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Palladium-Catalyzed Carbonylative Cross-Coupling Reaction of Arylboronic Acids with Aryl Electrophiles: Synthesis of Biaryl Ketones

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The carbonylative cross-coupling reaction of arylboronic acids with aryl electrophiles (ArI, ArBr, and ArOTf) to yield unsymmetrical biaryl ketones was carried out in anisole at 80 °C in the presence of a palladium catalyst and a base. The reaction selectively proceeded under an atmospheric pressure of carbon monoxide when $PdCl_2(PPh_3)_2$ (3 mol %)/K_2CO_3 (3 equiv) were used for aryl iodides and $PdCl_2(dppf)$ (3 mol %)/K_2CO_3 (3 equiv)/KI (3 equiv) for the bromides or the triflates. The carbonylation of arylboronic acids with benzyl halides gave aryl benzyl ketones.

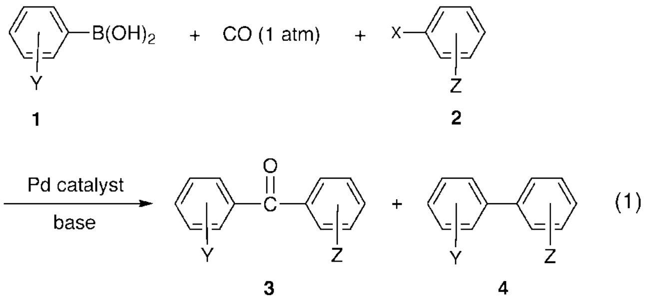
The transition metal-catalyzed three-component cross-coupling reaction between arylmetal reagents, carbon monoxide, and aryl electrophiles is a straightforward and convenient route for the synthesis of unsymmetrical biaryl ketones. Various arylmetal reagents including magnesium,[1] aluminum,[2] silicon,[3] and tin compounds[4] have been reported to undergo the carbonylative coupling, but the development of the protocol to electron-deficient aryl electrophiles is severely limited due to a side reaction that gives a direct coupling product without carbon monoxide insertion.

We previously reported the palladium-catalyzed cross-coupling reaction[5] of organoboron compounds with organic electrophiles and the carbonylative cross-coupling reaction of 9-alkyl-9-borabicyclo[3.3.1]nonane derivatives (9-alkyl-9-BBN) with aryl, 1-alkenyl, benzyl, and alkyl halides.[6] In this paper, we wish to report the synthesis of biaryl ketones (**3**) via the palladium-catalyzed carbonylative cross-coupling of arylboronic acids (**1**) with aryl iodides, bromides, or triflates (**2**) (eq 1).[7] The use of a dppf ligand for the palladium catalyst and the addition of NaI or KI were requisite to achieve a selective coupling for aryl bromides or triflates, though various palladium complexes were effective for aryl iodides in the absence of metal iodides.

Table 1. Carbonylative Coupling of Phenylboronic Acid with 4-Iodoacetophenone[a]

entry	catalyst	base	solvent	yield[b] (%) 3	yield[b] (%) 4
1	$PdCl_2(PPh_3)_2$	K_2CO_3	anisole	84	11
2		Cs_2CO_3		69	23
3		Tl_2CO_3		38	24
4		K_3PO_4		43	23
5	$PdCl_2(dppf)$[c]	K_2CO_3		82	9
6	$PdCl_2(CH_3CN)_2$			71	4
7	$Pd(PPh_3)_4$			74	7
8	$PdCl_2(PPh_3)_2$		toluene	68	11
9			dioxane	63	8
10			DMF	6	0

[a] Reactions between phenylboronic acid (1.1 mmol), CO (1 atm), and 4-iodoacetophenone (1.0 mmol) were carried out at 80 °C for 5 h in the presence of catalyst (3 mol %), base (3 mmol), and solvent (6 mL). [b] GLC yields based on 4-iodoacetophenone. [c] Dppf: 1,1′-bis(diphenylphosphino)ferrocene.



Results and Discussion

Reaction Conditions. The reaction of phenylboronic acid (1.1 equiv) with 4-iodoacetophenone was examined at 80 °C for 5 h under an atmospheric pressure of carbon monoxide to optimize the reaction conditions (Table 1).

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(5) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213. (c) Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419. (d) Suzuki, A. *Pure Appl. Chem.* **1985**, *57*, 1749. (e) Suzuki, A. *Acc. Chem. Res.* **1982**, *15*, 178.

(6) (a) Ishiyama, T.; Murata, M.; Suzuki, A.; Miyaura, N. *J. Chem. Soc., Chem. Commun.* **1995**, 295. (b) Ishiyama, T.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1991**, *32*, 6923. (c) Ishiyama, T.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1999. (d) Wakita, Y.; Yasunaga, T.; Akita, M.; Kojima, M. *J. Organomet. Chem.* **1986**, *301*, C17.

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Table 2. Carbonylative Coupling of Phenylboronic Acid with 4-Bromoacetophenone or 4-Acetylphenyl Triflate[a]

				yield[b] (%)	
entry	X	catalyst	additive	**3**	**4**
1	Br	$PdCl_2(PPh_3)_2$	none	55	36
2			KI	64	22
3		$PdCl_2(dppf)$[c]	none	66	18
4			KI	81	3
5			NaI	80	2
6			LiI	52	1
7		$Pd(dba)_2/dppf$[c]	KI	73	6
8		$Pd(dba)_2/dppb$[c]	KI	67	6
9		$Pd(dba)_2/dppp$[c]	KI	24	6
10		$Pd(dba)_2/dppe$[c]	KI	16	6
11	OTf	$PdCl_2(PPh_3)_2$	none	3	83
12		$PdCl_2(dppf)$[c]	KI	78	8

[a] Reactions between phenylboronic acid (1.1 mmol), CO (1 atm), and 4-bromoacetophenone or 4-acetylphenyl triflate (1.0 mmol) were carried out at 80 °C for 16 h in the presence of catalyst (3 mol %), K_2CO_3 (3 mmol), and additive (3 mmol) in anisole (6 mL). [b] GLC yields based on aryl electrophiles. [c] Dppf, dppe, dppp, and dppb: 1,1′-bis(diphenylphosphino)ferrocene, 1,2-bis(diphenylphosphino)ethane, 1,3-bis(diphenylphosphino)propane, and 1,4-bis(diphenylphosphino)butane, respectively.

The bases affected the selectivity of the reaction (entries 1−4). Cs_2CO_3, K_3PO_4, and Tl_2CO_3, which have been utilized in the cross-coupling reaction of organoboron compounds,[5] had a strong tendency to produce a direct coupling product, 4-acetylbiphenyl (23−24%). K_2CO_3 (3 equiv) suspended in anisole is very efficient to yield 4-acetylbenzophenone (82−84%) in the presence of $PdCl_2(PPh_3)_2$ or $PdCl_2(dppf)$ (3 mol %), which, however, was still accompanied the biaryl (9∼11%) (Table 1, entries 1 and 5). Most of the representative palladium catalysts, including the triphenylphosphine complexes, the dppf complex, and the phosphine-free complex $PdCl_2(CH_3CN)_2$, smoothly catalyzed the reaction, but the choice of less polar solvents was essential to achieve high yields (Table 1, entries 8−10). The reaction worked well in anisole, dioxane, or toluene, but low yields resulted in polar solvents such as DMF, presumably due to another side reaction leading to 4-acetylbenzoic acid (Table 1, entry 10).[8]

The results prompted us to investigate the reaction of aryl bromides or triflates (Table 2), but these substrates resulted in low yields under the conditions optimized for the iodides. The addition of NaI or KI (3 equiv) and the use of a dppf ligand for the palladium catalyst remarkably enhanced the selectivity of ketone (Table 2, entries 2−5 and 12). Although various palladium complexes were effective for iodides, the dppf complex was apparently better than the triphenylphosphine complexes for the bromide and the triflate (Table 2, entries 1−4, 11, and 12). The selectivity of ketone decreased in the order of dppf > dppb ≫ dppp > dppe (Table 2, entries 7−10), thus suggesting the superiority of bidentate phosphine ligands with a large bite angle.[9]

A comparison of various phenylboron derivatives in the reaction with 4-iodoacetophenone gave the following order of yields: $PhB(OH)_2$ (**3**/**4** = 84%/11%), the phenylboronic acid 1,3-propanediol ester (**3**/**4** = 17%/0%), and the phenylboronic acid pinacol ester (**3**/**4** = 3%/0%), 9-Ph-9-BBN (**3**/**4** = 69%/7%). The carbonylative coupling of 4-bromoacetophenone with phenylboron derivatives in the presence of KI (Table 2, entry 4) also afforded a similar order of reactivity; thus, suggesting the superiority of boronic acids.

Synthesis of Unsymmetrical Biaryl Ketones. The carbonylative cross-coupling reaction between various arylboronic acids and aryl electrophiles was carried out in anisole at 80 °C under an atmospheric pressure of carbon monoxide in the presence of $PdCl_2(PPh_3)_2$ (3 mol %)/K_2CO_3 (3 equiv) for the iodides (Table 1, entry 1) or $PdCl_2(dppf)$ (3−5 mol %)/K_2CO_3 (3 equiv)/KI (3 equiv) for the bromides and the triflates (Table 2, entries 4 and 12). The method provides a quite general route for the synthesis of unsymmetrical biaryl ketones having various functionalities. Although the iodide afforded better results in shorter reaction times, good yields of ketones were similarly obtained from aryl bromides and triflates. Representative results are summarized in Table 3.

The presence of a strong electron-attracting substituent such as NO_2 is known to promote the direct coupling giving biaryl **4**. For example, the carbonylative coupling reaction of triphenylalane with 4-iodonitrobenzene was reported to provide a 41% yield of 4-nitrobenzophenone and a 55% yield of 4-nitrobiphenyl,[2] and an analogous reaction with tributyltin hydride resulted in only a 9% yield of 4-nitrobenzaldehyde with an accompanying 84% yield of nitrobenzene.[10] Indeed, the reaction of phenylboronic acid with 4-iodonitrobenzene with $PdCl_2(PPh_3)_2$ resulted in **3**/**4** = 50%/35%, but the phosphine-free palladium catalyst of $PdCl_2(MeCN)_2$ gave a high yield of ketone (**3**/**4** = 89%/6%) (Table 3, entry 1). Other aryl halides and triflates having an electron-withdrawing group were successfully carbonylated and coupled with arylboronic acids with $PdCl_2(PPh_3)_2$ or $PdCl_2(dppf)$ (Table 3, entries 3−8). The bromo group in phenylboronic acid remained intact during the reaction with iodobenzene (Table 3, entry 9).

The reaction of mesitylboronic acid with 2-iodotoluene and that of *o*-tolylboronic acid with iodomesitylene took a longer reaction time due to their large steric hindrance (Table 3, entries 17 and 19). A more sterically hindered combination of mesitylboronic acid and iodomesitylene was further decelerated, but the reaction still yielded a 35% yield of dimesityl ketone.

The carbonylative coupling of heteroaromatic halides or triflates containing sulfur, nitrogen, and oxygen atoms afforded good yields of the corresponding ketones (Table 3, entries 21−28). $PdCl_2(dppf)$ was a good catalyst for 2-bromothiophene or 3-bromoquinoline (Table 3, entries 22 and 28), but the corresponding reaction of 2-bromopyridine or 2-bromofurane (Table 3, entries 24 and 25) suffered from low yields due to the exclusive formation of the direct coupling products **4**. For these two substrates, $Pd(PPh_3)_4$ exceptionally resulted in high yields of ketone (Table 3, entries 24 and 25).

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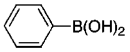
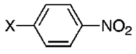
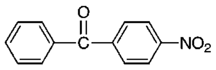
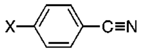
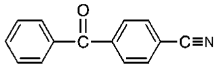
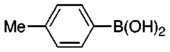
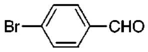
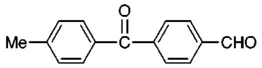
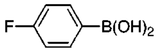
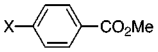
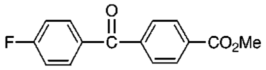
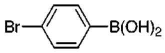
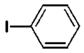
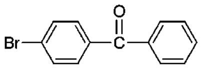
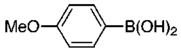
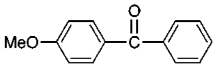
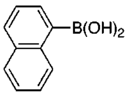
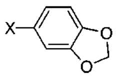
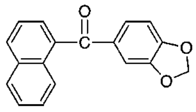
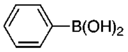
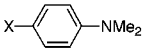
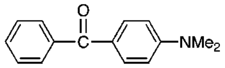
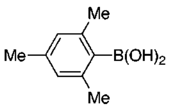
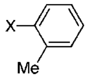
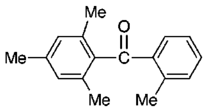
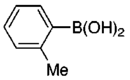
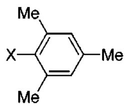
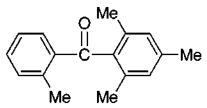
Table 3. Synthesis of Unsymmetrical Biaryl Ketones[a]

entry	borane	halide	product		time/h	yield/%[b]
1				X=I	5	89[c]
2				X=Br	16	17
3				X=Br	16	73
4				X=OTf	16	64
5					16	66
6				X=I	24	76
7				X=Br	16	75[d]
8				X=OTf	16	71
9					5	86
10				X=I	5	83
11				X=Br	16	66[d]
12				X=OTf	16	50
13				X=I	5	86
14				X=Br	16	75
15				X=I	5	89
16				X=Br	16	62[d]
17				X=I	24	63
18				X=Br	16	trace
19				X=I	24	66
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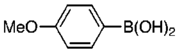
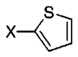
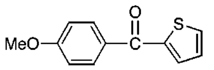
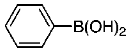
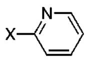
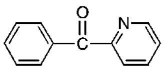
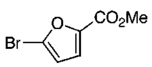
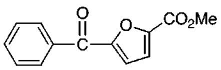
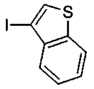
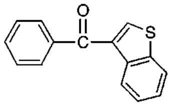
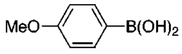
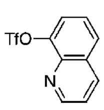
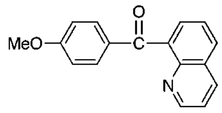
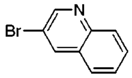
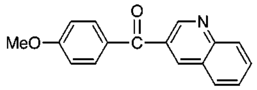
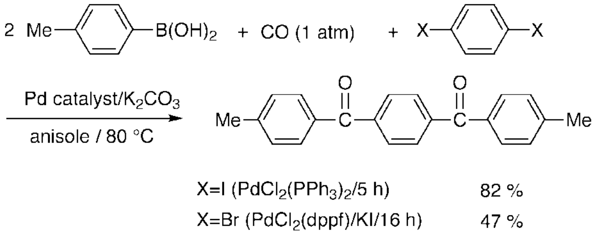
21				X=I	5	87
22				X=Br	16	64[d]
23				X=I	12	66
24				X=Br	16	68[e]
25					16	58[e]

Table 3 (Continued)

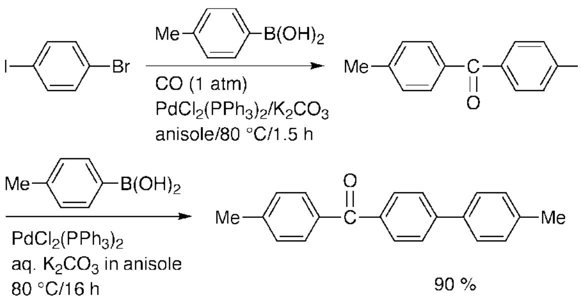
entry	borane	halide	product	time/h	yield/%[b]
26				5	89
27				16	43
28				16	66

[a] Reactions between arylboronic acids (1.1 mmol), CO (1 atm), and aryl electrophiles (1.0 mmol) were conducted at 80 °C in the presence of K_2CO_3 (3 mmol) in anisole (6 mL) by using $PdCl_2(PPh_3)_2$ (3 mol %) for iodides and $PdCl_2(dppf)$ (3 mol %) with KI (3 mmol) for bromides or triflates. [b] Isolated yields based on the halides or triflates. [c] $PdCl_2(MeCN)_2$ was used as catalyst. [d] 5 mol % of catalyst was used. [e] $Pd(PPh_3)_4$ was used as the catalyst in place of $PdCl_2(dppf)$.

A one-pot synthesis of diketone via the sequential double carbonylation is shown in eq 2. The reaction was very slow for the bromide, but the carbonylation of diiodobenzene with 2 equiv of *p*-tolylboronic acid provided the diketone in 82% yield after 5 h. On the other hand, the carbonylation of 4-bromoiodobenzene selectively occurred at the C−I bond in the presence of 2 equiv of *p*-tolylboronic acid (eq 3). The subsequent coupling with the remaining *p*-tolylboronic acid gave a 90% yield of biaryl monoketone.

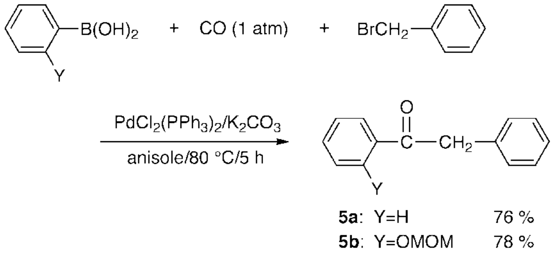


(2)

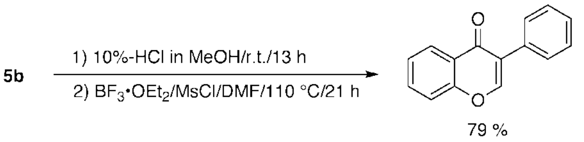


(3)

Synthesis of Aryl Benzyl Ketones. The reaction failed in other organic electrophiles such as 1-iodo-1-hexene, 1-iodo-1-hexyne, 1-iodohexane, and 3-bromo-2-phenyl-1-propene, but benzyl halides readily participated in the carbonylative cross-coupling reaction (eq 4). Under the conditions used for aryl iodides, the corresponding aryl benzyl ketones (**5a**,**b**) were obtained in 76% and 78% yields in the reaction of benzyl bromide with phenylboronic acid or [2-(methoxymethoxy)phenyl]boronic acid. The ketone **5b** thus obtained is a useful synthetic intermediate readily convertible to isoflavone (79%) (eq 5).[11]



(4)



(5)

Reaction Mechanism. The carbonylative cross-coupling of arylboronic acid with aryl electrophile may proceed through a catalytic cycle analogous to that proposed for other metal reagents (cycle A in Figure 1).[1−4] Oxidative addition of ArX to a palladium(0) complex provides Ar−Pd−X (**6**), which is followed by migratory insertion of carbon monoxide giving ArCO−Pd−X (**7**). Subsequent transmetalation between **7** and arylboronic acid with the aid of K_2CO_3 and reductive elimination of ketone **3** from ArCO−Pd−Ar′ (**8**) reproduce the palladium(0) species. Since **6** is a common intermediate for the carbonylation (cycle A) and the direct coupling giving biaryls (cycle B), a large amount of biaryls is often yielded when the carbon monoxide insertion (**6** → **7**) is slower than the transmetalation (**6** → **9**).

The carbon monoxide insertion into **6** is fast in electron-rich aryls, and the electron-withdrawing groups slow the insertion[12] by reversely accelerating the rate of transmetalation (**6** → **9**). Thus, low yields and low selectivity resulted in the reaction of electron-deficient substrates, especially for the bromides and the triflates. Iodo- and

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(12) The carbonylation of Ar−M−X complexes (M = Pd, Pt): (a) Dixon, K. R.; Dixon, A. C. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 9, p 208. (b) Anderson, G. K. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 9, p 460. (c) Alexander, J. J. In *The Chemistry of the Metal−Carbon Bond*; Hartley, F. R., Patai, S., Eds.; Wiley: New York, 1985; Vol. 2, p 349. (d) Cross, R. J.; Gemmill, J. *J. Chem. Soc., Dalton Trans.* **1981**, 2317. (e) Sugita, N.; Minkiewicz, J. V.; Heck, R. F. *Inorg. Chem.* **1978**, *17*, 2809. (f) Garrou, P. E.; Heck, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 4115.

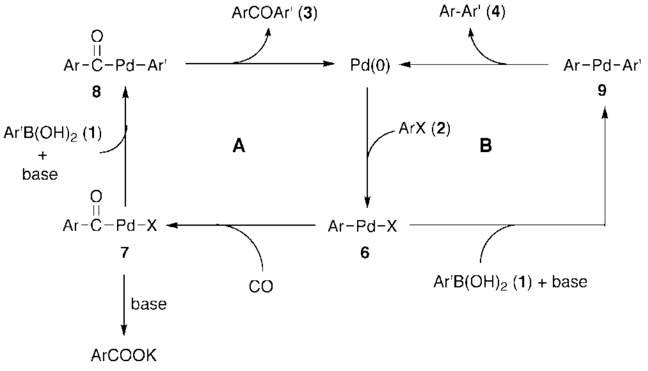
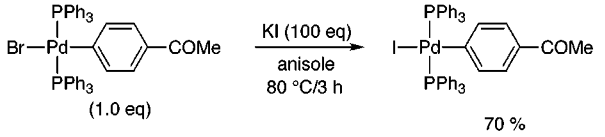


Figure 1. Catalytic cycle.

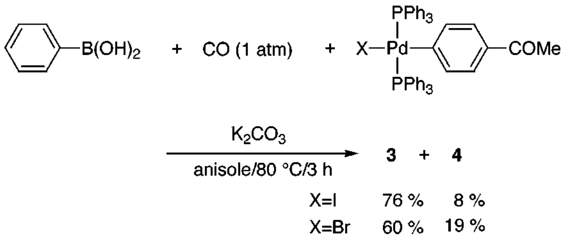
4-bromonitrobenzene (Table 3, entries 1 and 2) indeed exhibited a strong tendency to produce the direct coupling products.

The palladium–dppf complex is highly effective for the carbonylative coupling of aryl bromides and triflates. The order of yields and selectivity observed during the reaction of 4-bromoacetophenone is parallel to the bond angles of P–Pd–P (dppf > dppb ≫ dppp > dppe, Table 2, entries 7–10).[9] The rate of carbon monoxide insertion is accelerated by bidentate phosphine ligands having a large bite angle;[13] thus, the high catalytic efficiency and selectivity of $PdCl_2$(dppf) for the bromides and triflates can be attributed to its large P–Pd–P angle, which facilitates the CO insertion.

The carbon monoxide insertion to the Ar–Pd–I complexes (**6**, X = I) proceeds more readily than that into the corresponding Ar–Pd–Br complexes.[14] Thus, significant improvement of the yields and selectivity was observed by the addition of NaI or KI for aryl bromides and triflates. Indeed, the reaction of *trans*-PdBr(4-$MeCOC_6H_4$)$(PPh_3)_2$ with a large excess of KI gave *trans*-PdI(4-$MeCOC_6H_4$)$(PPh_3)_2$ in a yield of 70% (eq 6).[15] The superiority of the palladium iodides over the bromides was demonstrated by a stoichiometric reaction between phenylboronic acid and *trans*-PdX(4-$MeCOC_6H_4$)$(PPh_3)_2$ (X = I, Br) (eq 7). The carbonylative coupling of the Pd–I complex with phenylboronic acid resulted in a higher yield and selectivity (**3**/**4** = 76%/8%) than that of the Pd–Br complex (**3**/**4** = 60%/19%) in accordance with the selectivity of the catalytic reaction.



(6)



(7)

Experimental Section

Reagents. $PdCl_2$(dppf),[9b] $Pd(dba)_2$,[16] *trans*-PdBr(4-$MeCOC_6H_4$)$(PPh_3)_2$,[17] and *trans*-PdI(4-$MeCOC_6H_4$)$(PPh_3)_2$[18] were prepared. Arylboronic acids[19] and 9-phenyl-9-BBN[20] were synthesized by the reported procedures. The reaction of phenylboronic acid with diols in the presence of $MgSO_4$ in benzene gave phenylboronates. 4-Iodo-1,2-(methylenedioxy)benzene,[21] 4-iodo-*N*,*N*-dimethylaniline,[22] 2-iodopyridine,[15d] 3-iodobenzothiophene,[23] and aryl triflates[24] were prepared by the literature procedures.

Reaction Conditions (Tables 1 and 2). Palladium catalyst (0.03 mmol), base (3 mmol), phenylboronic acid (1.1 mmol), and 4-iodoacetophenone (1.0 mmol) were added to a flask fitted with a reflux condenser, a septum inlet, and a magnetic stirring bar. The flask was flushed with carbon monoxide and then charged with solvent (6 mL). The mixture was stirred at 80 °C for 5 h under an atmospheric pressure of carbon monoxide. The product was extracted with benzene (20 mL), washed with water, and dried over $MgSO_4$. The yields based on 4-iodoacetophenone were determined by GLC using pentadecane as an internal standard.

In a similar way, the reaction between phenylboronic acid (1.1 mmol), CO (1 atm), and 4-acetylphenyl bromide and triflate (1.0 mmol) was carried out in anisole (6 mL) at 80 °C for 16 h in the presence of palladium catalyst (0.03 mmol), K_2CO_3 (3 mmol), and powdered KI or NaI (3 mmol).

Synthesis of Unsymmetrical Biaryl Ketones (Table 3). The synthesis of 4-acetylbenzophenone[25] is representative. A flask equipped with a magnetic stirring bar, a septum inlet, and a reflux condenser was charged with $PdCl_2(PPh_3)_2$ (0.03

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mmol), K_2CO_3 (3 mmol), phenylboronic acid (1.1 mmol), and 4-iodoacetophenone (1.0 mmol). The flask was flushed with carbon monoxide, and anisole (6 mL) was then added. After being stirred at 80 °C for 5 h under CO (1 atm), the reaction mixture was cooled to room temperature, diluted with benzene, washed with water, and finally dried over $MgSO_4$. GC analysis revealed the formation of a 84% yield of 4-acetylbenzophenone. The isolation by chromatography over silica gel gave a pure compound: IR (Nujol) 1700, 1660 cm^{-1}; ^1H NMR δ 2.67 (s, 3 H), 7.51 (t, 2 H, $J = 7.8$ Hz), 7.63 (t, 1 H, $J = 7.4$ Hz), 7.81 (d, 2 H, $J = 7.3$ Hz), 7.87 (d, 2 H, $J = 8.1$ Hz), 8.06 (d, 2 H, $J = 8.1$ Hz); ^{13}C NMR δ 26.87, 128.14, 128.46, 130.02, 130.07, 132.96, 136.90, 139.55, 141.32, 195.92, 197.49; MS *m/e* 77 (9), 105 (9), 153 (15), 181 (14), 209 (100), 224 (M^+, 31); exact mass calcd for $C_{15}H_{12}O_2$ 224.0838, found 224.0826.

The reaction of arylboronic acids (1.0 mmol) with aryl bromides or triflates (1.0 mmol) was carried out in anisole (6 mL) at 80 °C for 16 h under CO (1 atm) in the presence of $PdCl_2(dppf)$ (0.03 mmol), K_2CO_3 (3 mmol), and KI (3 mmol).

1,4-Bis(4-methylbenzoyl)benzene (Eq 2).[26] The double carbonylative coupling was carried out in anisole (12 mL) at 80 °C for 5 h under CO (1 atm) by the use of $PdCl_2(PPh_3)_2$ (0.06 mmol), K_2CO_3 (6 mmol), *p*-tolylboronic acid (2.2 mmol), and 1,4-diiodobenzene (1.0 mmol). A similar reaction between *p*-tolylboronic acid (2.2 mmol), CO (1 atm), and 1,4-dibromobenzene (1.0 mmol) was carried out at 80 °C for 16 h in anisole (12 mL) by using of $PdCl_2(dppf)$ (0.06 mmol), K_2CO_3 (6 mmol), and KI (6 mmol): IR (Nujol) 1650 cm^{-1}; ^1H NMR δ 2.46 (s, 6 H), 7.31 (d, 4 H, $J = 8.5$ Hz), 7.75 (d, 4 H, $J = 8.1$ Hz), 7.86 (s, 4 H); ^{13}C NMR δ 21.66, 129.13, 129.51, 130.32, 134.30, 140.83, 143.84, 195.74; MS *m/e* 65 (14), 91 (38), 119 (100), 195 (7), 223 (21), 314 (M^+, 30); exact mass calcd for $C_{22}H_{18}O_2$ 314.1307, found 314.1280.

4-Methyl-4′-(*p*-tolyl)benzophenone (Eq 3). The carbonylative coupling between *p*-tolylboronic acid (2.2 mmol), CO (1 atm), and 4-bromoiodobenzene (1.0 mmol) was conducted in anisole (12 mL) at 80 °C for 1.5 h in the presence of $PdCl_2(PPh_3)_2$ (0.06 mmol) and K_2CO_3 (6 mmol). After being cooled to room temperature, the flask was flushed with nitrogen and charged with H_2O (2 mL). The resulting mixture was stirred at 80 °C for 16 h under N_2: IR (Nujol) 1650 cm^{-1}; ^1H NMR δ 2.42 (s, 3 H), 2.45 (s, 3 H), 7.29 (d, 2 H, $J = 8.3$ Hz), 7.30 (d, 2 H, $J = 8.3$ Hz), 7.55 (d, 2 H, $J = 8.3$ Hz), 7.68 (d, 2 H, $J = 8.3$ Hz), 7.75 (d, 2 H, $J = 8.3$ Hz), 7.86 (d, 2 H, $J = 8.3$ Hz); ^{13}C NMR δ 21.15, 21.65, 126.63, 127.11, 128.97, 129.67, 130.23, 130.60, 135.10, 136.31, 137.13, 138.09, 143.11, 144.93, 196.10; MS *m/e* 65 (11), 91 (33), 119 (67), 129 (10), 152 (27), 165 (17), 195 (100), 271 (16), 286 (M^+, 86); exact mass calcd for $C_{21}H_{18}O$ 286.1358, found 286.1380.

Synthesis of Aryl Benzyl Ketones (Eq 4). The procedure is the same as that employed for the reaction of aryl iodides.

Benzyl 2-(methoxymethoxy)phenyl ketone (5b): IR (film) 1680 cm^{-1}; ^1H NMR δ 3.47 (s, 3 H), 4.31 (s, 2 H), 5.26 (s, 2 H), 7.03 (t, 1 H, $J = 7.4$ Hz), 7.18 (d, 1 H, $J = 8.5$ Hz), 7.23 (d, 1 H, $J = 7.6$ Hz), 7.24 (t, 2 H, $J = 7.3$ Hz), 7.29 (d, 1 H, $J = 7.1$ Hz), 7.30 (t, 1 H, $J = 7.3$ Hz), 7.42 (t, 1 H, $J = 7.9$ Hz), 7.64 (d, 1 H, $J = 7.7$ Hz); ^{13}C NMR δ 50.10, 56.43, 94.55, 114.82, 121.84, 126.66, 128.40, 129.14, 129.61, 130.38, 133.31, 135.02, 155.87, 200.21; MS *m/e* 45 (87), 65 (8), 77 (5), 91 (15), 135 (25), 165 (100), 256 (M^+, 0.4); exact mass calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1124.

Synthesis of Isoflavone (Eq 5).[27] **5b** (0.47 mmol) was treated with 10% HCl in MeOH (5 mL) at room temperature for 13 h. Benzyl 2-hydroxyphenyl ketone thus obtained was directly subjected to the further transformation:[11] IR (Nujol) 1640 cm^{-1}; ^1H NMR δ 7.39 (t, 1 H, $J = 7.2$ Hz), 7.43 (t, 1 H, $J = 6.5$ Hz), 7.45 (t, 2 H, $J = 6.8$ Hz), 7.49 (d, 1 H, $J = 8.5$ Hz), 7.58 (d, 2 H, $J = 7.1$ Hz), 7.69 (t, 1 H, $J = 7.7$ Hz), 8.03 (s, 1 H), 8.33 (d, 1 H, $J = 8.1$ Hz); ^{13}C NMR δ 118.04, 124.62, 125.25, 125.44, 126.46, 128.21, 128.52, 128.96, 131.86, 133.61, 153.06, 156.23, 176.21; MS *m/e* 39 (20), 50 (24), 63 (56), 76 (24), 92 (51), 102 (18), 111 (7), 120 (21), 165 (9), 222 (M^+, 100); exact mass calcd for $C_{15}H_{10}O_2$ 222.0681, found 222.0680.

***trans*-$PdI(4\text{-}MeCOC_6H_4)(PPh_3)_2$ (Eq 6).** A mixture of *trans*-$PdBr(4\text{-}MeCOC_6H_4)(PPh_3)_2$ (0.06 mmol), KI (6 mmol), and anisole (12 mL) was stirred at 80 °C for 3 h under N_2. After removal of KI by filtration, the product was extracted with benzene, washed with water, and purified by recrystallization from benzene: IR (Nujol) 1680 cm^{-1}; ^1H NMR δ 2.28 (s, 3 H), 6.76 (s, 4 H), 7.23 (t, 12 H, $J = 7.4$ Hz), 7.32 (t, 6 H, $J = 7.2$ Hz), 7.52 (dd, 12 H, $J = 5.6$, 12.7 Hz); ^{13}C NMR δ 26.16, 126.45, 127.82 (t, $J = 5.4$ Hz), 129.90, 131.65 (t, $J = 23.6$ Hz), 134.80 (t, $J = 6.2$ Hz), 135.82 (t, $J = 4.1$ Hz), 172.47, 198.50; ^{31}P NMR ($CDCl_3$, H_3PO_4) δ 23.33.

Effect of Halogen Ligands (Eq 7). The reaction of phenylboronic acid (0.11 mmol) with *trans*-$PdX(4\text{-}MeCOC_6H_4)(PPh_3)_2$ (X = I, Br) (0.10 mmol) was carried out in the presence of K_2CO_3 (0.3 mmol) in anisole (1 mL) at 80 °C for 3 h under CO (1 atm).

Supporting Information Available: Spectral data and copies of ^1H NMR spectra of biaryl ketones (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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