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Pd-Catalyzed Olefination of Perfluoroarenes with Allyl Esters

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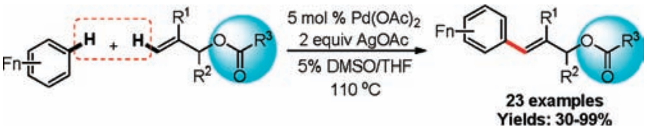
ABSTRACT



An efficient Pd(II)-catalyzed direct olefination of perfluoroarenes with allyl esters is demonstrated. Under the typical conditions, the coupling reaction of fluorinated-arenes with allylic esters proceeded via a β-H elimination rather than a β-OAc elimination to give the corresponding γ-substituted allylic esters.

Fluorinated arenes and derivatives represent a large class of important pharmaceuticals and agrochemicals.[1] In the past decades, a variety of methods have been developed to prepare these useful compounds.[2] Recently, Zhang,[3] Zhao,[4] Hirano and Miura,[5] Su,[6] and Shi[7] et al. reported several efficient protocols to synthesize substituted fluoroarenes by transition-metal-catalyzed coupling reactions of perfluoroarenes via C–H bond activation to form some new C–C bonds. Of particular interest is the oxidative Heck reaction of ArH with alkenes catalyzed by palladium which is also named the Fujiwara–Moritani reaction.[8] Although many efficient oxidative Heck-type coupling reactions of alkenes with arenes and heteroarenes have been developed, there is only one example of the direct olefination of highly electron-deficient perfluoroarenes via a Fujiwara–Moritani reaction reported by Zhang et al. in 2010.[3a] However, only the electron-deficient olefins, aliphatic olefins, and styrene derivatives were effective substrates in that system. Herein, we wish to report a first

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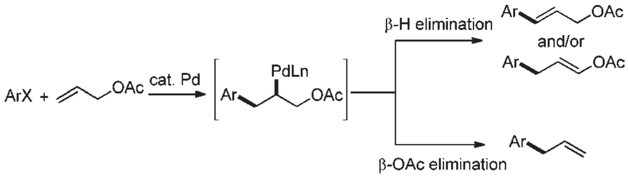
example of Pd-catalyzed oxidative olefination of perfluoroarenes with allyl esters.

Allylic esters have been widely used as allylation reagents in organic synthesis.[9] However, Pd-catalyzed Heck-type coupling reactions of organic halides and boronic acids with allyl esters are rarely achived. Recently, Jiao,[10]White,[11] and Xiao[12] et al. reported several examples of Heck reactions of allylic esters with arylhalides, arenes, and arylboronic acids proceeding via β-H elimination rather than β-OAc elimination (Scheme 1). We report herein an efficient olefination of fluorinated arenes with allylic esters via a highly selective β-H elimination process in the oxidative Heck reaction.

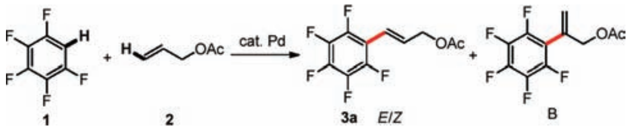
Scheme 1. β-H Elimination vs β-OAc Elimination in Heck-Type Reactions of Allylic Esters with Arylhalides and/or Arylboronic Acids



Initially, we chose pentafluorobenzene and allyl acetate as the model substrates to optimize suitable conditions for this reaction (Table 1). It was found that the solvent, catalysts, and additives affect the reaction efficiency critically. The solvent such as DMSO, THF, 5% DMSO/DMF (v/v), and 5% DMSO/DCE (v/v) were not effective (entries 1−4). The desired products were isolated in a yield of 73% by using a mixed solvent of 5% DMSO in THF (entry 5). The yield slightly decreased by using 10% DMSO/THF as the solvent (entry 6). The solvent effect indicates that a 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 7−10). The additive AgOAc was better than others such as Ag_2CO_3, Ag_2O, Ag_2SO_4, $Cu(OAc)_2$, and BQ (entries 11−15). Moreover, the yield decreased when the reaction mixture was stirred at 80 °C and was charged with equal moles of fluoroarene and allyl ester (entries 17 and 18). The desired products were obtained in 82% isolated yield under the typical conditions: 3.0 equiv of fluoroarene, 1.0 equiv of allyl ester, 5 mol % $Pd(OAc)_2$, 2.0 equiv of AgOAc, 5% DMSO/THF, 110 °C, 12 h (entry 16; also see Supporting Information).

To examine the scope of this system, the coupling reactions of various fluoroarenes with substituted allylic esters and ethers were studied (Table 2). A variety of fluorinated arenes have been proved to be very efficient substrates under the typical conditions. In these cases, olefination was generally observed at the more sterically accessible position (**3e**, **3g**, **3h**). Such selectivity might be attributed to the acidity of C−H of the fluorinated arenes even though it was located at a more sterical position.[13] Fluorinated arenes with an electron-donating methoxy group gave an excellent yield of the corresponding product (**3b**). Tetrafluorobenzene also gave a very high yield of the desired product (**3c**). It seems that the yields decrease with the decrease in the number of F-atoms substituted in the aromatic core (**3c**, **3d**, **3h**, **3i**, **3j**). Fluorobenzene gave an 81% yield of the olefination product when the reaction was carried out in a mixed solvent of 5% DMSO/fluorobenzene (**3k**). 2,6-Difluorotoluene gave only a 30% yield of the product (**3e**). Perfluoroarene with an electron-withdrawing group like CF_3 (**3f**) is also effective. Interestingly, the desired product with retention of the Br-atom was isolated

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



entry	catalyst	additive	solvent (v/v)	yield (%)[b]
1	$Pd(OAc)_2$	AgOAc	DMSO	12
2	$Pd(OAc)_2$	AgOAc	THF	43
3	$Pd(OAc)_2$	AgOAc	5% DMSO/DMF	34
4	$Pd(OAc)_2$	AgOAc	5% DMSO/DCE	55
5	$Pd(OAc)_2$	AgOAc	5% DMSO/THF	73
6	$Pd(OAc)_2$	AgOAc	10% DMSO/THF	65
7	$PdCl_2$	AgOAc	5% DMSO/THF	64
8	$Pd(TFA)_2$	AgOAc	5% DMSO/THF	51
9	$Pd(PCy_3)_2Cl_2$	AgOAc	5% DMSO/THF	21
10	$Pd(acac)_2$	AgOAc	5% DMSO/THF	41
11	$Pd(OAc)_2$	Ag_2CO_3	5% DMSO/THF	40
12	$Pd(OAc)_2$	Ag_2O	5% DMSO/THF	3
13	$Pd(OAc)_2$	Ag_2SO_4	5% DMSO/THF	9
14	$Pd(OAc)_2$	$Cu(OAc)_2$	5% DMSO/THF	11
15	$Pd(OAc)_2$	BQ	5% DMSO/THF	trace
16[c]	**$Pd(OAc)_2$**	**AgOAc**	**5% DMSO/THF**	**82**
17[d]	$Pd(OAc)_2$	AgOAc	5% DMSO/THF	72
18[e]	$Pd(OAc)_2$	AgOAc	5% DMSO/THF	44

[a] Reaction conditions: pentafluorobenzene (1.5 mmol), allyl acetate (0.5 mmol), additive (1 equiv), catalyst (5 mol %), 110 °C, 12 h, unless otherwise noted. [b] Isolated yields of the *E*/*Z* and B isomers. [c] AgOAc (2 equiv). [d] 2 equiv AgOAc, 80 °C. [e] **1**/**2** = 1/1.

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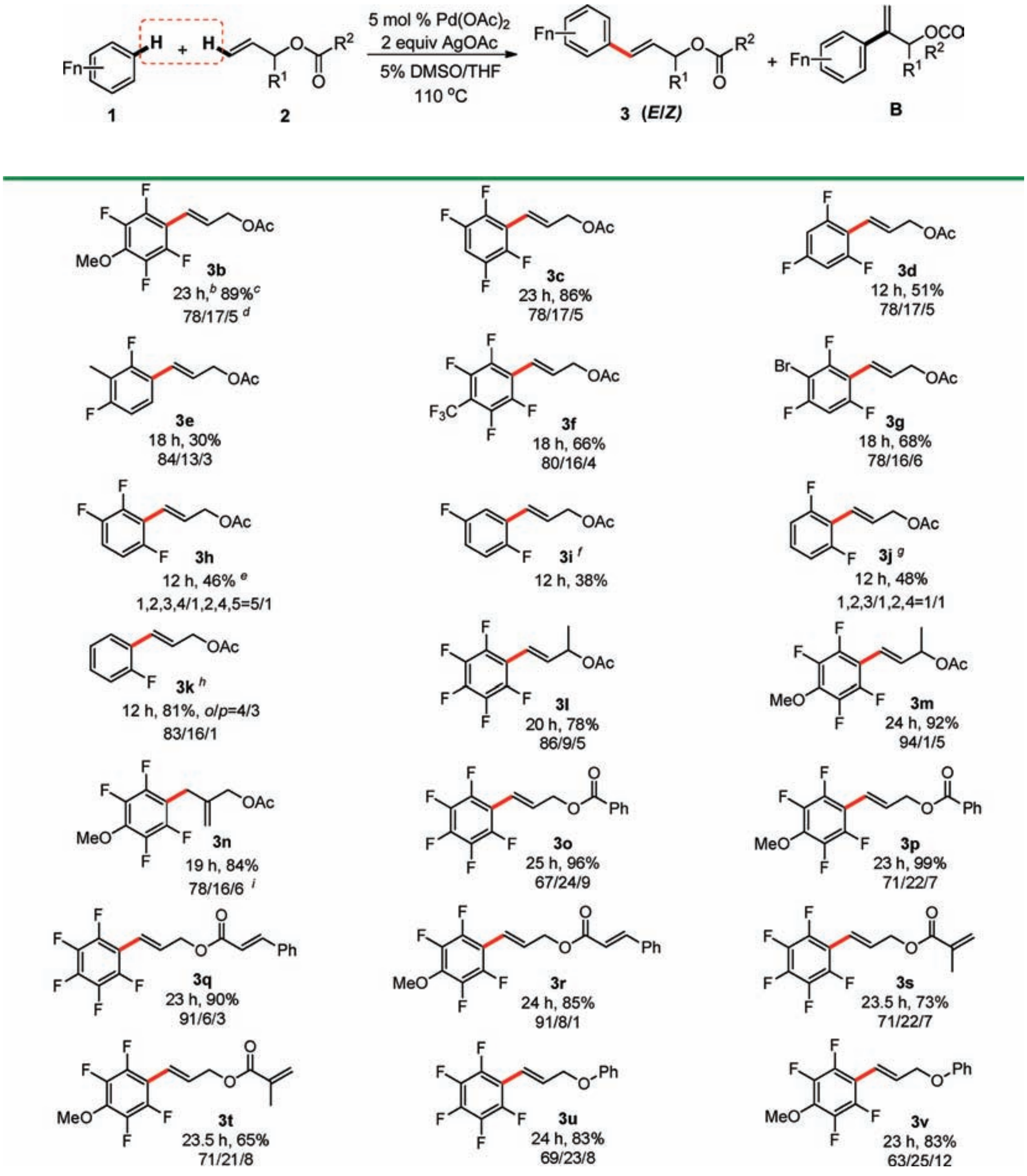
Table 2. Pd-Catalyzed Oxidative Heck Reaction of Fluoroarene with Allyl Ester[a]



[a] Reaction conditions: fluoroarene (1.5 mmol, 3 equiv), allyl esters or ethers (0.5 mmol, 1 equiv), AgOAc (2 equiv), $Pd(OAc)_2$ (5 mol %), 5% DMSO/THF (v/v), 110 °C, unless otherwise noted. [b] Reaction time, indicated by TLC. [c] Isolated overall yields of the *E*/*Z* and B isomers. [d] Ratio of *E*/*Z*/*B* determined by crude ^{1}H NMR. [e] Solvent: 5% DMSO/fluoroarene (v/v), isolated yields of the 1,2,3,4/1,2,4,5 substituted isomers. [f] Solvent: 5% DMSO/fluoroarene (v/v), isolated yields of the *E* isomer. [g] Solvent: 5% DMSO/fluoroarene (v/v), isolated yields of the 1,2,3/1,2,4 substituted isomers. [h] Solvent: 5% DMSO/fluoroarene (v/v), isolated yields of the 1,2/1,4 substituted isomers. [i] Ratio of *B*/*E*/*Z*.

in 68% yield by coupling of 1-bromo-2,4,6-trifluorobenzene with allyl acetate (**3g**).

Various substituted allylic esters gave excellent to quantitative yields of the desired products in this reaction (Table 2, **3l**–**3t**). A branched coupling product was isolated as the major product which might proceed via a β-elimination of the H-atom from the methyl group (**3n**). Both allyl benzoate and allyl cinnamate gave excellent yields of the products (**3o**–**3r**). Surprisingly, allyl acrylate and allyl methacrylate gave the desired products **3w**, **3p**, and **3q** in moderate to good yields. It indicates that the oxidative olefination site was located at the allylic rather than the acrylic double bond in this system. It is noteworthy that allylic ether is also used successfully as the olefination partner under these reaction conditions (**3u** and **3v**).

A competing olefination would occur between the allylic and the acrylic double bonds (Scheme 2). However, the C–C bond formation took place in the position of the terminal allylic C=C bond rather than the acrylic double bond under the typical conditions. 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.[9f,10,14] 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 highly electron-deficient perfluoroarenes by using allylic esters and ethers. In this system, various γ-substituted allylic esters have been prepared by an oxidative Heck-type reaction via β-H elimination rather than β-OAc elimination. As the olefination partner, a series of allylic esters even bearing another C=C bond such as allyl methacrylate and allylic ether give high yields of the desired products. The present protocol could be useful for the synthesis of perfluoroarenes and its derivatives which should be valuable to materials and life science. Further investigation of this procedure is underway in our laboratory.

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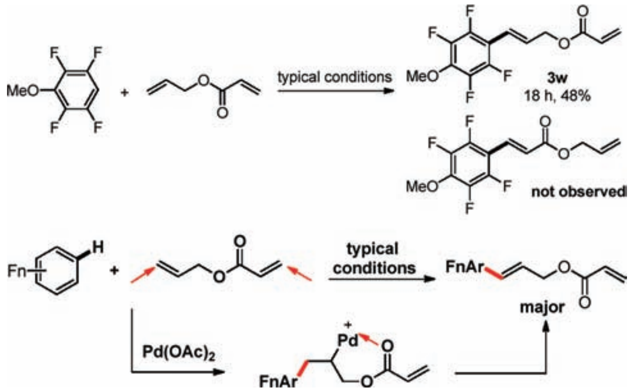
Scheme 2. Competing Olefination of Fluoroarene between the Allylic and Acrylic Double Bonds



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.

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