Drastic effect of bidentate phosphine ligands on Pd-catalyzed hydroarylation of ethyl propiolate: a simple route to arylbutadienes†

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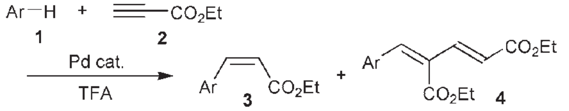
Palladium complexes with bidentate phosphine ligands, $Pd(dppe)(OAc)_2$ and $Pd(dppm)(OAc)_2$, were found to be effective catalysts for reactions of simple arenes with ethyl propiolate, affording arylbutadiene derivatives selectively.

Direct functionalization of C–H bonds is an attractive reaction because it is a powerful and straightforward method for transformation of organic compounds.[1] Especially, the C–H bond functionalization of a simple compound leading to a more complex molecule without pre-functionalization is of considerable interest from the viewpoint of green chemistry.

Arylbutadienes are useful and versatile compounds and frequently prepared by the Wittig and related reactions and by coupling reactions using transition metals.[2] Recently, it was reported that some transition metals catalyzed the reaction of aryl reagents with two molecule of alkynes to afford arylbutadienes.[3] These reactions provide a simple route for arylbutadienes but they need aryl reagents such as aryl iodides and boronic acids. To the best of our knowledge, little attention has been paid to the formation of arylbutadiene derivatives from simple arenes and alkynes by means of C–H bond functionalization methodology although the hydroarylation of alkynes with arenes has been studied extensively.[4,5]

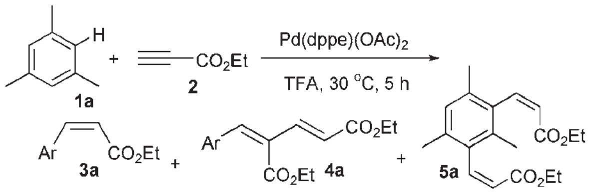
Previously, we reported that $Pd(OAc)_2$-catalyzed hydroarylation of alkynes with simple arenes in the presence of trifluoroacetic acid (TFA) proceeded in regio- and stereoselective manner to afford *cis*-aryl substituted alkenes.[6] In the case of ethyl propiolate (**2**), regio- and stereo-defined arylbutadiene derivatives **4** were also obtained as minor products, decreasing the yield of hydroarylation products, ethyl *cis*-cinnamates **3** (eqn (1)).[6a,b] However, we discovered that arylbutadienes **4** were obtained selectively from the reaction of a simple arene with ethyl propiolate when a palladium complex with a bidentate phosphine ligand, $Pd(dppe)(OAc)_2$ (dppe = 1,2-bis(diphenylphosphino)ethane), was used as a catalyst. Here, we report a simple route to arylbutadienes using hydroarylation of ethyl propiolate in the presence of a Pd complex with a bidentate phosphine.



(1)

First, we investigated the reaction of mesitylene (**1a**) with **2** in the presence of $Pd(dppe)(OAc)_2$ as a catalyst. The reaction afforded **4a** as a major product along with a small amount of *cis*-cinnamate **3a**. Investigation of the reaction conditions revealed that an amount of **1a** affected the selectivity of

Table 1 Investigation of reaction conditions[a]



Entry	**1a** (mmol)	**2** (mmol)	GC yield[b] (%) **3a**	**4a**	**5a**
1	3	2	17	83	0
2	2	2	17	83	0
3	1	2	7	68	4
4	1	3	0	25	2
5[c]	2	2	16	83	0
6[d]	2	2	9	91	0

[a] *Reaction conditions*: $Pd(dppe)(OAc)_2$ (0.005 mmol), **1a**, **2** and TFA (1 mL) at 30 °C for 5 h. [b] The yields based on **2**. [c] TFA (0.5 mL) and CH_2Cl_2 (0.5 mL). [d] TFA (0.25 mL) and CH_2Cl_2 (0.75 mL).

Table 2 Effect of phosphine ligands[a]

Entry	Pd catalyst	GC yield[b] (%) **3a**	**4a**	**5a**
1	$Pd(OAc)_2$	37	20	3
2	$Pd(PPh_3)_2(OAc)_2$	36	18	3
3	$[Pd(dppe)_2](OAc)_2$	0	1	0
4	$Pd(dppp)(OAc)_2$	23	57	1
5[c]	$Pd(dppm)(OAc)_2$	2	54	3
6[cd]	$Pd(dppm)(OAc)_2$	4	85	1

[a] *Reaction conditions*: Pd catalyst (0.005 mmol), **1a** (2 mmol), **2** (2 mmol), TFA (0.25 mL) and CH_2Cl_2 (0.75 mL) at 30 °C for 5 h. [b] The yields based on **2**. [c] $Pd(dppm)Cl_2$ (0.005 mmol) and AgOAc (0.02 mmol). [d] TFA (1 mL) and CH_2Cl_2 (0 mL).

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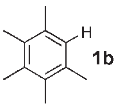
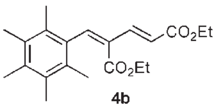
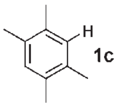
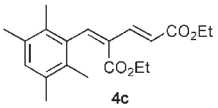
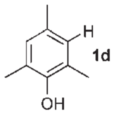
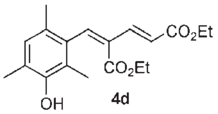
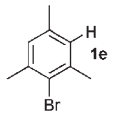
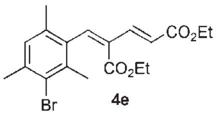
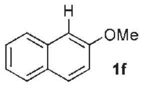
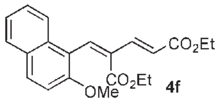
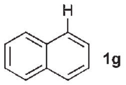
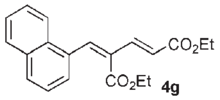
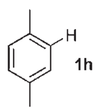
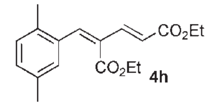
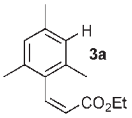
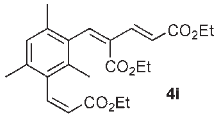
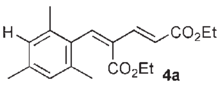
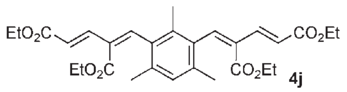
product **4a** (Table 1, entries 1–4). Use of an excess amount of **1a** prevented products **3a** and **4a** from further reaction, resulting in higher yields. The amount of TFA also affected the selectivity of **4a** (entries 5 and 6). A low amount of TFA is favorable for selective formation of **4a** although the reaction did not proceed in the absence of TFA. As a result, the best result was obtained when 0.25 mL of TFA was used (entry 6).

Furthermore, similar Pd complexes were examined as catalysts (Table 2). In contrast to Pd(dppe)$(OAc)_2$, Pd$(PPh_3)_2(OAc)_2$ bearing monodentate phosphine ligands resulted in low selectivity of **4a**, which was almost the same as that of Pd$(OAc)_2$ (entries 1 and 2). [Pd$(dppe)_2$]$(OAc)_2$ was completely inactive (entry 3). In the case of Pd(dppp)$(OAc)_2$ (dppp = 1,2-bis-(diphenylphosphino)propane), the selectivity of **4a** decreased

Table 3 Reaction of ethyl propiolate (**2**) with arenes[a]

		Solvent/mL		Product and isolated yield[b] (%)			
Entry	Ar–H	TFA	CH_2Cl_2	4		3	
1[c]	 **1b**	0.25	0.75	 **4b**	82	**3b**	9
2	 **1c**	0.25	0.75	 **4c**	76	**3c**	7
3	 **1d**	0.25	0.75	 **4d**	73	**3d**	5
4	 **1e**	1	0.5	 **4e**	66	**3e**	12
5[d]	**1e**	1	0.5	**4e**	69	**3e**	2
6	 **1f**	0.25	0.75	 **4f**	70	**3f**	11
7[e]	 **1g**	0.5	0.5	 **4g**	53	**3g**	18
8[de]	**1g**	1	0.5	**4g**	67	**3g**	8
9[f]	 **1h**	0.5	0	 **4h**	(54)	**3h**	(22)
10[dg]	**1h**	1	0	**4h**	75	**3h**	7
11	 **3a**	0.5	0.5	 **4i**	72	**5a**	6
12	 **4a**	1	0	 **4j**	75	**4i**	7

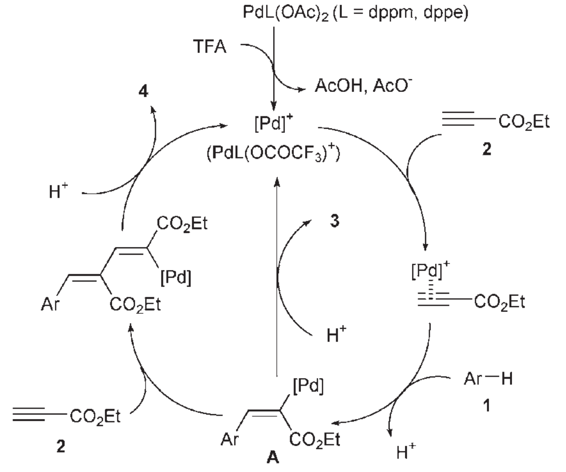
[a] *Reaction conditions*: Pd(dppe)$(OAc)_2$ (0.005 mmol), **2** (2 mmol), an arene (2 mmol), TFA and CH_2Cl_2 at 30 °C for 5 h. [b] The yields based on **2**. The yields in the parentheses were determined by GC. [c] **1b** (1.1 mmol) was used. [d] Pd(dppm)Cl_2 (0.005 mmol) and AgOAc (0.02 mmol) were used instead of Pd(dppe)$(OAc)_2$. [e] 10 h. [f] **1h** (0.5 mL, *ca.* 4.3 mmol) was used. [g] **1h** (3 mmol) was used.

compared to Pd(dppe)$(OAc)_2$ although it was higher than that of $Pd(OAc)_2$ (entry 4). On the other hand, Pd(dppm)$(OAc)_2$ (dppm = 1,2-bis(diphenylphosphino)methane) which was prepared *in situ* from Pd(dppm)Cl_2 and AgOAc showed high selectivity but the yield of **4a** was low (entry 5). However, Pd(dppm)$(OAc)_2$ gave **4a** in high yield when only TFA was used as solvent (entry 6). Among Pd complexes having bidentate phosphine ligands with different tether length, Pd(dppe)$(OAc)_2$ and Pd(dppm)$(OAc)_2$ were effective catalysts for formation of **4a**.

This reaction is also applicable to other arenes (Table 3). In all cases, the reactions gave arylbutadienes **4** regio- and stereoselectively. In the presence of Pd(dppe)$(OAc)_2$, pentamethylbenzene (**1b**), 1,2,4,5-tetramethylbenzene (**1c**) and 2,4,6-trimethylphenol (**1d**) gave the corresponding arylbutadienes **4** in good to high yields along with a small amounts of cinnamates **3** (entries 1–3). 2-Bromomesitylene (**1e**) also gave **4e** in good yield although 1 mL of TFA was required because of the lower reactivity of **1e**. Use of Pd(dppm)$(OAc)_2$ improved the selectivity but gave **4e** in similar yield (entry 5). For 2-methoxynaphthalene (**1f**), Pd(dppe)$(OAc)_2$ gave **4f** in good yield. In the case of naphthalene (**1g**) and *p*-xylene (**1h**), 1 mL of TFA was required to complete the reaction because of the low reactivity of **1g** and **1h**. However, Pd(dppe)$(OAc)_2$ showed low selectivity of arylbutadienes **4** when 1 mL of TFA was used. As a result, Pd(dppe)$(OAc)_2$ gave **4g** and **4h** in 53 and 54% yield, respectively when 0.5 mL of TFA was used (entries 7 and 9). In contrast, Pd(dppm)$(OAc)_2$ showed good selectivity by using 1 mL of TFA. Thus, **1g** and **1h** gave **4g** and **4h** in 67 and 75% yields, respectively (entries 8 and 10). These results indicate that Pd(dppm)$(OAc)_2$ is an effective catalyst for less reactive arenes which require a large amount of TFA. Hydroarylation products **3a** and **4a** also participated in the reaction, affording **4i** and **4j** in good yields, respectively. The reaction of **4a** explains clearly that an excess amount of **1a** is required in the reaction of **1a** with **2** to prevent further reaction of **4a**. Other substituted propiolates were not effective for this reaction.

The reaction of **3b** with **2** did not take place in the presence of Pd(dppe)$(OAc)_2$, indicating that **3** is not an intermediate of **4**. Although the reaction mechanism is not clear, the conjecture that products **3** and **4** formed *via* a similar intermediate is acceptable because the stereochemistry of **3** and **4** is similar. A possible reaction mechanism is depicted in Scheme 1.[6b,7] Ethyl propiolate (**2**) is first activated by coordination of a cationic Pd species generated *in situ* from a Pd catalyst and then undergoes electrophilic aromatic substitution to afford a 2-arylvinyl palladium intermediate **A**, followed by insertion of **2** into a Pd–C bond in *syn* fashion. Protonation of the resulting arylbutadienyl palladium intermediate gives **4** with concomitant regeneration of the catalyst. The protonation of intermediate **A** prior to insertion of **2** leads to the formation of **3**.

In summary, we have demonstrated that Pd(dppe)$(OAc)_2$ and Pd(dppm)$(OAc)_2$ show an effective, catalytic activity for the reaction of simple arenes with ethyl propiolate leading to regio- and stereo-defined arylbutadiene **4**. In the case of relatively reactive arenes, Pd(dppe)$(OAc)_2$ gave good selectivity in the presence of a smaller amount of TFA. Pd(dppm)$(OAc)_2$ was superior for less reactive arenes, giving higher selectivity in the presence of a larger amount of TFA. Further investigation on catalysts and extension of the scope are now in progress.



Scheme 1 A possible mechanism.

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