Palladium-catalyzed Cross-coupling of Benzylic Carbonates with Organostannanes

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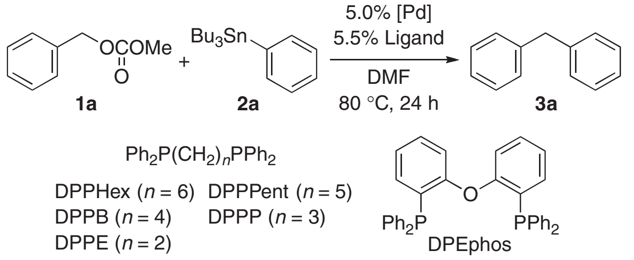
The cross-coupling of benzylic carbonates with arylstannanes proceeded in the presence of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$–DPPPent catalyst, affording the desired diarylmethanes in good yield.

Palladium-catalyzed cross-coupling of organohalides with organostannanes, i.e. the Kosugi–Migita–Stille coupling, is one of the reliable methods for selective formation of carbon–carbon bond in organic synthesis.[1] The catalytic reaction often employs sulfonates in place of halides as leaving groups on electrophilic substrates.[2] Use of carboxylate leaving group, which is easier to handle and more accessible than sulfonate, has been unexplored except allylic substrates.[3–5] Recently, we have devoted our efforts to develop the palladium-catalyzed reactions involving benzylic carbonates.[6,7] As a part of the research program, we report herein the use of benzylic carbonates as electrophilic substrates in the Kosugi–Migita–Stille coupling.[8–11]

In our initial attempt, a mixture of benzyl methyl carbonate (**1a**) with tributylphenylstannane (**2a**) was treated in DMF at 80 °C with 5 mol % of the palladium complex generated in situ from $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and DPPPent, which was the most effective catalyst for the Suzuki–Miyaura coupling of **1a**.[7a] The resulting mixture afforded diphenylmethane (**3a**) in 65% yield at 24 h (Table 1, Entry 1). As the result of further screening of phosphine ligands, the catalytic cross-coupling was found to proceed in moderate yield by using the bisphosphines possessing larger bite angle than DPPP (Entries 2–4). In contrast, DPPP- or DPPE-ligated palladium failed to catalyze the cross-coupling of **1a** with **2a** (Entries 5 and 6). To our surprise, a certain level of production of **3a** was observed in the reaction using triphenylphosphine–palladium catalyst, which was ineffective for the corresponding Suzuki–Miyaura coupling (Entry 7).[7a] However, the reaction of **1a** scarcely proceeded with sterically congested and electron-donating monophosphines, which are regarded as better ligands for many palladium-catalyzed cross-couplings than triphenylphosphine in general (Entries 8 and 9).[12] The palladium catalysis is sensitive to palladium catalyst precursor. Use of $Pd(dba)_2$ or $Pd(OAc)_2$ in place of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ resulted in little or no formation of **3a** (Entries 10 and 11). The catalytic reaction worked well in DMSO as well as in DMF (Entry 12). Use of a less polar solvent such as THF, 1,4-dioxane, and toluene caused significant decrease of the yield of **3a** (Entries 13–15). Bidentate bisphosphines affording **3a** in over 50% yield in the above ligand screening were reexamined on the reaction with 1% palladium loading. DPPPent gave the highest yields (69%) of the desired coupling product. The yield of **3a** was improved to 78% when the molar ratio of **1a** to **2a** was changed from 1:1.2 to 1.5:1 (Table 2, Entry 1).

As shown in Table 2, the cross-couplings of various benzylic carbonates **1** and organostannanes **2** were attempted under the reaction conditions optimized above. The yield of the cross-coupling product was remarkably enhanced by the electron-donating methoxy group of **1c** (Entry 3). Electron-withdrawing substituents did not disturb the formation of **3** significantly (Entry 4). Chloro group, which is possible to undergo an oxidative addition to palladium(0), was compatible with the catalytic cross-coupling, affording diarylmethane **3e** in 73% yield (Entry 5). In contrast, *p*-bromobenzyl carbonate **1e′** selectively reacted with **2a** at its bromo group and was transformed into biaryl **4** in 87% yield (Scheme 1). The observations indicate that the benzylic C–O bond of **1** possesses the reactivity between aryl C–Cl and C–Br bond. The *o*-methyl group of **1f** did not hinder the catalytic reaction (Entry 6). Benz-fused benzylic carbonates, **1g** and **1h**, worked as good electrophilic substrates in the cross-coupling with **2a** (Entries 7 and 8). However, use of benzylic substrates bearing a coordinative functional group, such as nitro or alkoxycarbonyl, resulted in no production of the desired diarylmethanes. Electronic property of the para substituent of aryl-

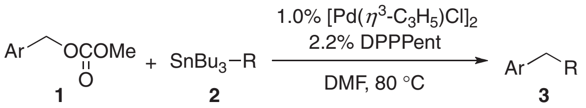
Table 1. Effect of phosphine ligand on the reaction of **1a** with **2a**[a]



Entry	[Pd]	Ligand	Solvent	Yield/%[b,c]
1	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPPent	DMF	65 (69)
2	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPEphos	DMF	64 (45)
3	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPHex	DMF	56 (56)
4	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPB	DMF	80 (56)
5	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPP	DMF	0
6	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPE	DMF	1
7[d]	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	PPh_3	DMF	31
8[d]	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	P(*o*-Tol)$_3$	DMF	0
9[d]	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	P(*t*-Bu)$_3$	DMF	0
10	$Pd(dba)_2$	DPPPent	DMF	4
11	$Pd(OAc)_2$	DPPPent	DMF	0
12	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPPent	DMSO	73 (51)
13	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPPent	THF	27
14	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPPent	dioxane	28
15	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	DPPPent	toluene	18

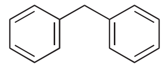
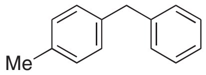
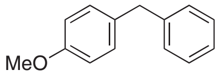
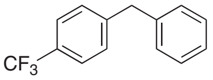
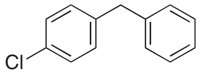
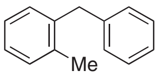
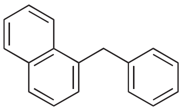
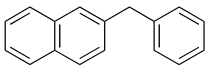
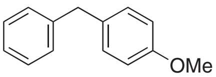
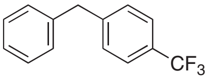
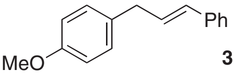
[a]Reactions were conducted in DMF at 80 °C for 24 h. The molar ratio of **1a**:**2a**:[Pd]:ligand was 20:24:1.0:1.1 unless otherwise noted. [b]GC yield (average of two runs). [c]The yields in parentheses were GC yields at 72 h in the reaction with 1.0% catalyst loading. [d]The molar ratio of [Pd]:ligand was 1.0:2.2.

Table 2. Palladium-catalyzed cross-coupling of benzylic carbonates **1** with organostannanes **2**[a]



1b: Ar = 4-MeC_6H_4
1c: Ar = 4-$MeOC_6H_4$
1d: Ar = 4-$CF_3C_6H_4$
1e: Ar = 4-ClC_6H_4
1f: Ar = 2-MeC_6H_4
1g: Ar = 1-naphthyl
1h: Ar = 2-naphthyl

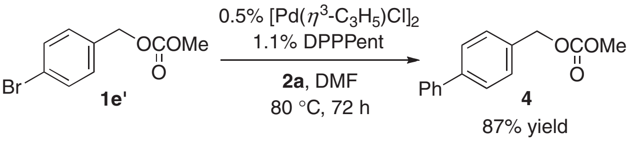
2b: R = 4-$MeOC_6H_4$
2c: R = 4-$CF_3C_6H_4$
2d: R = (*E*)-PhCH=CH

Entry	1	2	Time/h	Product 3	Yield/%[b]
1[c]	**1a**	**2a**	72	 **3a**	78
2	**1b**	**2a**	72	 **3b**	66
3[c]	**1c**	**2a**	72	 **3c**	99
4	**1d**	**2a**	24	 **3d**	64
5[c]	**1e**	**2a**	72	 **3e**	73
6	**1f**	**2a**	72	 **3f**	70
7[c]	**1g**	**2a**	24	 **3g**	86
8[c]	**1h**	**2a**	24	 **3h**	88
9	**1a**	**2b**	72	 **3c**	70
10	**1a**	**2c**	72	 **3d**	78
11	**1c**	**2d**	36	 **3i**	96

[a]Reactions were conducted in DMF at 80 °C. The molar ratio of **1**:**2**:[Pd(η^3-C_3H_5)Cl]$_2$:ligand was 75:50:0.5:1.1 unless otherwise noted. [b]Isolated yield. [c]Reactions were conducted with 1% catalyst loading.

stannanes scarcely affected the reaction rate of the catalytic reaction. As with arylstannanes, (*E*)-alkenylstannane **2d** reacted with benzyl carbonate **1c**, giving (*E*)-allylbenzene **3i** in high yield without any undesirable alkene migration (Entry 11).

In this paper, we have proved benzylic carbonates useful as electrophilic substrates for the Kosugi–Migita–Stille coupling. The palladium complex prepared from [Pd(η^3-C_3H_5)Cl]$_2$ and DPPPent ligand was the most effective catalyst for the catalytic cross-coupling.[13]



Scheme 1. Reaction of *p*-bromobenzyl carbonate **1e**′ with **2a**.

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