An Efficient Heterogeneous Pd Catalyst for the Suzuki Coupling: Pd/Al_2O_3

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Pd^{II}-loading alumina catalyst, which is simply prepared through impregnation of γ–alumina with $Pd(OAc)_2$ followed by calcination in the air, shows a high catalytic activity for the Suzuki coupling of aryl bromides with arylboronic acids under phosphine ligand-free conditions. Only 0.25 mol % of palladium is sufficient for the promotion of the couplings in ethanol.

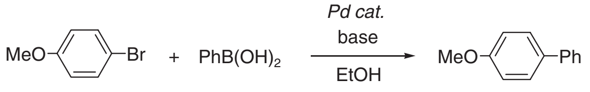
The Suzuki coupling,[1] which is one of the most commonly used methods for biaryls synthesis, has conventionally been performed by homogeneous palladium catalysts in the presence of various phosphine ligands. Such catalysts are highly active for the coupling, but the separation of the catalyst components from products is often a troublesome operation. By contrast, heterogeneous palladium catalysts are much easier upon the separation. Among various immobilized Pd catalysts, palladium on activated carbon (Pd^0/C and Pd^{II}/C) is readily available and recognized highly active.[2] Generally, more than 2–3 mol % of Pd are employed for Pd/C-catalyzed reactions except a few examples,[3] and the catalysis of Pd/C is sensitive to the air, reaction solvents, and reaction temperatures.[4]

Palladium particles in Pd/C, which are finely but weakly fixed on activated carbon, are apt to be reduced to form less active palladium agglomerates (palladium black) under harsh conditions. To suppress such agglomeration, porous oxides such as Al_2O_3 and SiO_2 which strongly interact with palladium would be favored as a Pd support. Such heterogeneous palladium catalysts have been employed not only for selective hydrogenation of olefins,[5] but also for a C–C bond formation like the Heck reaction.[6] Recently, Hell et al. reported the Suzuki coupling with palladium loaded on magnesium–lanthanum mixed oxides.[7] Here, we report that palladium-loading alumina, Pd/Al_2O_3, is a highly effective catalyst for the Suzuki coupling.

The Pd/Al_2O_3 catalyst was prepared via the impregnation of three kinds of γ–Al_2O_3 (ALO-2, ALO-3, and ALO-7)[8] with $Pd(OAc)_2$ in toluene followed by calcination in the air at 573 K. One wt % of palladium to the alumina was loaded. The color of the impregnated catalyst was light orange, and quite different from that of palladium black derived from the calcination of $Pd(OAc)_2$ without alumina, implying that the palladium species on Al_2O_3 existed mainly in the Pd^{II} oxidation state, which was also confirmed by XPS. X-ray diffraction of the Pd/Al_2O_3 did not match that of commercial Pd black as well as PdO. Nitrogen adsorption analysis of the Pd/Al_2O_3 indicated the pore structure of the parent γ–alumina was almost maintained.

We performed the coupling of 4-bromoanisole (**1a**) with phenylboronic acid (**2a**) in EtOH in the presence of concomitant base under phosphine ligand-free conditions (Table 1). Among inorganic bases (K_2CO_3, Cs_2CO_3, KF, CsF, K_3PO_4, and NaOH), potassium fluoride (KF) was found the best (Entry 3), while an organic base, NEt_3, gave a very low yield (Entry 7).[9]

Table 1. Suzuki coupling with various bases and catalysts[a]



1a (1 mmol) **2a** (1.5 mmol) **3a**

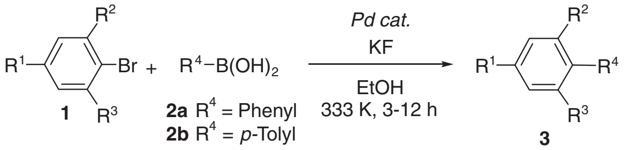
Entry	Catalyst	Base /mmol	Temp /K	Time /h	Yield[b] /%
1	Pd/ALO-7	K_2CO_3 (2)	333	3	79
2	Pd/ALO-7	Cs_2CO_3 (2)	333	3	89
3	Pd/ALO-7	KF (4)	333	3	96
4	Pd/ALO-7	CsF (4)	333	3	93
5	Pd/ALO-7	K_3PO_4 (1.3)	333	3	89
6	Pd/ALO-7	NaOH (4)	333	3	15
7	Pd/ALO-7	Et_3N (4)	333	3	8
8	Pd/ALO-7	none	333	3	0
9[c]	Pd/ALO-2	KF (4)	318	2.5	73
10[c]	Pd/ALO-3	KF (4)	318	2.5	43
11[c]	Pd/ALO-7	KF (4)	318	2.5	59
12[c]	Pd/C[d]	KF (4)	318	2.5	31
13[c]	$Pd(OAc)_2$	KF (4)	318	2.5	35

[a]The reaction was carried out with 1.0 mmol of **1a**, 1.5 mmol of **2a**, and 0.005 mmol of palladium-including catalyst in 5 mL of ethanol. [b]Isolated yield. [c]A smaller amount of palladium (0.0015 mmol) was used. [d]10 wt % Pd K-Type from N. E. Chemcat was used.

More interestingly, the catalysis of Pd/Al_2O_3 was strongly influenced by the impurities included in the alumina supports: Acidic ALO-2 containing sulfate ions was found more effective than basic ALO-3 having Na ions and neutral ALO-7 (Entries 9–11). And the catalysis of Pd/ALO-2 was obviously superior to that of Pd^0/C and $Pd(OAc)_2$ (Entries 9, 12, and 13). Examining solvent effects, we found alcoholic solvents, especially ethanol, are suitable for the reaction. In water, the reaction also proceeded, but the yield was much lower due to insolubility of reactants **1a** and **2a** in water.

Using KF as a base, we then applied the Pd/ALO-2 catalyst to various couplings of aryl bromides with arylboronic acids in EtOH (Table 2). Most of the couplings with electron-rich and poor aryl bromides proceeded well to yield the corresponding biaryls **3** in good to quantitative yields by use of only 0.25 mol % Pd. Only 2-nitrobenzene gave an unsatisfactory result, probably due to the strong coordination of a nitro group to palladium. In the coupling with 4-methoxybromobenzene (**1a**), the use of 0.01 mol % palladium promoted the reaction with a turnover number (TON) of 8400 (Entry 1). We also examined the catalysis of $Pd(OAc)_2$ and commercial Pd/C under the same conditions. Toward electron-rich aryl bromides, these catalysts were less effective. Especially, with $Pd(OAc)_2$, rapid reduction

Table 2. Suzuki coupling of aryl bromides with arylboronic acids[a]



Entry	1	R^1	R^2	R^3	2	Time/h	Catalyst	Yield/%[b]	
1	**1a**	MeO	H	H	**2a**	3	Pd/ALO-2	**3a**	97 (84[c])
2							Pd/C[d]		50
3							Pd(OAc)$_2$		31
4	**1b**	Me	H	H	**2a**	3	Pd/ALO-2	**3b**	97
5							Pd/C[d]		68
6							Pd(OAc)$_2$		67
7	**1c**	H	OMe	H	**2a**	6	Pd/ALO-2	**3c**	73
8							Pd/C[d]		28[e]
9							Pd(OAc)$_2$		29[e]
10	**1d**	H	Me	Me	**2a**	12	Pd/ALO-2	**3d**	64[e]
11							Pd/C[d]		trace[e]
12							Pd(OAc)$_2$		17[e]
13	**1e**	H	Me	H	**2a**	3	Pd/ALO-2	**3e**	96
14	**1f**	H	H	H	**2a**	3	Pd/ALO-2	**3f**	95
15	**1g**	CN	H	H	**2a**	3	Pd/ALO-2	**3g**	96
16	**1h**	H	NO$_2$	H	**2a**	3	Pd/ALO-2	**3h**	<10[e]
17	**1i**	Ac	H	H	**2a**	3	Pd/ALO-2	**3i**	96
18	**1j**	CF$_3$	H	H	**2a**	3	Pd/ALO-2	**3j**	99
19	**1k**	H	CF$_3$	H	**2a**	3	Pd/ALO-2	**3k**	98
20	**1l**	F	F	H	**2a**	3	Pd/ALO-2	**3l**	96
21	**1m**	CO$_2$H	H	H	**2a**	3	Pd/ALO-2	**3m**	82
22	**1n**	OH	H	H	**2a**	3	Pd/ALO-2	**3n**	98
23	**1f**	H	H	H	**2b**	3	Pd/ALO-2	**3b**	96

[a]Carried out with 1.0 mmol of **1**, 1.2 mmol of **2**, and 4 mmol of KF in the presence of palladium (0.0025 mmol) in 5 mL of ethanol, for 3 h. [b]Isolated yield. [c]0.0001 mmol (0.01 mol %) of Pd/ALO-2 was used. TON = 8400. [d]10 wt % Pd K-Type from N. E. Chemcat was used. [e]NMR yield.

occurred and the deposition of palladium black was observed.

In order to obtain the active Pd catalyst, the calcination process is requisite: The Pd/ALO-2 catalyst which had been prepared via loading Pd(OAc)$_2$ on the alumina followed by the thermal treatment in the air was highly active, while a simply loading catalyst of Pd(OAc)$_2$/ALO-2 which had not underwent the calcination only showed as low catalytic activities as unloaded Pd(OAc)$_2$. The tight interaction of the oxide anions in ALO-2 with Pd^{II} ions upon the calcination seems to be indispensable for an efficient catalyst precursor.

The strong coordination of the alumina to Pd^{II} would also enhance the stabilities of the Pd species in the catalytic system. To compare the stability between Pd/ALO-2 and Pd(OAc)$_2$, we immersed the two catalysts in an EtOH solution of **1a** and **2a** in the absence of KF for a specified period (1 or 6 h) followed by addition of KF: Although no coupling occurred without KF, the reaction started to yield **3a** just upon addition of KF. No change in the activities of Pd/ALO-2 was observed after the catalyst was immersed in EtOH for 1 and 6 h: 90% yield of **3a** for 1 h and 90% yield for 6 h. By contrast, Pd(OAc)$_2$ gradually lost its activities depending on the time in EtOH in the absence of KF: 20% of **3a** for 1 h and 14% for 6 h.

We compared the amount of Pd leaking in EtOH for Pd/ALO-2 and commercial Pd/C during the reaction of **1a** with **2a**. After the catalysts were filtered off, ICP analysis of the EtOH solutions showed that less than 3 wt % of Pd was contained in the solutions, indicating that the Pd leakage took place to almost the same extent for the both Pd-loading catalysts. When the filtered Pd/ALO-2 was reused in the same reaction, the yield of **3a** was 80%.

In summary, we discovered that the Pd/ALO-2 catalyst prepared by the simple impregnation–calcination of Al$_2$O$_3$ with Pd(OAc)$_2$ was an effective catalyst for the Suzuki coupling using aryl bromide. The feature of the catalyst is that 1) a very low amount of Pd is sufficient for the coupling, 2) there is no need to use phosphine-based organic additives, 3) the coupling smoothly proceeds in pure EtOH without the aid of water, and 4) since Pd^{II} species are loaded on the alumina support, Pd/ALO-2 is stabilized and safe to handle in the air.

The authors are indebted to Dr. Kouhei Okitsu of the University of Tokyo for his help in XPS analysis. This study was financially supported by Development of Microspace and Nanospace Reaction Environment Technology for Functional Materials Project of NEDO, Japan.

This article is dedicated to the late Professor Yoshihiko Ito.

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8 The alumina samples were supplied by the Catalysis Society of Japan, and contain the following impurities: ALO-2: 0.03% Fe$_2$O$_3$, 0.22% SiO$_2$, 0.04% Na$_2$O, 0.50% SO$_4^{2-}$; ALO-3: 0.01% Fe$_2$O$_3$, 0.01% SiO$_2$, 0.3% Na$_2$O, 0.01% TiO$_2$; ALO-7: $<$ 0.01% Fe$_2$O$_3$, $<$ 0.1% SiO$_2$, $<$ 0.0015% Na$_2$O; $<$ 0.1% Cl$^-$.
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