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Palladium-catalyzed allylic alkenylation of allylic alcohols with *n*-butyl acrylate†

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Various allylic alcohols reacted with *n*-butyl acrylate in the presence of *p*-toluenesulfonic anhydride and palladium catalysts to yield the corresponding *n*-butyl 2,5-dienoates with high regioselectivity.

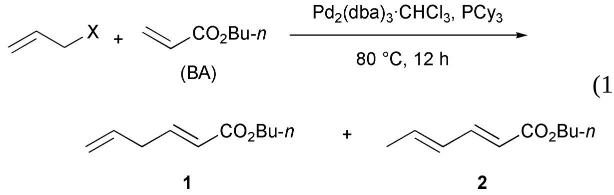
Catalytic transformations of allylic compounds *via* π-allylpalladium complexes have been extensively applied to organic synthesis.[1] Among them, allylic alkylation with soft carbon nucleophiles has attracted much attention and been widely investigated. However, allylic alkenylation is also one of the most efficient and versatile methods for synthesis of 1,4-dienes. Although various alkenylmetal reagents including tin,[2] silane,[3] and boron[4] have been employed for this purpose, alkenylation with non-metalated alkenes is more desirable in terms of simplicity and atom economy.[5] However, to our knowledge, this type of catalytic alkenylation has not been reported,[6] except for intramolecular metallo-ene reactions,[7] while a wide range of alkenes has been applied in Mizoroki–Heck reactions.[8] Although the reactions were not catalyzed by a palladium complex, Mitsudo *et al.* reported that ruthenium complexes catalyzed reactions of allyl carbonates and *N*,*N*-dimethylacrylamide.[9] However, the products obtained were 1,3-dienes, not 1,4-dienes. Recently, we found that rhodium-catalyzed reactions of allyl tosylate with styrene derivatives yielded 1-aryl-1,4-dienes in most cases.[10] Here, we report palladium-catalyzed alkenylation of allylic alcohols with *n*-butyl acrylate in the presence of *p*-toluenesulfonic anhydride (Ts_2O) to yield *n*-butyl 2,5-dienoates.

Reactions of allyl tosylate and mesylate with *n*-butyl acrylate were investigated first because we found that they are excellent allylating agents in reactions with alkynes,[11] arylalkenes,[10] and aromatic compounds.[12] Treatment of allyl tosylate (0.5 mmol) with *n*-butyl acrylate (2.0 mmol) in benzene in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%) and PCy_3 (5.0 mol%) at 80 °C for 12 h afforded *n*-butyl 2,5-hexadienoate (**1**) and *n*-butyl 2,4-hexadienoate (**2**) in 42% combined yield with moderate selectivity (eqn. (1) and Table 1, entry 1). A trace amount of *n*-butyl acrylate dimer was also produced. Although the reaction of allyl mesylate gave similar results (entry 2), no product was obtained by reaction of other allylic compounds such as allyl bromide, allyl acetate, or allyl trifluoroacetate. Using triphenylphosphine or tri(*n*-butyl)phosphine as a ligand, **1** and **2** were obtained in low yields. In contrast, other phosphorus ligands, such as tri(*tert*-butyl)phosphine, tri(*o*-tolyl)phosphine, and triphenyl phosphite, were ineffective under the same conditions. When the reaction was conducted in acetic acid, the selectivity for **1** improved dramatically (entry 3). Satisfactory yield and selectivity for **1** were achieved by using *n*-butyl acrylate both as solvent and reagent (entry 4). The reaction at 60 °C afforded similar results after 24 h (entry 5). Recently, we found that allyl alcohol exhibited reactivity similar to allyl tosylate in the presence of Ts_2O in the palladium-catalyzed reaction with alkynes.[10] Although trifluoromethanesulfonic anhydride (Tf_2O) was not effective (entry 8), presumably due to instability ($t_{\frac{1}{2}}$ = 10 min at rt)[13] of allyl triflate generated *in situ*, the alkenylation of allyl alcohol with *n*-butyl acrylate in the presence of Ts_2O or methanesulfonic anhydride (Ms_2O) gave **1** with good selectivity (entries 6 and 7). This system enhances the value of alkenylation as a synthetic tool, because most of the substituted allyl tosylates cannot be prepared owing to their thermal instability.

Table 1 Pd-catalyzed alkenylation of allylic compounds with *n*-butyl acrylate (BA)[a]

Entry	X	Additive	Solvent (mL)	Yield[b] (%)	Ratio[c] (**1** : **2**)
1	OTs		Benzene (0.5)	42	75 : 25
2	OMs		Benzene (0.5)	37	77 : 23
3	OTs		AcOH (3)	69	99 : 1
4	OTs		BA (4[d])	90	98 : 2
5[e]	OTs		BA (4[d])	81	99 : 1
6	OH	Ts_2O	BA (4[d])	63	96 : 4
7	OH	Ms_2O	BA (4[d])	56	96 : 4
8	OH	Tf_2O	BA (4[d])	9	65 : 35

[a] Reaction conditions: allylic compound (0.5 mmol), BA (2.0 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (13 μmol), PCy_3 (25 μmol) at 80 °C, 12 h. [b] GC yields. [c] Determined by GC. [d] Total amount. [e] Reaction was carried out at 60 °C for 24 h.



(1)

Next, the alkenylation reactions of various allylic alcohols in the presence of Ts_2O were investigated and the results are summarized in Table 2. The reactions of 2-hexen-1-ol (**3a**) and 1-hexen-3-ol (**3b**) yielded the same product, **4a** (entries 1 and 2). Neither branched isomers nor stereoisomers were obtained in either case. Similarly, only (*E*,*E*)-1,4-diene **4b** formed by reaction using cinnamyl alcohol (**3c**) and 1-phenyl-2-propen-1-ol (**3d**) (entries 3 and 4). These results indicate that the alkenylation reactions proceed *via* common π-allylpalladium intermediates. The reactions of prenyl alcohol (**3e**) and 3-penten-2-ol (**3f**) selectively gave 1,4-dienes **4c** and **4d**, respectively, although small amounts of isomers also were obtained (entries 5 and 6). The reaction of methallyl alcohol (**3h**) yielded a large amount of a polymer, and the yield of desired 1,4-diene **4f** was low (entry 8). No product was obtained using other alkenes such as acrylonitrile, *N*,*N*-dimethylacrylamide, or styrene.

Brookhart studied reactivity of the cationic π-allylpalladium complex $[(\pi\text{-allyl})Pd(OEt_2)(PCy_3)]^+[BAr_4]^-$ (Ar = $[3,5\text{-}(CF_3)_2C_6H_3]$) **5** with methyl acrylate by low-temperature NMR spectroscopy, in which the formation of methyl 2,5-hexadienoate was observed at 15 °C, and the reaction intermediates were detected at lower temperature.[6] The alkenylation reported here may proceed *via* similar reaction intermediates as shown in Scheme 1. Oxidative addition of allylic tosylates (**6**)[14] generated *in situ* from allylic alcohols and Ts_2O would give the

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† Electronic supplementary information (ESI) available: spectral data for compounds **1**, **2**, **4**, and **5**. See http://www.rsc.org/suppdata/cc/b3/b307705e/

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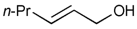
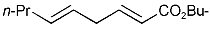
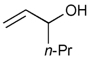
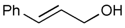
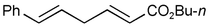
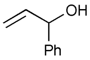
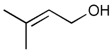
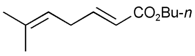
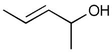
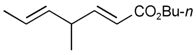
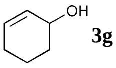
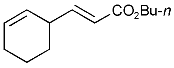
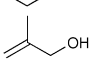
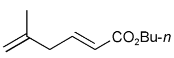
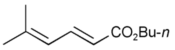
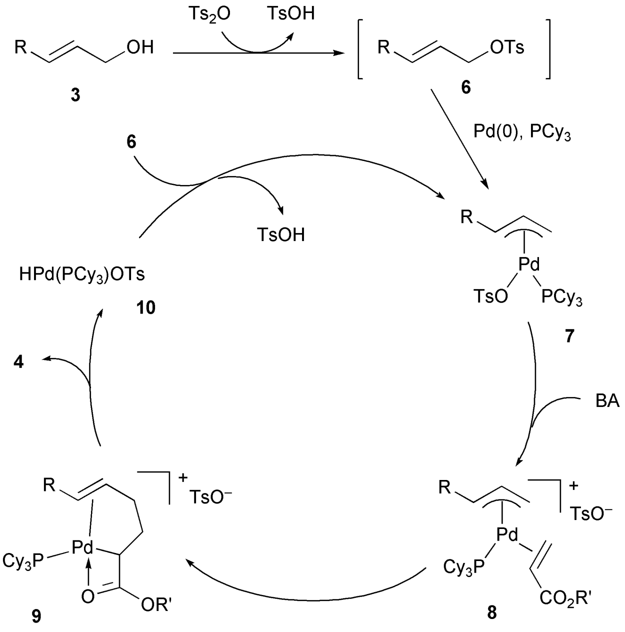
Table 2 Pd-catalyzed alkenylation of allylic alcohols with *n*-butyl acrylate (BA) in the presence of Ts_2O[a]

Entry	Alcohol	Product	Isolated yield (%)
1	 **3a**	 **4a**	73
2	 **3b**	**4a**	74
3	 **3c**	 **4b**	70
4	 **3d**	**4b**	78
5	 **3e**	 **4c**	70^b
6	 **3f**	 **4d**	64^b
7	 **3g**	 **4e**	32
8	 **3h**	 **4f**	28^c
		 **5**	(**4f** : **5** = 53 : 47)

[a] Reaction conditions: **3** (0.5 mmol), BA (4 mL), Ts_2O (0.6 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (13 μmol), PCy_3 (25 μmol) at 80 °C for 12 h. [b] Contaminated with a small amount of inseparable isomers. [c] GC yield.



Scheme 1

allylpalladium intermediate **7**. Replacement of tosylate with *n*-butyl acrylate is followed by its insertion, giving complex **9**. Elimination of product **4** from **9** affords hydride complex **10**, which reacts with **6**, affording allylpalladium intermediate **7**. When allyl acetate and allyl halide were used instead of allyl tosylate, a cationic complex corresponding to **8** would not form because acetate and halide coordinate to palladium more firmly than does tosylate.

In summary, we found that the reaction of allyl tosylate with *n*-butyl acrylate in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ and PCy_3 selectively gave *n*-butyl 2,5-hexadienoate (**1**). Moreover, the regioselective alkenylation of various allylic alcohols **3** to the corresponding 1,4-dienes **4** was accomplished by addition of Ts_2O.

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14 Another possible intermediate is allyl acrylate, generated by transesterification between allyl alcohol and BA under acidic conditions. However, allyl acrylate was not detected in the reaction of allyl alcohol with BA in the presence of TsOH at 70 °C for 17 h in acetic acid.