

Palladium catalyzed atom-efficient cross-coupling reactions of triarylbiismuths with aryl iodides and aryl triflates

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Abstract—The atom-efficient cross-coupling of triarylbiismuths with aryl iodides or aryl triflates using catalytic Pd(OAc)₂/PPh₃ and K₃PO₄ as base in DMF at 90 °C to afford the corresponding functionalized biaryls in high yields is reported.

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The cross-coupling reactions of organometallic reagents with electrophilic reagents is an important route for carbon–carbon bond formation. The versatility of these methods have been well exploited in organic synthesis.¹ The cross-coupling of aryl halides and aryl triflates with aryl organometallic reagents is a useful methodology for the synthesis of various functionalized biaryls. Biaryls are important due to their presence in a variety of natural products, pharmaceuticals and in liquid crystalline materials applications. The Suzuki coupling involving organoboron reagents, the Stille coupling using organotin and the Negishi coupling with organozinc reagents are popular methods for biaryl synthesis.^{1,2}

The development of atom-efficient organometallic reagents is important as many of these reagents are used in industrial scale synthesis.² Atom-efficient reagents which can react with more than 1 equivalent of electrophilic reagents such as triarylindiums³ and triarylbiismuths would lower the stoichiometric loading of organometallic reagents. Reactions of triarylbiismuths with electrophilic reagents under metal catalyzed conditions are of present interest.^{4,5} Hence, we report a new palladium catalyzed protocol for the cross-coupling of triarylbiismuths with aryl iodides or aryl triflates for the synthesis of various functionalized biaryls.

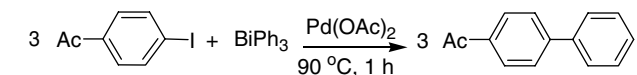
To date, a generalized palladium catalyzed protocol for the cross-coupling of triarylbiismuths with aryl bromides, aryl iodides and aryl triflates is not available.

Keywords: Cross-coupling; Atom-efficient; Triarylbiismuth; Aryl iodides; Aryl triflates.

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Currently, different activators in the form of a base or a fluoride reagent in different solvents are required.^{4b} Thus, in our efforts to establish the cross-coupling reactivity of triarylbiismuths with aryl iodides, an initial screening was performed using Pd(OAc)₂ as catalyst.^{4d} The cross-coupling reaction of *p*-iodoacetophenone

Table 1. Screening conditions^{a,b}



Entry	Solvent	Base	Conv. ^c (%)
1	DMF	NaOAc	57
2	DMF	Ba(OH) ₂	43
3	DMF	DABCO	65
4	THF	K ₃ PO ₄	0
5	CH ₃ CN	K ₃ PO ₄	0
6	Toluene	K ₃ PO ₄	0
7	Dioxane	K ₃ PO ₄	7
8	DME	K ₃ PO ₄	22
9	NMP	K ₃ PO ₄	88
10	DMF	K ₃ PO ₄	94
11	DMF	K ₃ PO ₄	0 ^d
12	DMF	K ₃ PO ₄	53 ^e
13	DMF	None	30
14	DMF	K ₃ PO ₄	87 ^f

^a Conditions: equiv ratios are based on BiAr₃: BiAr₃ (1 equiv), Ar-I (3.5 equiv), Pd(OAc)₂ (0.1 equiv)/PPh₃ (0.4 equiv), base (6 equiv), solvent (3 mL), 90 °C.

^b Homo-coupled biphenyls resulted from triarylbiismuths when no cross-coupling occurred.

^c Based on GC analysis.

^d Control reaction without Pd(OAc)₂.

^e Control reaction without PPh₃.

^f With 4 equiv of K₃PO₄.

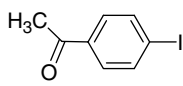
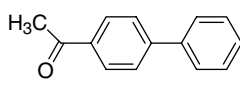
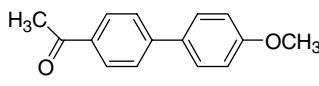
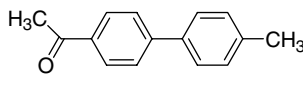
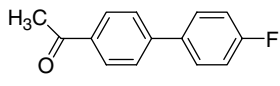
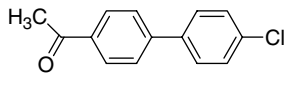
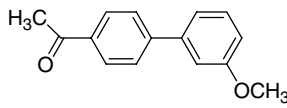
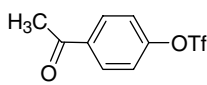
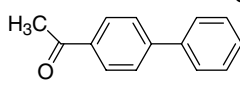
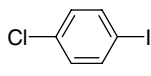
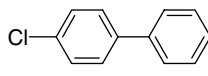
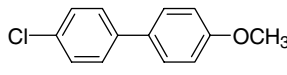
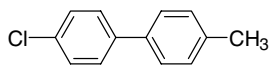
(3.5 equiv) was examined with triphenylbismuth under various conditions, Table 1.

From the initial screening, it was found that bases such as sodium acetate, barium hydroxide and DABCO gave moderate conversion to the cross-coupled product, 4-acetylbiphenyl in DMF (entries 1–3). Further screening with K_3PO_4 as base afforded different extents of conversion in various solvents. In solvents such as tetrahydrofuran, acetonitrile, toluene, dioxane, 1,2-dimethoxyethane, poor or no conversion to a cross-coupled product occurred (entries 4–8). Solvents such as NMP (entry 9) and DMF (entry 10) resulted in high conversion to 4-acetylbiphenyl with K_3PO_4 as base. A control experiment carried out in the absence of $Pd(OAc)_2$ did not afford any cross-coupled product (entry 11). The absence of PPh_3 as ligand gave only a 53% conversion to 4-acetylbiphenyl (entry 12). Further, we have carried out reactions involving varied amounts of base equivalents. It was found that in the absence of K_3PO_4 , only

30% conversion to the product occurred (entry 13). Under similar conditions with K_3PO_4 (4 equiv), an 87% conversion to the cross-coupled product was obtained (entry 14). As the solubility of the base was not good in DMF, we found it was beneficial to use 6 equiv of base to obtain a high cross-coupling conversion between the aryl iodide (3.5 equiv) and triphenylbismuth (1 equiv) at 90 °C in 1 h (entry 10). The present protocol was found to be very efficient, as a high conversion to 4-acetylbiphenyl was obtained in a very short reaction time under relatively mild conditions.^{4b}

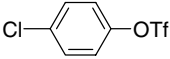
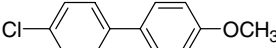
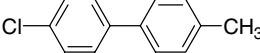
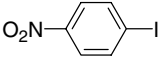
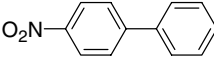
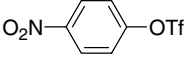
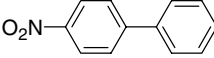
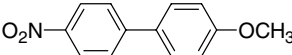
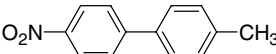
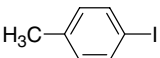
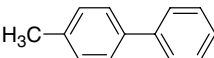
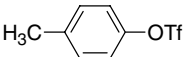
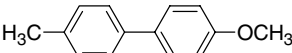
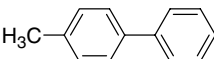
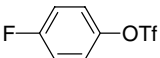
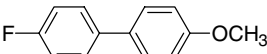
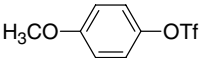
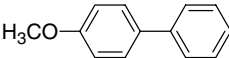
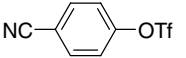
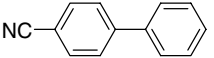
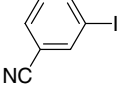
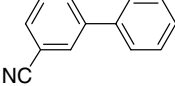
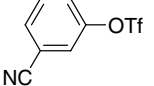
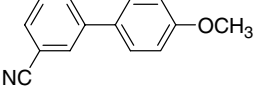
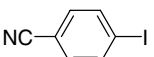
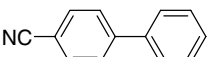
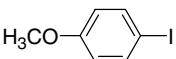
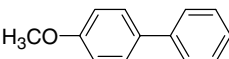
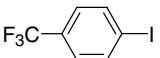
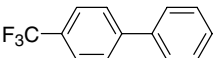
Encouraged by this, further screening of the reactions of various aryl iodides with triarylbiaryls was carried out to determine the generality of the present protocol (Table 2).⁶ As the rate of oxidative addition of aryl triflates to $Pd(0)$ falls in between aryl iodides and aryl bromides, similar cross-coupling reactivity with aryl triflates^{1f} was expected. Hence, we studied the cross-coupling reactivity of aryl triflates under the same conditions⁶ and the

Table 2. Synthesis of various functionalized biphenyls

Entry	Ar-X	BiAr ₃	Product	Yield ^{a,b} (%)
$3 \text{ Ar-X} + \text{Bi}(\text{Ar}_3) \xrightarrow[\text{DMF, 90 } ^\circ\text{C, 1 h}]{\text{Pd(OAc)}_2 \text{ (0.1 equiv), PPh}_3 \text{ (0.4 equiv), K}_3\text{PO}_4 \text{ (6 equiv)}} 3 \text{ Ar-Ar'}$				
1		4-H		91
2		4-OCH ₃		90
3		4-CH ₃		77
4		4-F		91
5		4-Cl		82
6		3-OCH ₃		95
7		4-H		68
8		4-H		77
9		4-OCH ₃		90
10		4-CH ₃		90

(continued on next page)

Table 2 (continued)

Entry	Ar-X	BiAr ₃	Product	Yield ^{a,b} (%)
11		4-OCH ₃		79
12		4-CH ₃		73
13		4-H		94
14		4-H		71
15		4-OCH ₃		73
16		4-CH ₃		73
17		4-H		58
18		4-OCH ₃		61
19		4-H		61
20		4-OCH ₃		82
21		4-H		44
22		4-H		56
23		4-H		85
24		4-OCH ₃		83
25		4-H		81
26		4-H		45
27		4-H		83

^a Conditions: equiv ratios are based on BiAr₃: BiAr₃ (1 equiv), Ar-X (3.5 equiv), Pd(OAc)₂ (0.1 equiv)/PPh₃ (0.4 equiv), K₃PO₄ (6 equiv), DMF (3 mL), 90 °C, 1 h.

^b Isolated yields after purification by column chromatography. All the products were characterized by ¹H, ¹³C NMR and IR spectroscopy and by comparison with the literature data.

results are given in Table 2. The cross-coupling reaction of *p*-iodoacetophenone with triarylbismuths containing

p-methyl, *p*-fluoro, *p*-chloro, *p*-methoxy and *m*-methoxy substituents produced the corresponding functionalized

biphenyls in high yields (entries 1–6). The cross-coupling reaction of *p*-acetylphenyl triflate with triphenylbismuth afforded a moderate yield of the product (entry 7). In contrast, *p*-chlorophenyl iodide and *p*-chlorophenyl triflate reacted well giving good to high yields of the cross-coupled products (entries 8–12). Electron-deficient *p*-nitrophenyl iodide and *p*-nitrophenyl triflate produced the corresponding cross-coupled biphenyls in good yields (entries 13–16). The cross-coupling reactions with electron rich *p*-tolyl iodide and *p*-tolyl triflate produced moderate yields of the corresponding biphenyls (entries 17–19). Substituted phenyl triflates possessing a *p*-methoxy or *p*-cyano group gave 44% and 56% yields (entries 21 and 22), while that with a *p*-fluoro substituent gave an 82% yield of the cross-coupled product (entry 20). *m*-Cyanophenyl iodide and *m*-cyanophenyl triflate also produced high yields with different triaryl bismuths (entries 23 and 24). The cross-coupling of *p*-methoxyphenyl iodide gave a moderate yield of the corresponding cross-coupled product (entry 26). The reactivity of *p*-cyanophenyl iodide and *p*-trifluoromethylphenyl iodide produced high yields of cross-coupled products (entries 25 and 27). In this study, electron-deficient aryl iodides and aryl triflates reacted efficiently with triaryl bismuths furnishing high yields of the corresponding cross-coupled products. It is noteworthy that electron-rich aryl iodides and aryl triflates which are otherwise known to be less reactive also afforded moderate yields of the cross-coupled products with triaryl bismuths.^{4b} Evidently, the cross-coupling reactivity of the electronically different triaryl bismuths was proved to be efficient with different aryl iodides or aryl triflates under the present conditions.

In conclusion, we have disclosed a palladium catalyzed, atom-efficient cross-coupling reaction of triaryl bismuths with aryl iodides and aryl triflates. The catalytic protocol developed involves the use of a readily available metal catalyst, ligand and base. In addition, the short reaction time is an added advantage.

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References and notes

- Selected references on metal catalyzed coupling reactions, see: (a) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442–4489; (b) Kotha, S.; Lahiri,

- K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633–9695; (c) *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; (d) Christmann, U.; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366–374; (e) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263–303; (f) Hassan, J.; Seignion, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1469; (g) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.
- (a) Corbet, J. P.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651–2710; (b) Rouhi, A. M. *Chem. Eng. News* **2004**, *82*, 49–58.
- (a) Perez, I.; Sestelo, J. P.; Sarandeses, L. A. *Org. Lett.* **1999**, *1*, 1267–1269; (b) Perez, I.; Sestelo, J. P.; Sarandeses, L. A. *J. Am. Chem. Soc.* **2001**, *123*, 4155–4160; (c) Pena, M. A.; Sestelo, J. P.; Sarandeses, L. A. *J. Org. Chem.* **2007**, *72*, 1271–1275; (d) Pena, M. A.; Sestelo, J. P.; Sarandeses, L. A. *Synthesis* **2005**, *3*, 485–492.
- (a) *Organobismuth Chemistry*; Suzuki, H., Matano, Y., Eds.; Elsevier: Amsterdam, 2001; (b) Rao, M. L. N.; Yamazaki, O.; Shimada, S.; Tanaka, T.; Suzuki, Y.; Tanaka, M. *Org. Lett.* **2001**, *3*, 4103–4105; (c) Rao, M. L. N.; Venkatesh, V.; Jadhav, D. N. *Tetrahedron Lett.* **2006**, *47*, 6975–6978; (d) Rao, M. L. N.; Banerjee, D.; Jadhav, D. N. *Tetrahedron Lett.* **2007**, *48*, 2707–2711; (e) Asano, R.; Moritani, I.; Fujiwara, Y.; Teranishi, S. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2910–2911; (f) Kawamura, T.; Kikukawa, K.; Takagi, M.; Matsuda, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2021–2024; (g) Barton, D. H. R.; Ozbalik, N.; Ramesh, M. *Tetrahedron* **1988**, *44*, 5661–5668; (h) Wada, M.; Ohki, H. *J. Synth. Org. Chem. Jpn.* **1989**, *47*, 425–435; (i) Ohe, T.; Tanaka, T.; Kuroda, M.; Cho, C.-S.; Ohe, K.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1851–1855.
- Other organobismuths for carbon–carbon bond formation: (a) Rao, M. L. N.; Shimada, S.; Tanaka, M. *Org. Lett.* **1999**, *1*, 1271–1273; (b) Rao, M. L. N.; Shimada, S.; Yamazaki, O.; Tanaka, M. *J. Organomet. Chem.* **2002**, *659*, 117–120; (c) Shimada, S.; Yamazaki, O.; Tanaka, T.; Rao, M. L. N.; Suzuki, Y.; Tanaka, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1845–1848; (d) Yamazaki, O.; Tanaka, T.; Shimada, S.; Suzuki, Y.; Tanaka, M. *Synlett* **2004**, 1921–1924.
- Representative procedure for the cross-coupling reaction of aryl iodides and triflates (Table 2): A hot oven-dried Schlenk tube was charged with *p*-iodoacetophenone (0.215 g, 0.87 mmol) and triphenylbismuth (0.110 g, 0.25 mmol). To this, K₃PO₄ (0.318 g, 1.5 mmol), PPh₃ (0.026 g, 0.1 mmol), Pd(OAc)₂ (0.0056 g, 0.025 mmol) and solvent DMF (3 mL) were added under a nitrogen atmosphere. The mixture was stirred at 90 °C in an oil bath for 1 h. The contents were cooled to room temperature and the reaction was quenched with dil HCl (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extract was washed with water, brine and dried over anhydrous MgSO₄. The organic extract was concentrated under reduced pressure. The crude product thus obtained was further purified by column chromatography on silica gel (100–200 mesh) using hexane–ethyl acetate (8:2) as eluent to afford pure 4-acetylbiphenyl (0.133 g) in 91% yield. The product was characterized by comparing ¹H, ¹³C NMR and IR data with the reported data.