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Pd(II)-Catalyzed Dehydrogenative Olefination of Vinylic C−H Bonds with Allylic Esters: General and Selective Access to Linear 1,3-Butadienes

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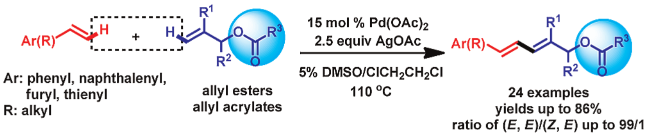
ABSTRACT



This work demonstrates a general and efficient method to prepare conjugated dienes by Pd(II)-catalyzed direct olefination of unactivated alkenes with allylic esters and acrylates via vinylic C−H activation. Various aryl and heteroaryl alkenes as well as aliphatic alkenes all give the desired linear 1,3-butadienes with retention of the traditional leaving groups such as OAc and other carboxylic acid ester groups.

Conjugated dienes and polyenes represent a large class of important natural products and pharmaceutically active compounds such as vitamin A, lissoclinolide, carotenes, bombykol, scyphotatin, viridenomycin, etc.[1] Methods for the preparation of these molecules can be divided into two general categories.[1d] One is the carbonyl olefination reactions[2] represented by the Wittig reaction[3] and its variants such as the Horner−Wadsworth−Emmons reaction,[4] Still−Gennari modification,[5] Julia olefination,[6] and the Peterson reaction.[7] The second strategy is the alkenylation *via* C−C cross-coupling reactions such as Stille cross-coupling,[8] Heck alkenylation,[9] and Negishi coupling.[10] Recently, several interesting direct methods *via* oxidative cross-coupling of alkenes with acrylates and styrenes have been developed by Ishii,[11] Loh,[12] Yu,[13] and Glorius[14] et al.

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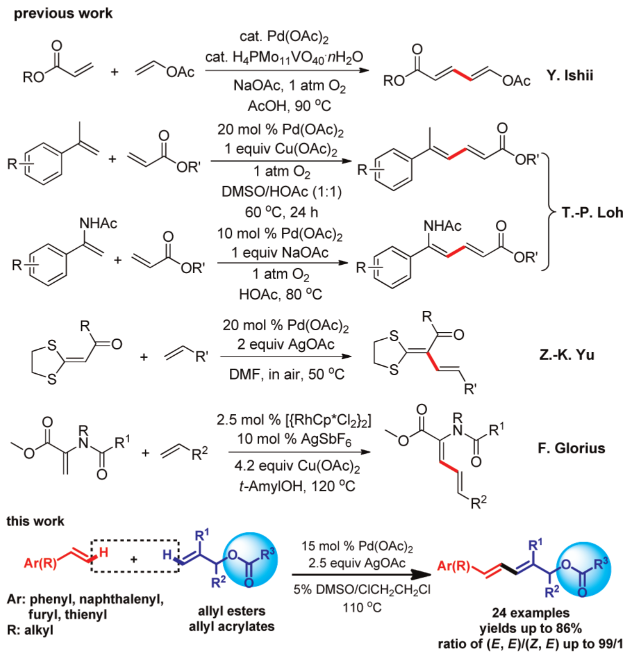
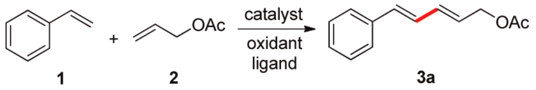
Scheme 1. Direct Oxidative Olefination of Vinylic C−H Bonds



(Scheme 1). Although these systems provide very efficient and direct strategies for the construction of conjugated alkenes by olefination of alkenes *via* vinylic C−H bond activation, most of them suffer from a limited substrate scope and acidic conditions. For example, only vinyl carboxylates and acrylates are tolerated in Ishii's system.[11] Alkenes without α-substituents give no products in Loh's.[12] The α-oxoketene dithioacetals[13] and specific alkenes with directing or activating groups[14] are the only effective substrates in the latter two procedures, respectively. In addition, acetic acid was used as solvent in some cases, which would not tolerate certain functional groups.[11,12] Therefore, more efficient and general protocols to prepare butadienes by direct oxidative vinylic C−H cross-coupling reactions would be highly desirable. Herein, we report a general and efficient strategy for conjugated diene synthesis by Pd(II)-catalyzed direct oxidative olefination of various unactivated alkenes with allyl esters and acrylates under nearly neutral conditions (Scheme 1). In addition, a variety of phenyl, naphthalenyl, furyl, thienyl, and alkyl alkenes could be selectively olefinated by allyl esters and acrylates to form the corresponding 1,3-butadienes in moderate to good yields.

Allylic esters have been widely used as allylation reagents in organic synthesis.[15]However, Pd-catalyzed Heck-type coupling reactions of boronic acids and halides with allyl esters are rarely achieved.[16]As anticipated from the mechanism for the oxidative Heck-type reaction, the *β*-H elimination may be promoted by an electron-rich arene to stabilize the positively charged benzylic carbon in the four-membered transition state. Otherwise, an allylation would occur by *β*-OAc elimination.[9] Inspired by our previous work in the oxidative olefination of arenes with allyl esters,[17] we began to wonder about the possibility of direct oxidative Heck cross-coupling of alkenes with allyl esters. Fortunately, we successfully accomplished the first example of $Pd(OAc)_2$-catalyzed direct olefination of various unactivated alkenes with allylic esters, which would provide an efficient and general approach to 1,3-butadienes and their derivatives.

Table 1. Modification of the Typical Reaction Conditions[a]



entry	catalyst	oxidant	solvent (v/v)	yield (%)[b]
1	$Pd(OAc)_2$	AgOAc	DMSO	trace
2	$Pd(OAc)_2$	AgOAc	DMSO/HOAc (1:1)	trace
3	$Pd(OAc)_2$	AgOAc	5% DMSO/DMF	7
4	$Pd(OAc)_2$	AgOAc	5% DMSO/THF	18
5	$Pd(OAc)_2$	AgOAc	5% DMSO/$ClCH_2CH_2Cl$	34
6	$PdCl_2$	AgOAc	5% DMSO/$ClCH_2CH_2Cl$	22
7	$Pd(TFA)_2$	AgOAc	5% DMSO/$ClCH_2CH_2Cl$	trace
8	$Pd(PCy_3)_2Cl_2$	AgOAc	5% DMSO/$ClCH_2CH_2Cl$	11
9	$Pd(acac)_2$	AgOAc	5% DMSO/$ClCH_2CH_2Cl$	18
10	$Pd(OAc)_2$	Ag_2CO_3	5% DMSO/$ClCH_2CH_2Cl$	16
11	$Pd(OAc)_2$	Ag_2O	5% DMSO/$ClCH_2CH_2Cl$	trace
12	$Pd(OAc)_2$	$Cu(OAc)_2$	5% DMSO/$ClCH_2CH_2Cl$	trace
13[c]	$Pd(OAc)_2$	AgOAc	5% DMSO/$ClCH_2CH_2Cl$	50
14[d]	**$Pd(OAc)_2$**	**AgOAc**	**5% DMSO/$ClCH_2CH_2Cl$**	**81**[e]
15[f]	$Pd(OAc)_2$	AgOAc	5% DMSO/$ClCH_2CH_2Cl$	41

[a] Reaction conditions: styrene (0.5 mmol), allyl acetate (1.5 mmol), oxidant (2 equiv), catalyst (10 mol %), 110 °C, 15 h, unless otherwise noted. [b] Isolated yields of the *E*/*E* and *Z*/*E* isomers. [c] $Pd(OAc)_2$ (15 mol %). [d] $Pd(OAc)_2$ (15 mol %), AgOAc (2.5 equiv). [e] Conversion of styrene is 75%; Isolated yield based on conversion of styrene. [f] $Pd(OAc)_2$ (15 mol %), AgOAc (2.5 equiv), 80 °C.

Initially, we chose styrene and allylic acetate as the model substrates to optimize suitable conditions for this reaction (Table 1). It was found that the solvent, catalysts, and oxidants critically affect the reaction efficiency. Solvents such as DMSO, DMSO/HOAc (v/v = 1:1), 5% DMSO/DMF (v/v), and 5% DMSO/THF were not effective (entries 1−4). The desired products were isolated in a yield of 34% by using a mixed solvent of 5% DMSO/$ClCH_2CH_2Cl$ (v/v) (entry 5). The yield decreased with increasing or decreasing the amount of DMSO (see Supporting Information). The solvent effect indicates that a

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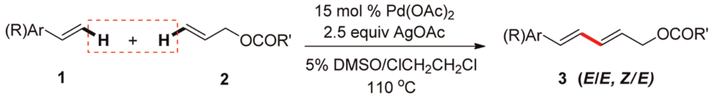
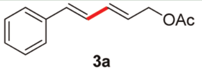
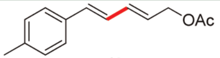
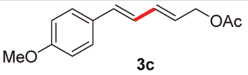
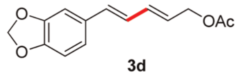
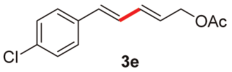
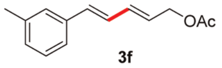
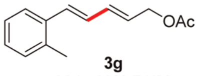
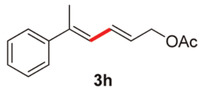
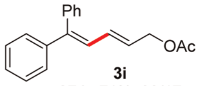
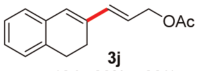
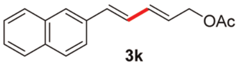
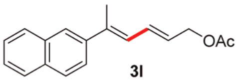
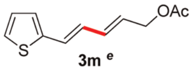
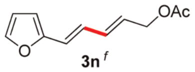
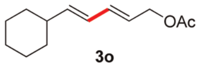
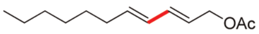
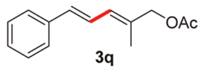
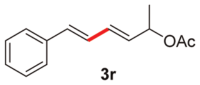
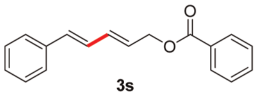
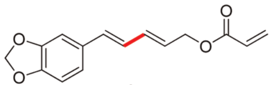
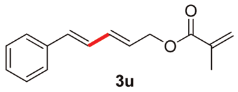
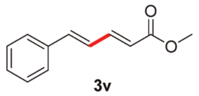
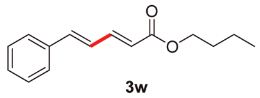
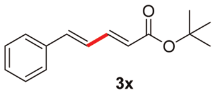
Table 2. Olefination of Various Alkenes with Allylic Acetates and Acrylates[a]



product time, yield, (*E*/*E*)/(*Z*/*E*)	product time, yield, (*E*/*E*)/(*Z*/*E*)	product time, yield, (*E*/*E*)/(*Z*/*E*)
 **3a** 20 h,[b] 81%,[c] 85/15[d]	 **3b** 11 h, 65%, 81/19	 **3c** 14 h, 68%, 88/12
 **3d** 22.5 h, 81%, 81/19	 **3e** 30 h, 50%, 80/20	 **3f** 22 h, 63%, 72/28
 **3g** 22 h, 68%,74/26	 **3h** 13 h, 73%, 82/18	 **3i** 27 h, 71%, 83/17
 **3j** 13 h, 60%, >99/1	 **3k** 14 h, 63%, 63/37	 **3l** 12 h, 84%, 79/21
 **3m**[e] 20.5 h, 85%, 86/14	 **3n**[f] 14 h, 86%, 88/12	 **3o** 24 h, 70%, 74/26
 **3p** 25 h, 80%, 76/24	 **3q** 12 h, 79%, 61/39	 **3r** 20 h, 76%, 83/17
 **3s** 10.5 h, 70%, 80/20	 **3t** 18 h, 46%, 76/24	 **3u** 19 h, 66%, 83/17
 **3v** 20.5 h, 60%, 92/8	 **3w** 20.5 h, 56%, 94/6	 **3x** 20.5 h, 56%, 90/10

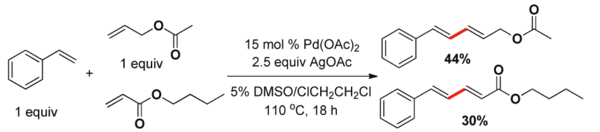
[a] Reaction conditions: alkene (0.5 mmol, 1 equiv), allyl esters or acrylates (1.5 mmol, 3 equiv), AgOAc (2.5 equiv), $Pd(OAc)_2$ (15 mol %), 5% DMSO/$ClCH_2CH_2Cl$ (v/v), 110 °C, unless otherwise noted. [b] Reaction time, indicated by TLC. [c] Isolated yields of the *E*/*E* and *Z*/*E* isomers. [d] Ratio of *E*/*E* and *Z*/*E* isomers determined by ^{1}H NMR. [e] The reaction was performed at 70 °C. [f] The reaction was performed at 60 °C.

specified volume of DMSO plays an important role in this reaction. As the catalyst, $Pd(OAc)_2$ was more efficient than $PdCl_2$, $Pd(O_2CCF_3)_2$, $PdCl_2(Cy_3P)_2$, and $Pd(acac)_2$ (entries 6–9). The oxidant AgOAc was better than others such as Ag_2CO_3, Ag_2O, and $Cu(OAc)_2$ (entries 10–12). Moreover, the yields increased with increasing the amount of catalyst and oxidant (entries 13 and 14). A lower temperature gave a lower yield (entry 15). The desired product **3a** was obtained in 81% isolated yield under the typical conditions: 1.0 equiv of styrene, 3.0 equiv of allyl ester, 15 mol % $Pd(OAc)_2$, 2.5 equiv of AgOAc, 5% DMSO/$ClCH_2CH_2Cl$, 110 °C, 15 h. Entries 1–15 are only a sampling of over 60 reactions which have been screened by using different catalysts, ligands, additives, oxidants, bases, and solvents (see Supporting Information).

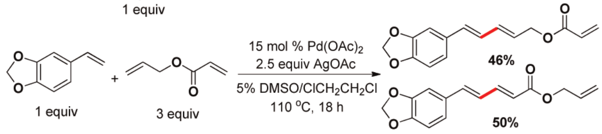
To examine the scope of this system, the coupling reactions of various alkenes with substituted allylic esters and acrylates were studied (Table 2). A variety of substituted styrenes gave the desired products in moderate to good yields (**3b**–**3j**). Among them, electron-rich styrenes gave slightly higher yields than the electron-poor ones (**3b**–**3e**). The *meta*- and *ortho*-substituted styrenes gave comparative yields to the *para*-substituted ones (**3f**, **3g**). The α-methyl and α-phenyl styrenes were tolerated in this reaction (**3h**, **3i**). In addition, an internal alkene reacted with allyl acetate to furnish **3j** in 60% isolated yield. The 2-vinylnaphthalene and 2-isopropenylnaphthalene were also effective substrates, and the corresponding products **3k** and **3l** were obtained in 63% and 84% yields, respectively. Surprisingly, heteroaryl-substituted ethylenes such as 2-vinylthiophene and 2-vinylfuran were also successfully employed for the vinylic C–H oxidative olefination reaction which has never been reported before, and the desired products **3m** and **3n** were isolated in 85% and 86% yields, respectively. Moreover, the oxidative olefination of aliphatic alkenes with allylic esters also gave good yields of the corresponding dienes, though the conversion of aliphatic olefins was low (**3o** and **3p**).

On the other hand, various substituted allylic esters gave moderate yields of the desired products in this reaction (Table 2, **3q**–**3u**). The coupling reaction of styrene with α-methyl and β-methyl allyl acetates afforded products **3q** and **3r** in 79% and 76% yields, respectively. Additionally, allyl benzoate gave a good yield of **3s**. Moreover, allyl acrylate and allyl methacrylate also gave the allyl vinylic C–H bond olefination products **3t** and **3u** in 46% and 66% yields, respectively. It is noteworthy that acrylates could also be used as the olefination partners with styrene to produce the desired dienes in moderate yields under the reaction conditions (**3v**, **3w**, and **3x**). However, in the system by Loh et al., olefination of styrene with acrylates gave no desired products.[12]

To investigate the mechanism for this oxidative olefination, an intermolecular competition reaction was carried out (eq 1), which indicates that the difference between allyl acetate and butyl acrylate in the olefination of styrene is not remarkable. The same conclusion can be obtained from an intramolecular competition reaction of allyl acrylate with 5-vinylbenzo[*d*][1,3]dioxole under the typical conditions (eq 2).



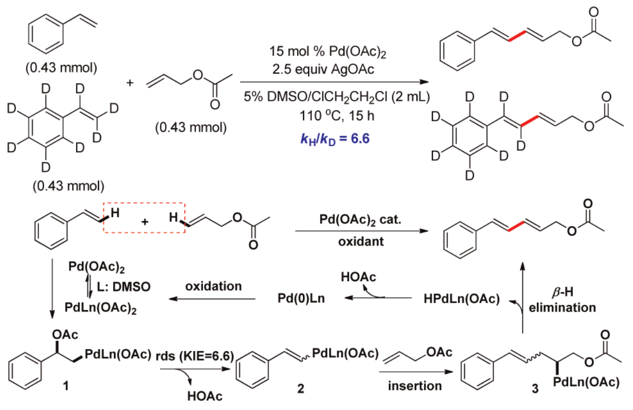
(1)



(2)

In addition, an intermolecular kinetic isotope effect (KIE) experiment was carried out. As a result, a significant KIE was observed with the $k_H/k_D = 6.6$ (Scheme 2). It indicates that the C–H bond cleavage is involved in the rate-determining step of this procedure. A plausible mechanism that is consistent with the experimental data and literature precedent is depicted in Scheme 2. Addition of $Pd(OAc)_2$ to alkene generates intermediate **1**, which would precede an elimination of HOAc to give an alkenyl-Pd-OAc intermediate **2**.[10,12] The insertion of **2** to the double bond of the allyl ester would form intermediate **3**. The desired product diene is obtained by β-H elimination, and the catalyst is regenerated following oxidation of the low-valent Pd complex.[9,12,17]

Scheme 2. Mechanistic Studies on the Oxidative Olefination of Alkenes with Allyl Esters



In conclusion, we developed a general and direct protocol to prepare conjugated dienes *via* a Pd(II)-catalyzed oxidative olefination of unactivated alkenes with allylic esters and acrylates. This strategy exhibits the broadest substrate scope with respect to both alkenes and allylic esters/acrylate partners among the existing systems. Various aryl and heteroaryl alkenes as well as aliphatic alkenes all give the expected 1,3-dienes as the major products. In addition, as the olefination partner, a series of substituted allylic esters bearing another C=C bond such as allyl acrylates also give moderate to good yields of the desired products. Further investigation of this procedure is underway in our laboratory.

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Supporting Information Available. Full experimental details and characterization data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.