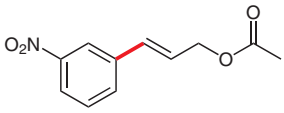
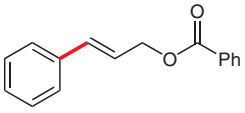
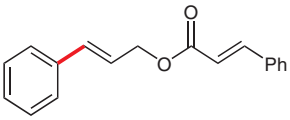
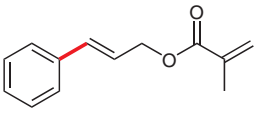
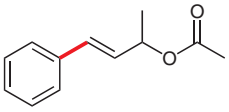
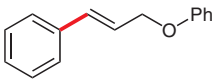
Entry	Product	Yield of *E*-isomer (%)[b]
4	 **2d** +  **2d′**	55 (**2d**/**2d′** = 3:1)
5	 **2e** +  **2e′**	45 (**2e**/**2e′** = 5:1)
6	 **2f**	32
7	 **2g**	56
8	 **2h** +  **2h′**	71 (**2h**/**2h′** = 5:4)
9	 **2i** +  **2i′**	46 (**2i**/**2i′**/**2i″** = 5:3:2)

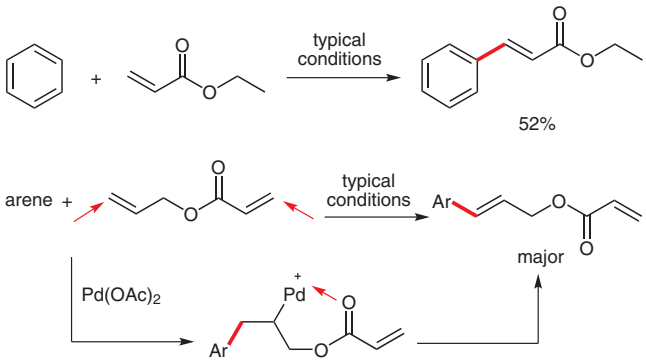
Table 2 Olefination of Arenes with Allyl Esters and Ethers[a] (continued)

Entry	Product	Yield of *E*-isomer (%)[b]
	 **2i′**	
10	 **2j**	17
11	 **2k**	35
12	 **2l**	34
13	 **2m**	30
14	 **2n**	47
15	 **2o**	43

[a] Reaction conditions: arene (1–2 mL), DMSO (5% v/v relative to arene), allylic ester or ether (0.6 mmol), $Pd(OAc)_2$ (10 mol%, 0.06 mmol), AgOAc (2 equiv, 1.2 mmol), 110 °C, 12 h.
[b] Isolated yield of the *E*-isomer.

A competing olefination would occur between the allylic and the acrylic double bonds. However, the C–C bond formation took place in the position of the terminal allylic C=C bond although 52% yield of ethyl cinnamate was produced in the olefination of benzene with ethyl acrylate under the typical conditions (Scheme 2). The selectivity might be attributed to the stability of the alkyl–Pd intermediate via chelation of Pd atom by the carbonyl O atom which was previously proposed.[13] Additionally, this chelation effect could also result in the high regioselectivity since the (Pd)C–C(O) bond cannot rotate freely.

In conclusion, we demonstrated an efficient Pd(II)-catalyzed direct olefination of unactivated arenes, fluorinated arenes, and heteroarenes by using allylic esters and ether. As the olefination partner, various allylic esters bearing another C=C bond and allylic ether give moderate to good yields of the desired products. The present protocol would



Scheme 2 Competing coupling of arenes with allyl ester and acrylate catalyzed by Pd

be useful to prepare substituted allylic alcohols. Further investigation of this procedure is under way in our laboratory.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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(11) The cinnamyl acetate was also generated in the absence of toluene when $PdCl_2(Ph_3P)_2$ was used as catalyst.

(12) **Typical Procedure**
A mixture of mesitylene (1.9 mL, as solvent), allyl acetate (0.6 mmol, 60 mg), $Pd(OAc)_2$ (0.06 mmol), AgOAc (1.2 mmol), and DMSO (0.1 mL) was added to a round-bottom flask. After stirring for 12 h at 110 °C, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent: PE–EtOAc = 20:1) to afford (*E*)-3-mesitylallyl acetate (73 mg, 56%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88 (s, 2 H), 6.64 (d, *J* = 16.0 Hz, 1 H), 5.84–5.76 (m, *J* = 16.0, 6.4 Hz, 1 H), 4.76 (dd, *J* = 6.4, 1.2 Hz, 2 H), 2.28 (s, 9 H), 2.12 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 136.4, 135.8, 132.9, 131.9, 128.6, 128.5, 65.4, 21.0, 20.9, 20.8, 20.7. HRMS: *m/z* calcd for $C_{14}H_{18}NaO_2$: 241.1199; found: 241.1197.

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