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Hydroalkenylation: palladium catalyzed co-dimerization of unactivated alkenes

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ABSTRACT

A highly efficient co-dimerization of styrene and cyclopentene was developed in the presence of palladium and a BF_3 source, selectively forming a new C–C bond. The complex $[Pd(PPh_3)_2]^+BF_4^-$ is believed to generate palladium hydride (Pd-H), which catalyzes the reaction between various styrenes and cyclopentene in excellent yields as single isomers. This co-catalytic system provides a new efficient C–C bond forming method.

Seminally, the discovery of palladium catalyzed cross-coupling reactions has changed the field of modern organic chemistry.[1] Recently, many transition metal catalyzed hydroalkenylation reactions have been reported in the literature,[2] utilizing palladium catalysts in conjunction with tetrafluoroborate additives in order to activate various alkenes.[3] Sen,[4] Shmidt,[5] and Tkach,[6] among others, have used this co-catalytic system in order to dimerize or polymerize olefins; however, they have not been able to couple two different alkenes efficiently. Herein we report a vinyl arene coupling reaction utilizing a palladium(0) source and a tetrafluoroborate co-catalyst. In sharp contrast to the previous work, this reaction is a chemoselective and stereoselective cross-coupling of different alkenes without the need of a leaving or activating group on the olefins.

Initially, we used our NHC-amidate Pd(II) complex **1** (Fig. 1) by activating with $AgBF_4$ to remove the chlorine ligand and form a cationic palladium(II) complex.[7] Under mild conditions, we were able to successfully couple styrene and cyclopentene in a high yield, while minimizing the homo-coupled side product of styrene (Scheme 1).

We then endeavored to determine the most favorable source of palladium by screening different palladium and silver complexes (Table 1). Similarly to **1**, other palladium sources provided the desired product as well. Palladium(II) sources such as $Pd(OAc)_2$ and $Pd(TFA)_2$ (entries 1 and 2), yielded low to good results, respectively. $Pd(dba)_2$ (entry 3) was slightly less effective as $Pd(TFA)_2$; however, $Pd(PPh_3)_4$ (entry 4) produced the desired product in comparable yields as **1**. No reaction took place in the absence of a palladium source (entry 5) or in the absence of $AgBF_4$ (entry 6). Using $AgPF_6$ as the silver source drastically lowered the yield of the reaction (entry 7), while other silver(I) salts provided no catalytic activity (entries 8 and 9). This led us to discover the significance of $AgBF_4$.

Since $AgBF_4$ was previously used to remove chloride in **1**, its necessity with $Pd(PPh_3)_4$ was tested by screening $Pd(PPh_3)_4$ against various tetrafluoroborate and boron trifluoride additives (Table 2). $NaBF_4$ by itself or in the presence of acids such as hydrochloric or *p*-toluenesulfonic acid provided no products (entries 1–3). However, $NaBF_4$ in the presence of acids such as methanesulfonic or sulfuric acid provided the product in low yields (entries 4 and 5). Importantly, in the absence of the tetrafluoroborate salt, no

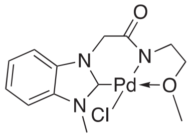

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Figure 1. Structure of our NHC-amidate Pd(II) complex.

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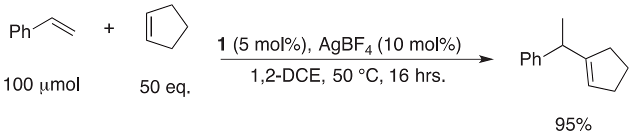


Scheme 1. Initial reaction conditions utilizing complex **1**.

Table 1
Screening of varying palladium and silver sources[a]

Entry	Palladium source	Silver source	Yield[b] (%)
1	$Pd(OAc)_2$	$AgBF_4$	37
2	$Pd(TFA)_2$	$AgBF_4$	79
3	$Pd(dba)_2$	$AgBF_4$	73
4	$Pd(PPh_3)_4$	$AgBF_4$	93
5	–	$AgBF_4$	–
6	$Pd(PPh_3)_4$	–	–
7	$Pd(PPh_3)_4$	$AgPF_6$	13
8	$Pd(PPh_3)_4$	AgOTf	–
9	$Pd(PPh_3)_4$	$AgNO_3$	–

[a] Reaction conditions: 100 μmol styrene, 1250 μmol cyclopentene, 5 μmol palladium source, and 20 μmol silver source were dissolved in 0.7 mL 1,2-DCE and stirred at 50 °C for 16 h.

[b] Determined by ^{1}H NMR using DMSO as an internal standard.

Table 2
Screening of varying tetrafluoroborate and boron trifluoride additives[a]

Entry	Additive 1	Additive 2	Yield[b] (%)
1	$NaBF_4$	–	–
2	$NaBF_4$	HCl	–
3	$NaBF_4$	TsOH	–
4	$NaBF_4$	MsOH	15
5	$NaBF_4$	H_2SO_4	35
6	–	MsOH	–
7	–	H_2SO_4	–
8	HBF_4	–	85
9	$BF_3{\cdot}OEt_2$	–	76
10	$AlCl_3$	–	–

[a] Reaction conditions: 100 μmol styrene, 1250 μmol cyclopentene, 5 μmol Pd$(PPh_3)_4$, 20 μmol additive 1, and 20 μmol additive 2 were dissolved in 0.7 mL 1,2-DCE and stirred at 50 °C for 16 h.

[b] Determined by ^{1}H NMR using DMSO as an internal standard.

products were observed when methanesulfonic or sulfuric acid was used alone (entries 6 and 7). The best results were observed when HBF_4 was used as the tetrafluoroborate additive, producing the product in 85% yield (entry 8). Further, boron trifluoride diethyl etherate was also used as a trifluoride additive, which produced a significant amount of the desired product, revealing that the reaction may not solely be catalyzed by fluoroboric acid (entry 9). Critically, employing other Lewis acids such as $AlCl_3$ did not produce any product (entry 10). These results strongly suggested that the tetrafluoroborate or boron trifluoride additives were responsible for activating the catalytic system.

Based on these results and the work done by Shmidt et al., it is believed that trace amounts of fluoride in the solution form palladium-fluorine dimers (Scheme 2). With increasing amounts of BF_3, the active catalytic species is formed, wherein BF_3 is complexed to the palladium source either via a fluorine atom ($F{\cdot}BF_3$) or as a BF_4^- anion.[8]

The ratio between palladium source and the boronic cocatalyst has been extensively studied, in the dimerization or oligomerization of alkenes. The loading of both tetrafluoroboric acid and boron trifluoride was examined under our standard reaction conditions (Table 3). Stoichiometric equivalents of the boronic source to the palladium catalyst produced low yields (entry 1). Doubling the ratio of tetrafluoroboric acid significantly increased the yield, while doubling the ratio of boron trifluoride modestly increased the yield of the desired product (entry 2). A four-time excess of either tetrafluoroborate or boron trifluoride loading to the palladium catalyst produced the highest amount of the desired product (entry 3), while the yield of the reaction decreased, with higher ratio amounts (entry 4). These results further support our belief of the activated catalyst complex, since increased amounts of the boronic cocatalyst would shift the equilibrium of the palladium complex toward more of an ionic character species.

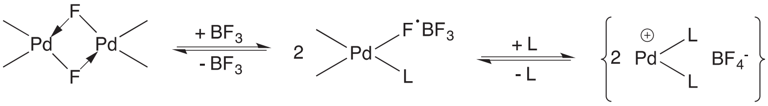
The solvent effect of both $AgBF_4$ and HBF_4 was then tested separately (Table 4). Both $AgBF_4$ and HBF_4 reacted similarly in polar and nonpolar halogenated solvents (entries 1–3). In the case of using benzene as the solvent, HBF_4 produced moderate yields, while the same reaction using $AgBF_4$ did not produce the desired product (entry 4). Other polar solvents inhibited the reaction (entries 5–8). This is thought to be due to the solvent's interaction with BF_3, deactivating the cocatalyst.

We then examined the electronics of the reaction by varying the substituents on styrene in order to determine how electron withdrawing or donating groups would affect the yield of the desired product. These reactions were tested with HBF_4 as the boronic cocatalyst (Table 5). Interestingly, electron deficient styrene substrates produced the highest amount of the desired product (entries 2–6). Electron rich styrene substrates produced drastically lower yields (entries 7 and 8), while the most electron rich substituent, 4-methoxystyrene, produced the lowest yield. Regardless of acid loading and temperature variations, 4-methoxystyrene polymerized under these reaction conditions. Such electronic trends imply that the electron deficient styrene substrates are the most reactive in these reaction conditions, since they are more readily activated by palladium hydride complexes (vide infra).

Preforming the reaction using deuterated styrene revealed interesting mechanistic implications (Scheme 3). Critically, the final product was not deuterated on the cyclopentene ring. The deuterated ratio at the benzylic position of the product was 2:1, revealing that there were no proton or deuterium shifts during the reaction.

Sen et al. suggested a carbocationic mechanism for the dimerization of styrene, using $Pd(PPh)_2(BF_4)_2$ in the late 1980's;[4b] however, this theory has been long challenged. Such a carbocationic mechanism involves the participation and abstraction of free H^+ and would be very sensitive to the temperature fluctuations. Later findings have refuted this belief and proposed that the coupling of unactivated alkenes with similar catalytic systems may be propagated by palladium hydride complexes[9] or hydrido-palladium species.[10] Though hydrido-palladium species selectively provide head-to-tail products, we favor the palladium hydride complex as the active catalytic species, due to its direct methodology and long list of precedence.

It is well known that Brønsted acids, such as HBF_4, complex with Pd(0) sources, forming palladium hydride complexes, for example, $HPd(L_2)BF_4$.[11] Moreover, in the presence of trace amounts of water from solvent and substrates, silver hexafluorophosphate, tetrafluoroborate counter ions, and boron trifluoride diethyl etherate have been shown to hydrolyze and form HF and activate palladium species.[8a,d,12] Scheme 4 proposes the coupling of styrene and cyclopentene via a palladium hydride complex.[9,13] Initially, the coordinately unsaturated palladium hydride species **I** coordinates to the alkene of styrene, while two monodentate phosphine ligands also coordinate to the palladium center, forming structure **II**. The palladium then forms a π complex with the abundant cyclopentene, forming structure **III** and initiating the cross-coupling reaction. Lastly, beta-elimination of **IV** terminates the



Scheme 2. Catalytically active complexes.

Table 3
Effects of tetrafluoroborate and boron trifluoride loading[a]

Entry	HBF_4 (μmol)	Yield[b] (%)	$BF_3 \cdot OEt_2$ (μmol)	Yield[b] (%)
1	5	24	5	8
2	10	66	10	20
3	20	85	20	76
4	40	49	40	23

[a] Reaction conditions: 100 μmol styrene, 1250 μmol cyclopentene, 5 μmol Pd$(PPh_3)_4$, and varying amounts of HBF_4 or $BF_3 \cdot OEt_2$ were dissolved in 0.7 mL 1,2-DCE and stirred at 50 °C for 16 h.
[b] Determined by ^1H NMR using DMSO as an internal standard.

Table 4
Solvent screened with $AgBF_4$ or HBF_4[a]

Entry	Solvent	$AgBF_4$ yield[b] (%)	HBF_4 yield[b] (%)
1	DCM[c]	86	88
2	1,2-DCE	93	85
3	Chloroform	90	74
4	Benzene	—	59
5	Acetonitrile	—	—
6	THF	—	—
7	MeOH	—	—
8	1,2-Dioxane	—	—

[a] Reaction conditions: 100 μmol styrene, 1250 μmol cyclopentene, 5 μmol Pd$(PPh_3)_4$, and 20 μmol $AgBF_4$ or HBF_4 were dissolved in 0.7 mL solvent and stirred at 50 °C for 16 h.
[b] Determined by ^1H NMR using DMSO as an internal standard.
[c] Reaction was run at 25 °C.

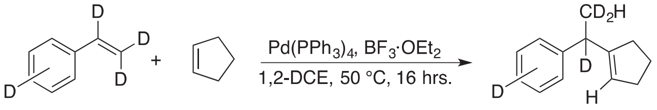
Table 5
Screening styrene derivatives with HBF_4[a]

Entry	Substrate	Yield[b] (%)
1	Styrene	85
2	4-Trifluoromethylstyrene	96
3	4-Nitrostyrene	91
4	4-Chlorostyrene	91
5	2-Fluorostyrene	82
6	4-Fluorostyrene	80
7	4-Methylstyrene	40
8	2-Vinylnaphthalene	57
9	4-Methoxystyrene	14

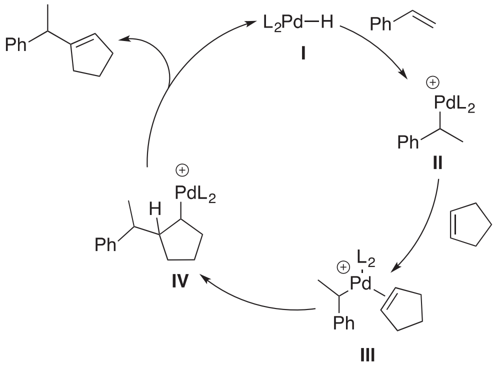
[a] Reaction conditions: 100 μmol styrene substrate, 1250 μmol cyclopentene, 5 μmol Pd$(PPh_3)_4$, and 20 μmol HBF_4 were dissolved in 0.7 mL 1,2-DCE and stirred at 50 °C for 16 h.
[b] Determined by ^1H NMR using DMSO as an internal standard.

chain, providing the desired product and regenerating the palladium hydride active species **I**.

In conclusion, we have found a set of reaction conditions, which selectively couple styrene and cyclopentene, providing a cross-coupling product. In the presence of palladium and a BF_3 source, the active catalytic species is formed, wherein BF_3 is complexed to the palladium source. Palladium hydride complexes initiate the reaction and are more selective toward electron poor substrates.



Scheme 3. Styrene-d_8 study.



Scheme 4. Proposed mechanism via a palladium hydride complex.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2016.01.034.

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