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Suzuki-type cross-coupling reaction of pentavalent triarylantimony diacetates with arylboronic acids without a base

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Abstract—Novel base-free Suzuki-type cross-coupling reaction by the use of triarylantimony diacetates and arylboronic acids in the presence of $Pd(PPh_3)_4$ catalyst led to the formation of biaryl derivatives in moderate to excellent yields. The reaction is applicable to a variety of arylboronic acids bearing base-sensitive functional groups.

The Suzuki–Miyaura cross-coupling reaction is one of the most versatile and utilized reactions for carbon–carbon bond formation, in particular for the synthesis of biaryls.[1] In these reactions, however, it is inevitable to add a stoichiometric or excess amount of bases for smooth transformation, which makes it difficult to apply the reaction to base-sensitive substrates and, moreover, the formation of an equivalent amount of waste salts is unavoidable. Consequently, the development of transition metal-catalyzed cross-coupling reactions of organoboron compounds without bases has been a challenging and urgent issue.[2,3] On the other hand, transition metal-catalyzed coupling reaction by the use of organoantimony compounds has recently been the focus of attention. Among these compounds, pentavalent triarylantimony dichloride and diacetate were known to be effective in carbon–carbon bond formation such as Heck-,[4] Stille-,[5] and Hiyama-type[6] cross-coupling reactions. We have recently reported that the reaction of organoantimony(III) compounds with acid halides, aryl halides, and vinyl halides in the presence of Pd-catalyst resulted in cross-coupling reaction to give alkynyl ketones, diarylacetylenes, and enyne compounds.[7] We present here a novel base-free Pd-catalyzed Suzuki-type cross-coupling reaction of organoantimony(V) compounds, triphenylantimony diacetate, with a variety of arylboronic acids.

We initially focused our attention on the determination of the best experimental conditions for the cross-coupling of organoantimony compounds **1a**–**c** with *p*-methylphenylboronic acid **3a** without any bases. The results including the search for active substrates and suitable catalysts for the reaction are summarized in Table 1. The progress of the reaction was monitored by gas–liquid chromatography (GLC) and the reaction time was determined when the yields of products **4a** and **5** show a maximum value because it is impossible to detect the disappearance of the starting material by thin-layer chromatography (TLC) or GLC. First, we performed the reaction of **3a** (3 equiv) and antimony derivatives, such as triphenylantimony **1a**, triphenylantimony dichloride **1b**, and diacetate **1c**,[4b] to compare the reactivity using 5 mol % of $Pd(OAc)_2$ as a catalyst in 1,4-dioxane at 60 °C (entries 1–3). The expected cross-coupling compound **4a** was obtained in a good yield along with homo-coupling product **5** when **1c** was employed as a substrate. In this reaction, one of the three phenyl groups on antimony is involved in the carbon–carbon bond formation. On the other hand, pentavalent dichloride **1b** was found to be less reactive toward the cross-coupling reaction and the major product was biphenyl **5** formed by the homo-coupling reaction of phenyl group on **1b**. It is also known that pentavalent triarylbismuth dichloride **2b** and diacetate **2c** were effective reagents as a pseudo-halogen compound in carbon–carbon

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Keywords: Base-free; Suzuki-type cross-coupling; Antimony; Triphenylantimony diacetate; Palladium; Biaryl.

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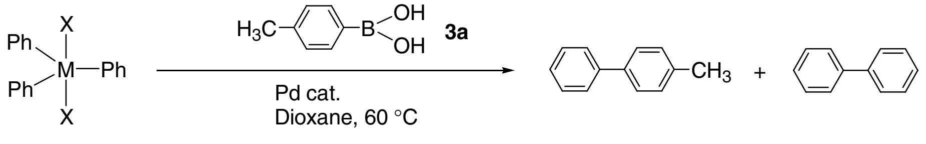
Table 1. Palladium-catalyzed Suzuki-type cross-coupling reaction of organo-antimony **1** and -bismuth **2** compounds with 4-methylphenyllboronic acid **3a**[a]



1: M = Sb
2: M = Bi
4a
5

Entry	Substrate	M	X	Pd cat.	Time (h)	Yield[b,c]	
						4a	**5**
1	**1a**	Sb(III)	—	$Pd(OAc)_2$	12	ND	ND
2	**1b**	Sb(V)	Cl	$Pd(OAc)_2$	12	8	84
3	**1c**	Sb(V)	OAc	$Pd(OAc)_2$	12	92	6
4	**2a**	Bi(III)	—	$Pd(OAc)_2$	12	6	26
5	**2b**	Bi(V)	Cl	$Pd(OAc)_2$	12	3	122
6	**2c**	Bi(V)	OAc	$Pd(OAc)_2$	12	39	97
7	**1c**	Sb(V)	OAc	$PdCl_2$	12	60	3
8	**1c**	Sb(V)	OAc	$PdCl_2(PPh_3)_2$	12	95	2
9	**1c**	Sb(V)	OAc	$Pd(dba)_2$	12	73	4
10	**1c**	Sb(V)	OAc	$Pd(PPh_3)_4$	6	98 (94)[f]	ND (0)
11[d]	**1c**	Sb(V)	OAc	$Pd(PPh_3)_4$	36	91	5
12[e]	**1c**	Sb(V)	OAc	$Pd(PPh_3)_4$	36	95	ND
13	**1c**	Sb(V)	OAc	None	36	ND	ND

[a] Compound **1** or **2** (0.5 mmol), **3a** (1.5 mmol), Pd cat. (5 mol %).

[b] The yields of **4a** and **5** were determined by GLC using tetradecane or octadecane as an internal standard, and the yield 100% correspond to the involvement of one phenyl group on **1** or **2**.

[c] ND: not detected.

[d] Compound **3a** (0.75 mmol).

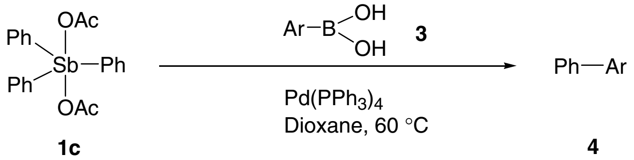
[e] Pd cat. (1 mol %).

[f] Isolated yield.

bond formation such as Heck-[8] and Stille-type[9] cross-coupling reactions. However, the homo-coupling reaction took precedence over the expected cross-coupling reaction when bismuth agents **2a–c** were used instead of antimony reagents in the present reaction (entries 4–6). These results showed that the reactivity of the metal reagents was considerably affected by not only the valence [(III), (V)] and the kind (Sb, Bi) of the constitutive metal, but also the substituent (Cl, OAc) on the metal. Next, several available palladium catalysts were also screened by means of the reaction between **1c** and **3a** (entries 3, 7–10). All catalysts examined here afforded **4a** in good yields. Among these, $Pd(PPh_3)_4$ appeared to be the best catalyst for this reaction in terms of the yield (98%) of the cross-coupling product **4a** and reaction time (6 h), and no homo-coupling product **5** was formed (entry 10). When the reaction was carried out at rt, **4a** was formed in 41% yield after 24 h. We also tested the reaction without a palladium catalyst, but the formation of coupling products **4a** and **5** was not detected by GLC analysis (entry 13). When loading of boron reagent (1.5 equiv, entry 11) and catalyst (1 mol %, entry 12) was decreased, prolonged time was required to finish the reaction and the formation of **5** was observed in the former reaction. Utilization of other solvents such as toluene (44%) and 5:1 mixture of dioxane–water (5%) gave inferior results under the same reaction conditions (60 °C, 6 h). Consequently, the best result was obtained when **1c** was treated with **3a** (3 equiv) by the use of $Pd(PPh_3)_4$ (5 mol %) in 1,4-dioxane at 60 °C. Similar reactions by the use of tri(*p*-tolyl)antimony diacetate $[(p\text{-}CH_3C_6H_4)_3Sb(OAc)_2]$[4b] and tri(*p*-chlorophenyl)antimony diacetate $[(p\text{-}ClC_6H_4)_3Sb(OAc)_2]$[10] with **3a** afforded 4,4′-dimethylbiphenyl (96%) and 4-chloro-4′-methylbiphenyl **4f** (93%) in good yields (60 °C, 6 h), respectively.

The scope of the present coupling was evaluated by investigating the reaction of **3a** with a variety of arylboronic acids **3b–o**.[11] The reaction was carried out for 6 h for **3b–d** bearing an electron-donating group and for 18 h for **3f–m** having an electron-withdrawing group, because the reaction rate was sensitive to the electronic nature of the acids and the decrease of **1c** in the course of the reaction could not be monitored by TLC and GLC as noted above (Table 2). Thus, **3b–d** afforded the corresponding cross-coupling product **4b–d** in good yields in a shorter reaction time (6 h, entries 1–3), while **3f–m** gave **4f–m** in satisfactory yields in a longer reaction time (18 h, entries 5–12). The results also showed that the present base-free reaction allows employment of acids **3i,j**, and **3l** with a relatively base-sensitive group. Moreover, the reaction can be applied to the cross-coupling-active substrate, 2-bromophenylbronic acid **3g**, whose carbon–bromine bond remained intact (entry 6). Additionally, the reaction of heterocyclic boronic acids **3n** and **3o** gave the corresponding biaryls **4n** and **4o**, respectively (entries 13 and 14). Unfortunately, sterically hindered 2,6-dimethylphenylboronic acid and basic 4-pyridylboronic acid did not afford cross-coupling products.

Table 2. Base-free palladium-catalyzed Suzuki-type cross-coupling reaction of triphenylantimony diacetate **1c** with arylboronic acids **3**[a]



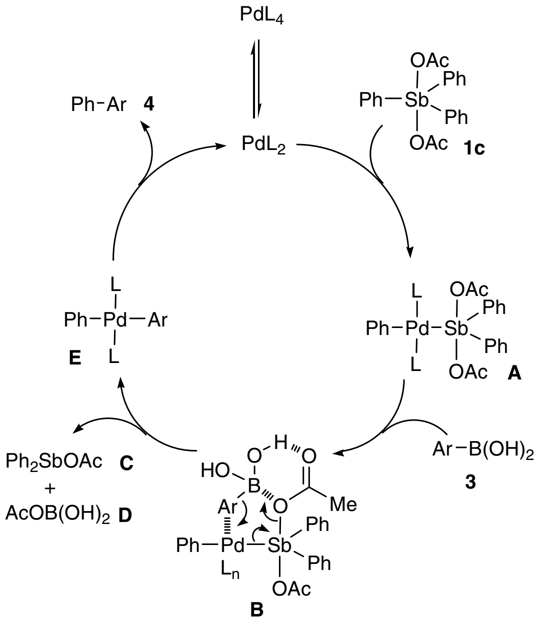
Entry	ArB(OH)$_2$	Time (h)	Product	Yield[b] (%)
1	3,4-(Methylenedioxy)phenyl **3b**	6	**4b**	95
2	4-*t*-Butylphenyl **3c**	6	**4c**	96
3	4-Methoxyphenyl **3d**	6	**4d**	92
4	1-Naphthyl **3e**	6	**4e**	97
5	4-Chlorophenyl **3f**	18	**4f**	98 (55)[c]
6	2-Bromophenyl **3g**	18	**4g**	95
7	4-Formylphenyl **3h**	18	**4h**	82
8	4-(Methoxycarbonyl)phenyl **3i**	18	**4i**	85
9	4-Acetylphenyl **3j**	18	**4j**	88
10	4-(Trifluoromethyl)phenyl **3k**	18	**4k**	83
11	4-Cyanophenyl **3l**	18	**4l**	71 (32)[c]
12	4-Nitrophenyl **3m**	18	**4m**	65 (30)[c]
13	2-Benzothienyl **3n**	6	**4n**	96
14	2-Benzofuryl **3o**	6	**4o**	88

[a] Compound **1** (0.5 mmol), **3a** (1.5 mmol), Pd(PPh$_3$)$_4$ (5 mol %).

[b] Isolated yield (the yield 100% correspond to the involvement of one phenyl group on **1c**).

[c] Reaction time, 6 h.

A plausible mechanism of the present base-free Suzuki-type cross-coupling reaction is depicted in Scheme 1. As reported by Gushchin and co-workers,[4b] the initial step of this reaction should involve oxidative addition of the Ar–Sb bond of **1c** onto the L$_2$Pd(0) species. Taking into account the results that the reaction does not need a base as an additive for the activation of boronic acid, the formation of intermediate **B** with B- - -O and OH- - -O inter-coordination is anticipated from **A** and boronic acids **3**. In intermediate **B**, the boronic acid moiety should be activated by the acetoxy group on the antimony by constructing a six-membered ring **B**.[12] This interpretation should be also supported by the following facts. The antimony compounds (Ph$_3$Sb, Ph$_3$SbCl$_2$) without an acetoxy group on the antimony are ineffective (Table 1, entries 1 and 2). In addition, the arylboronic ester, 5,5-dimethyl-2-*p*-tolyl-1,3,2-dioxaborinane which has no ability to form the six-membered intermediate **B** was ineffective in the present reaction under the same conditions.[13] Pentavalent organoantimony(V) compounds were well known to be reduced to Sb(III) compounds with ease.[14] As a result, diorganopalladium complex **E** thus formed via intermediate **B** undergoes reductive elimination to give coupling products **4** and reproduces the Pd(0) species.



Scheme 1. Proposed mechanism.

In summary, we have found that triphenylantimony diacetate is an efficient substrate in palladium-catalyzed cross-coupling reactions with arylboronic acids, which can be conducted under mild conditions without any bases. Various boronic acids having electron-donating or -withdrawing functional groups afforded the corresponding cross-coupling product in 65–98% yields. Organoantimony(V) compound **1** is a new class of pseudo-halogen compound for base-free Suzuki-type cross-coupling reaction. Synthetic application of this reaction and work on the detailed reaction mechanism are in progress.

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10. *Preparation and structural data of tri(p-chlorophenyl)antimony diacetate*: A mixture of tri(*p*-chlorophenyl)antimony (2.0 mmol) and (diacetoxyiodo)benzene (2.2 mmol) in dichloromethane (CH_2Cl_2: 10 mL) was stirred for 24 h at rt. The solvent was concentrated under reduced pressure to a small volume. Hexane (10 mL) was added and the solution was stirred in an ice bath. The solid was filtered and recrystallized from a mixture of CH_2Cl_2–hexane to give tri(*p*-chlorophenyl)antimony diacetate 0.81 g (71%) as colorless prisms, mp 117–120 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 1.83 (6H, s), 7.46 (6H, d, $J = 8.7$ Hz), 7.88 (6H, d, $J = 8.7$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7 (s), 129.4 (d), 135.0 (d), 137.6 (s, ×2), 176.8 (s); MS (EI) *m*/*z*: 515 $(M-OAc)^+$; IR (KBr): 1633 cm^{-1} (C=O). Anal. Calcd for $C_{22}H_{18}O_4Cl_3Sb$: C, 45.99; H, 3.16. Found: C, 46.08; H, 3.29.
11. *Typical experiment*: A solution of triphenylantimony diacetate **1c** (0.5 mmol), arylboronic acids **3** (1.5 mmol), and tetrakis(triphenylphosphine)palladium (0.025 mmol) in 1,4-dioxane (3 mL) was heated at 60 °C for 6–18 h under an argon atmosphere. After dilution with ether (40 mL) and water (20 mL), the reaction mixture was separated and the aqueous layer was extracted with ether (20 mL). The combined organic layer was washed with water, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude residue was purified by short column chromatograph on silica gel with hexane (for **4a**,**c**,**e**–**g**) or hexane–CH_2Cl_2 (for **4b**,**d**,**h**–**o**) to give biaryl derivatives **4**. The structure of the products was confirmed by comparison of the NMR and MS spectral data with that in the literature.
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