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Palladium-Catalyzed Cross-Coupling Reaction of Triarylbismuths with Aryl Halides and Triflates

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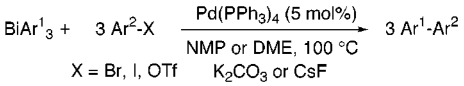
ABSTRACT

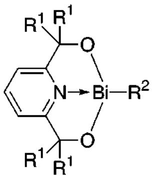


$$\mathrm{BiAr^1_3} + 3\ \mathrm{Ar^2\text{-}X} \xrightarrow[\text{NMP or DME, 100 °C}]{\mathrm{Pd(PPh_3)_4}\ (5\ \text{mol\%})} 3\ \mathrm{Ar^1\text{-}Ar^2}$$

X = Br, I, OTf $\quad$ K_2CO_3 or CsF

Palladium-catalyzed cross-coupling reaction of triarylbismuths with aryl bromides, iodides, and triflates proceeded efficiently in the presence of K_2CO_3 or CsF.

Transition metal-catalyzed cross-coupling reaction of organometallic compounds with organic halides and triflates is one of the most important reactions for making C−C bonds.[1] Although various organometallic compounds such as organotin, -boron, -silicon, -zinc, and -magnesium compounds have been successfully utilized for the cross-coupling reactions, organobismuth compounds have not been well studied.[2,3] Since bismuth is known to be a low-level toxic element, organobismuth compounds are potentially useful candidates for environmentally benign reagents. We have recently demonstrated that organobismuth compounds are actually useful reagents for the palladium-catalyzed cross-coupling reaction with aryl and vinyl triflates by using organobismuth dialkoxides **1**.[4,5] Triarylbismuths are more



1: R^1 = Me, Et, ^{i}Pr
R^2 = Ph, Me

favorable reagents than **1** because they are easier to prepare than the dialkoxides (some triarylbismuths are commercially available), are stable to moisture, and can be handled and stored under air, while **1** are sensitive to moisture. However, triarylbismuths were found to be much less reactive than **1** for the cross-coupling reaction with organic triflates.[4] Here we have examined the effect of additives on the reactivity

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(1) *Metal-Catalyzed, Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998.

(2) Suzuki, H.; Ikegami, T.; Matano, Y. *Synthesis* **1997**, 249. Suzuki, H.; Matano, Y. In *Chemistry of Arsenic, Antimony and Bismuth*; Norman, N. C., Ed.; Blackie Academic & Professional: London, 1998; Chapter 6. Elliott, G. I.; Konopelski, J. P. *Tetrahedron* **2001**, *57*, 5683.

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(4) Rao, M. L. N.; Shimada, S.; Tanaka, M. *Org. Lett.* **1999**, *1*, 1271.

(5) Shimada, S.; Rao, M. L. N.; Tanaka, M. *Organometallics* **2000**, *19*, 931.

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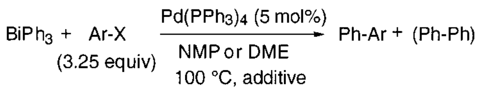
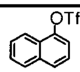
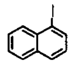
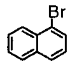
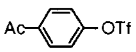
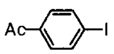
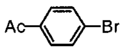
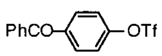
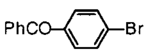
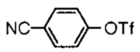
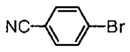
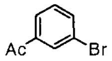
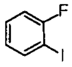
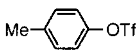
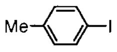
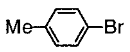
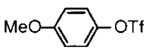
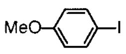
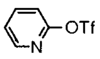
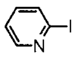
Table 1. Reaction of $BiPh_3$ with Aryl Triflates, Iodides, and Bromides[a]



entry	Ar-X	additive (equiv)	time / h	Ph-Ar[b] / %	Ph-Ph[b] / %
1		no	5	11	9
2		K_2CO_3 (3)	5	92	0
3		no	6	13	12
4		K_2CO_3 (4)	6	85	0
5[c,d]		no	18	2	11
6[c,d]		K_2CO_3 (3)	18	20	15
7[c]		CsF (8)	18	76	5
8		no	5	8	1
9		K_2CO_3 (3)	5	75	2
10		no	6	32	6
11		K_2CO_3 (4)	6	86(86)	0
12		no	6	3	4
13		CsF (8)	6	95	0
14		K_2CO_3 (3)	5	92	2
15		CsF (8)	8	84	0
16		K_2CO_3 (3)	5	quant	0
17		CsF (8)	6	quant	0
18		CsF (8)	6	77	0
19		K_2CO_3 (4)	6	93	7
20		K_2CO_3 (3)	5	0	0
21		K_2CO_3 (4)	16	55	45
22		CsF (8)	18	39	7
23		K_2CO_3 (3)	5	0	0
24		K_2CO_3 (4)	6	26	59
25		K_2CO_3 (3)	5	28	3
26		K_2CO_3 (4)	16	65	10

[a] Unless indicated otherwise, the reaction was performed in NMP for aryl triflates and iodides and in DME for aryl bromides. [b] Yields were determined by GLC analysis of the crude reaction mixture by using hexadecane as an internal standard. Isolated yield is shown in parentheses. [c] 10 mol % of $Pd(PPh_3)_4$ was used. [d] The reaction was performed in NMP.

of triarylbismuths for the cross-coupling reaction and found that K_2CO_3 or CsF remarkably improve the reactivity of triarylbismuths toward aryl halides and triflates. All three of the aryl groups of triarylbismuths can be used for the cross-coupling reaction.

Under reaction conditions suitable for the cross-coupling reaction of **1** with aryl and vinyl triflates ($Pd(PPh_3)_4$ (5 mol %), triflate:$BiPh_3$ = 3.25:1, NMP, 100 °C, 5 h), the reaction of $BiPh_3$ with 1-naphthyl triflate (**2**) gave only 11% of cross-coupled product, 1-phenylnaphthalene (**3**), along with 9% of homo-coupled product, biphenyl (Table 1, entry 1). Even in the case of 4-acetylphenyl triflate, an activated substrate, only 8% of 4-acetylbiphenyl (**4**) was obtained under the same reaction conditions (Table 1, entry 8). However, the addition of 3 equiv (to $BiPh_3$) of K_2CO_3 under identical reaction conditions improved the yield of **3** and **4** to 92% and 75%, respectively. In the reaction of $BiPh_3$ and **2**, smaller amounts of K_2CO_3 largely decreased the yield of **3** (2 equiv, 35%; 1 equiv, 25%). Other additives (amounts of the additives, yield of **3**) such as CsF (4 equiv, 89%), KOAc (4 equiv, 85%), NaOAc (4 equiv, 88%), LiOAc (4 equiv, 85%), and Cs_2CO_3 (3 equiv, 53%) are also effective. $Ni(PPh_3)_4$ and $Pt(PPh_3)_4$ have no or little catalytic activity even in the presence of 4 equiv of K_2CO_3 (0% and 6% yield, respectively).

K_2CO_3 (4 equiv) is also effective on the reaction of $BiPh_3$ with 1-iodonaphthalene and 4′-iodoacetophenone, giving **3** and **4** in 85% and 86% yields, respectively, while only 13% and 32% of **3** and **4** were obtained in the absence of K_2CO_3 (Table 1, entries 3−4 and 10−11). On the other hand, K_2CO_3 (3 equiv) is not very effective in the reaction of $BiPh_3$ with 1-bromonaphthalene and increased the yield of **3** from 2% to 20% (Table 1, entries 5−6). However, this reaction was significantly improved by the combination of CsF as an additive and DME (1,2-dimethoxyethane) as a solvent and gave 76% of **3** (Table 1, entry 7). Cs_2CO_3 (8 equiv) afforded 57% of **3** under identical reaction conditions, while LiOAc, NaOAc, KOAc, KF, Bu_4NF, Bu_4NI, KOtBu, KSCN, and CaF_2 had little or no effect. The performance of other solvents (yield of **3** in parentheses) with 7−8 equiv of CsF is as follows: NMP (59%), MeCN (58%), and 1,4-dioxane (12%).

Table 1 shows a preliminary summary of the scope and limitation of the cross-coupling reaction of $BiPh_3$ with various aryl triflates, iodides, and bromides.[6] Substrates with electron-withdrawing substituents gave cross-coupled products in good to quantitative yields irrespective of the position of the substituents (Table 1, entries 8−19). On the other hand, substrates with electron-donating substituents were considerably less reactive; *p*-tolyl triflate and 4-methoxyphenyl triflate did not react with $BiPh_3$ at all, while 4-iodotoluene and

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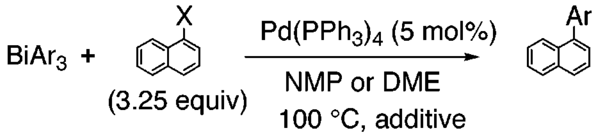
(6) **Representative procedures:** An NMP solution (3 mL) of $BiPh_3$ (55.3 mg, 0.126 mmol), 4′-iodoacetophenone (100 mg, 0.406 mmol), K_2CO_3 (70 mg, 0.51 mmol), and $Pd(PPh_3)_4$ (7.4 mg, 0.0064 mmol) was stirred at 100 °C for 6 h under nitrogen. After cooling, the mixture was analyzed by GLC with hexadecane as an internal standard to determine the yield of the product (4-acetylbiphenyl, 86%). The crude mixture was dissolved in EtOAc (90 mL) and washed with water (10 mL), 10% aqueous HCl (10 mL), water (10 mL), and brine (10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by preparative TLC to give 64 mg (86%) of 4-acetylbiphenyl.

4-iodoanisole gave moderate or low yields of cross-coupled products (Table 1, entries 20−24).

Table 2. Reaction of $BiAr_3$ with 1-Naphthyl Triflate, Iodide, and Bromide[a]



entry	Ar	X	additive (equiv)	time/h	yield[b]/%
1	4-MeC_6H_4	OTf	K_2CO_3 (3)	5	quant
2		I	K_2CO_3 (4)	6	quant
3		Br	CsF (8)	18	76
4	4-FC_6H_4	OTf	K_2CO_3 (3)	5	95
5		I	K_2CO_3 (4)	6	93
6		Br	CsF (8)	18	31

[a] The reaction was performed in NMP for 1-naphthyl triflate and 1-iodonaphthalene and in DME for 1-bromonaphthalene. [b] Yields were determined by GLC analysis of the crude reaction mixture by using hexadecane as an internal standard.

Table 2 provides the results of two representative $BiAr_3$ compounds with electron-donating substituents, Bi(4-$MeC_6H_4)_3$, and electron-withdrawing substituents, Bi(4-$FC_6H_4)_3$, for the reaction with 1-naphthyl compounds. In most cases, similar or better results were obtained than those of $BiPh_3$, while the reaction of Bi(4-$FC_6H_4)_3$ with 1-bromonaphthalene gave a poor yield of cross-coupled product (Table 2, entry 6).

In summary, we have demonstrated that readily available triarylbismuths are useful reagents for the palladium-catalyzed cross-coupling reaction with aryl halides and triflates in the presence of additives such as K_2CO_3 and CsF. Further studies are underway to elucidate the reaction mechanism and to broaden the applicability of organobismuth compounds in organic synthesis.

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