



Ligandless Palladium Catalyzed Reactions of Arylboronic Acids and Sodium Tetraphenylborate with Aryl Halides in Aqueous Media

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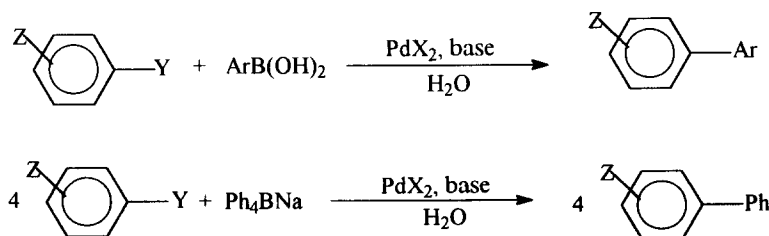
Abstract: Polyfunctional biaryls are prepared by a modified Suzuki cross-coupling reaction between arylboronic acids or sodium tetraphenylborate and aryl halides ArX, X = I, Br, Cl in aqueous solvents or neat water using a phosphine-free palladium catalyst, and in the presence of bases (Na₂CO₃ or NaOH). All four phenyl groups of Ph₄BNa participate in the reaction. The reaction of Ph₄BNa with aryl halides proceeds in water with high catalytic efficiency (250,000 catalytic cycles).
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INTRODUCTION

Palladium catalyzed cross-coupling reaction of organoboron compounds with organic halides is a versatile synthetic method for new carbon-carbon bond formation.¹ Organoboron reagents are easily accessible, stable in air and inert to various functional groups which otherwise require a protection-deprotection sequence.

Usually, cross-coupling reactions of organoboranes are carried out in an organic solvent or in a mixture of organic solvent and aqueous base in the presence of phosphine palladium complexes such as Pd(PPh₃)₄ and PdCl₂(dppf). Recently water-soluble ligands PPh₂(*m*-C₆H₄SO₃Na) and P(*m*-C₆H₄SO₃Na)₃ have been successfully used.²

In our preliminary communication³ we reported that cross-coupling reactions between arylboranes and aryl halides are effectively catalyzed by palladium salts without phosphine ligands in the presence of bases in neat water.



X = Cl, OAc; Y = I, Br, Cl

Recently, such modified Suzuki coupling reactions have been reported for the synthesis of biaryls and 1,3-diarylpropenes.⁴ Here we report in detail results of our investigations in this field.

RESULTS AND DISCUSSION

Palladium catalyzed arylation of aryl bromides and iodides by arylboronic acids or sodium tetraphenylborate. At first, we studied the effect of catalyst and base on the yield of *m*-phenylbenzoic acid in the reaction of phenylboronic acid with *m*-iodobenzoic acid in water as a solvent and in the presence of 1 mol% of palladium compounds as a catalyst. The results are presented in Table 1. The reaction proceeded rapidly at room temperature in the presence of different palladium catalysts. Palladium salts PdX₂ (X=Cl, OAc) were found to be the most effective catalysts for the cross-coupling with phenylboronic acid. The reaction occurred more slowly in the presence of phosphine-palladium catalysts, but the yield of cross-coupling product remained high. Pd-black can be also used as a catalyst precursor (Table 1, entry 9).

Table 1. Cross-Coupling of 3-Iodobenzoic Acid with PhB(OH)₂ under Various Reaction Condition^a

Entry	Catalyst	Base (mol. eq.)	t, min	Yield ^b , %
1	Pd(OAc) ₂	NaOH (4)	15	99
2	Pd(OAc) ₂	NaOH (2.1)	30	97
3	Pd(OAc) ₂	NaOH (7.5)	90	96
4	Pd(OAc) ₂	NaOAc (3)	8 h	24
5	Pd(OAc) ₂	NaHCO ₃ (4)	60	70
6	Pd(OAc) ₂	Na ₂ CO ₃ (3)	30	96
7	Pd(OAc) ₂	K ₂ CO ₃ (3)	60	96
8	Pd(OAc) ₂	K ₃ PO ₄ (2)	30	95
9	Pd-black	NaOH (4)	3 h	80
10	PdCl ₂ (dppf)	NaOH (4)	30	100
11	PdCl ₂ (PPh ₃) ₂	NaOH (4)	20 h	73
12	PdCl ₂ [PPh ₂ (<i>m</i> -C ₆ H ₄ SO ₃ Na)] ₂	NaOH (4)	45	95
13	PdCl ₂	NaOH (4)	10	100

^a Reactions were carried out at room temperature in water (1 mL) by using 0.5 mmole of *m*-IC₆H₄CO₂H, 0.55 mmol of PhB(OH)₂, base and 1 mol% of catalyst under argon. ^b GLC yield of *m*-PhC₆H₄CO₂H based on the *m*-iodobenzoic acid employed.

Representative results of reactions of arylboronic acids and Ph₄BNa with iodo(and bromo)arenes, bearing carboxy and hydroxy groups, are summarised in Tables 2 and 3. These haloarenes are soluble in water in the presence of bases.

The coupling reaction of arylboronic acids was completed within 5 min to 2 h at room temperature in aqueous solution of Na_2CO_3 or NaOH in the presence 1 mole % of $\text{Pd}(\text{OAc})_2$ or PdCl_2 when *m*- or *p*-halobenzoic acids and halophenols are used. The reactions of *o*-iodo(and bromo)benzoic acids occurred slowly under such conditions, and the yield of cross-coupling product did not exceed 60%. While *m*- and *p*-halobenzoic acids reacted smoothly in the presence of both Na_2CO_3 and NaOH , in the case of halophenols relatively weak bases such as K_2CO_3 gave high product yield.

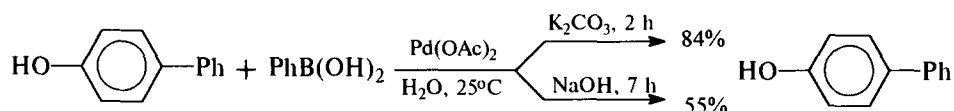


Table 2. Cross-Coupling Reaction of Arylboronic Acids with Aryl Halides in Water^a

ArX	Ar'B(OH) ₂ or Ar'B(OEt) ₂	Base (mmol)	t, h	Yield ^b , %
<i>m</i> -HO ₂ CC ₆ H ₄ I	PhB(OH) ₂	Na ₂ CO ₃ (3)	10 min	(94)
<i>m</i> -HO ₂ CC ₆ H ₄ I	<i>p</i> -FC ₆ H ₄ B(OH) ₂	NaOH (4)	5 min	(96)
<i>p</i> -HO ₂ CC ₆ H ₄ I	PhB(OH) ₂	Na ₂ CO ₃ (2.5)	1	(80)
<i>p</i> -HO ₂ CC ₆ H ₄ I	<i>p</i> -TolB(OH) ₂	NaOH (4)	1	(80)
<i>o</i> -HO ₂ CC ₆ H ₄ I	PhB(OH) ₂	Na ₂ CO ₃ (2.5)	25	(60)
<i>p</i> -HOC ₆ H ₄ I	PhB(OH) ₂	K ₂ CO ₃ (3)	2	(84)
<i>p</i> -HOC ₆ H ₄ Br	PhB(OEt) ₂	Na ₂ CO ₃ (3)	1	(82)
<i>m</i> -HOC ₆ H ₄ Br	PhB(OEt) ₂	Na ₂ CO ₃ (3)	1	(83)
<i>m</i> -HO ₂ CC ₆ H ₄ Br	PhB(OEt) ₂	Na ₂ CO ₃ (3)	1	(80)
<i>m</i> -HO ₂ CC ₆ H ₄ Br ^c	<i>p</i> -FC ₆ H ₄ B(OH) ₂	NaOH (3)	10 min	(95)
<i>o</i> -HO ₂ CC ₆ H ₄ Br	PhB(OEt) ₂	Na ₂ CO ₃ (3)	1	39
<i>o</i> -HO ₂ CC ₆ H ₄ Br ^d	TolB(OH) ₂	NaOH (5)	5	(60)
	PhB(OEt) ₂	Na ₂ CO ₃ (3)	2	99
	<i>p</i> -FC ₆ H ₄ B(OH) ₂	Na ₂ CO ₃ (3)	1	(90)

^a Reactions were carried out in water (4 mL) at room temperature using 1 mmole of ArX, 1.1 mmole of Ar'B(OH)₂ or Ar'B(OEt)₂, base and 1 mol% $\text{Pd}(\text{OAc})_2$ under argon, unless otherwise noted. ^b GLC yields are based on ArX, and the isolated yields are in parentheses. ^c 1 mol% PdCl_2 . ^d 0.1 M PdCl_2 in H_2O (2 mol%), *p*-TolB(OH)₂ (2.2 mmol), at 100°C.

Cross-coupling of sodium tetraphenylborate with halobenzoic acids and halophenols occurred easily under such conditions. It is important to note that all four phenyl groups of Ph_4BNa can be transferred in the presence of base.

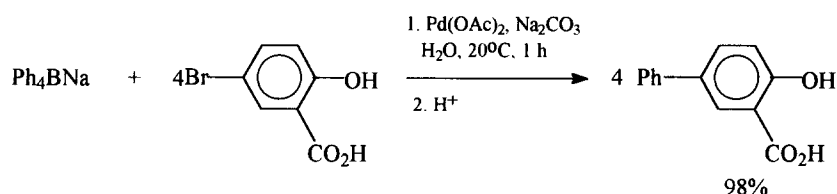
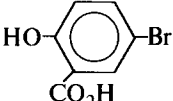


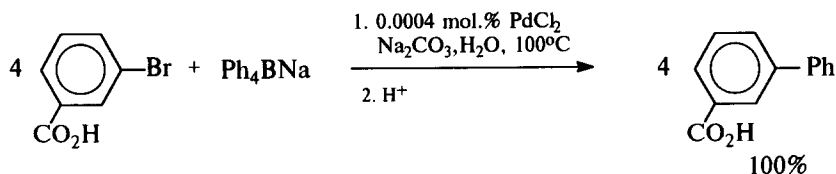
Table 3. Cross-Coupling Reaction of Ph_4BNa with Aryl Halides^a

ArX	Base (mmol)	t, h	Yield ^b , %
<i>m</i> -HO ₂ CC ₆ H ₄ I	Na ₂ CO ₃ (1.75)	1	(98)
<i>p</i> -HO ₂ CC ₆ H ₄ I	Na ₂ CO ₃ (1.75)	1.5	(95)
<i>o</i> -HO ₂ CC ₆ H ₄ I ^c	Na ₂ CO ₃ (1)	16	(53)
<i>p</i> -HOC ₆ H ₄ I	Na ₂ CO ₃ (3)	3	(83)
<i>m</i> -HO ₂ CC ₆ H ₄ Br	Na ₂ CO ₃ (1.75)	0.5	(99)
<i>m</i> -HO ₂ CC ₆ H ₄ Br	NaOH (1.84)	2	100
<i>p</i> -HO ₂ CC ₆ H ₄ Br	Na ₂ CO ₃ (1.75)	1	(91)
<i>m</i> -HOC ₆ H ₄ Br	NaOH (2)	2	96
<i>p</i> -HOC ₆ H ₄ Br	Na ₂ CO ₃ (1.75)	0.5	98
	Na ₂ CO ₃ (3)	1	98 (79)

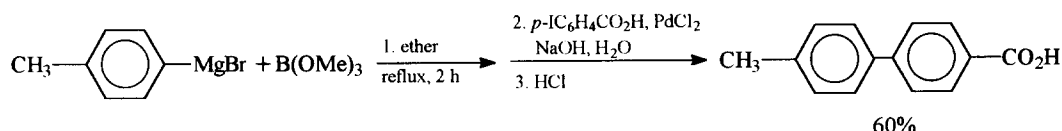
^a Reactions were carried out in water (4 mL) at room temperature by using 1 mmole of ArX, 0.27 mmole of Ph_4BNa , base and 1 mol% of $\text{Pd}(\text{OAc})_2$ under argon, unless otherwise noted. ^b GLC yields are based on ArX, and the isolated yields are in parentheses.

^c 1.1 mmol Ph_4BNa , at 90°C.

Reactions of bromophenols and bromobenzoic acids with organoboron compounds proceeded with longer induction periods, with Ph_4BNa than with $\text{PhB}(\text{OH})_2$. The induction period was reduced if the alkali concentration was decreased or Na_2CO_3 was used as base. Preliminary tests showed that reduction of $\text{Pd}(\text{II})$ salt to $\text{Pd}(0)$ with out aryl halide obeys the same rules. Therefore we suppose the delay to be accounted for this step. At higher temperatures the reaction starts immediately and the amount of catalyst can be significantly decreased. For example, the reaction of *m*-bromobenzoic acid with Ph_4BNa at 100°C was completed in 4 h in the presence of 0.0004 mol% of PdCl_2 , corresponding a turnover number as high as 250, 000.

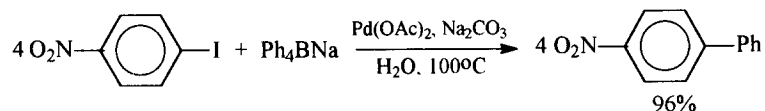


The mixture of *p*-tolylboranes (*p*-Tol₄BMgBr, *p*-Tol₃B, *p*-Tol₂BOH, *p*-TolB(OH)₂) prepared *in situ* from B(OMe)₃ and *p*-TolMgBr reacted with *p*-iodobenzoic acid in water giving 60% isolated yield of *p*-(*p*-tolyl)benzoic acid.

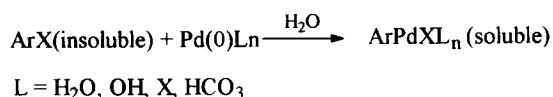


This one-pot modification seems to be the most suitable for unstable boron compounds.

Reactions of aryl halides insoluble in water such as *p*-iodonitrobenzene, *p*-iodobenzaldehyde etc. occurred slowly in water and the yields were only 50-60%. However, the yields can be increased up to quantitative by carrying out the reaction at higher temperature (Table 4).

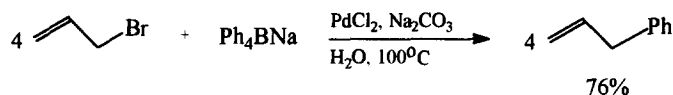


One may suppose that under such conditions palladium intermediates act not only as catalyst, but also as phase transfer agents.



The solubility of ArPdXL_n in water is due to the hydrophilicity of ligands (L). Water-insoluble aryl halides can easily react with arylboronic acid and sodium tetraphenylborate at room temperature in aqueous organic solvents (DMF or acetone). Water dramatically affects the reaction as shown in Table 5. For example, the reaction of *p*-O₂NC₆H₄I with Ph₄BNa practically does not occur in DMF, but proceeds smoothly in a mixture of DMF and water (2:1) despite the low solubility of ArX. The reaction is also facilitated by the presence of bases such as Na₂CO₃ and NaOAc. These facts may be accounted for by formation of palladium complexes with oxygen-containing ligands ArPdZ (Z = OH, OAc, HCO₃, H₂O etc.) which are more reactive towards organoboranes in the transmetallation step.

Other halides studied in the cross-coupling with Ph₄BNa were allylbromide and benzoyl chloride. Reaction of allylbromide yielded 60% allylbenzene at 25°C and 76% at 100°C.



Benzoyl chloride was converted to benzophenone by the reaction with Ph_4BNa (0.27 equiv.) in mixed acetone-water (2:1) solvent at ambient temperature.

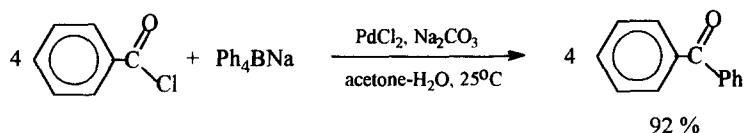
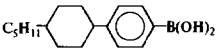
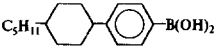


Table 4. Cross-Coupling of Ph_4BNa or $\text{ArB}(\text{OH})_2$ with Water-Insoluble Aryl Halides.^a

ArX	Borane	Solvent	PdX_2^b	T (°C)	t, h	Yield ^c , %
<i>p</i> -O ₂ NC ₆ H ₄ I	Ph_4BNa	DMF-H ₂ O (2:1)	A	25	10	99(81)
<i>p</i> -O ₂ NC ₆ H ₄ I	Ph_4BNa	H ₂ O	A	25	21	50
<i>p</i> -O ₂ NC ₆ H ₄ I	Ph_4BNa	H ₂ O	A	100	2	96
<i>p</i> -OHCC ₆ H ₄ I	Ph_4BNa	acetone-H ₂ O (3:2)	A	25	4	83
<i>p</i> -OHCC ₆ H ₄ I	Ph_4BNa	H ₂ O	A	100	1	(84)
<i>m</i> -O ₂ NC ₆ H ₄ I	Ph_4BNa	acetone-H ₂ O (3:2)	A	25	7	98
<i>o</i> -BrC ₆ H ₄ I	Ph_4BNa	acetone-H ₂ O (3:1)	A	25	50	43 ^d
<i>o</i> -BrC ₆ H ₄ I	Ph_4BNa	acetone-H ₂ O (2:1)	A	56	1	99(98) ^e
C ₆ H ₅ I	<i>p</i> -FC ₆ H ₄ B(OH) ₂	H ₂ O	B	100	2	(85)
<i>p</i> -AcC ₆ H ₄ Br	<i>p</i> -FC ₆ H ₄ B(OH) ₂	H ₂ O	B	100	3	(86)
<i>p</i> -HOC ₆ H ₄ I		DMF-H ₂ O (4:1)	A	80	2	(64)
<i>p</i> -F ₂ HCSC ₆ H ₄ I		DMF-H ₂ O (1.2:1)	A	80	2	(95)

^a Reactions were carried out in a mixture DMF(acetone)-H₂O or water by using ArX (1 mmol), Ph_4BNa (0.27 mmol) or $\text{ArB}(\text{OH})_2$ (1.1 mmol), Na_2CO_3 (1-3 mmol), and 1 mol% PdX_2 , unless otherwise noted. ^b PdX_2 : A = $\text{Pd}(\text{OAc})_2$, B = 0.1 mL of 0.1 M PdCl_2 in H₂O. ^c GLC yields are based on ArX, and the isolated yields are in parentheses. ^d 43% *o*-BrC₆H₄Ph, 17% *o*-PhC₆H₄Ph, 40% *o*-BrC₆H₄I. ^e 0.54 mmol Ph_4BNa , 99% *o*-PhC₆H₄Ph.

In conclusion, a new modification of the cross-coupling reaction of aryl halides and organoboron reagents have been developed based on simple palladium salts as catalyst precursors and water as solvent thus rendering this process more economic and ecologically acceptable.

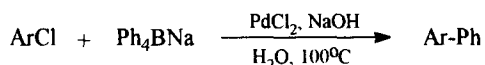
Table 5. The Influence of Water and Base on the Reaction of Ph₄BNa with 1-Iodo-4-nitrobenzene

Solvent (DMF:H ₂ O)	Base (mmol)	Yield ^b , %
DMF	-	10
9:1	-	13
2:1	-	77
1:1	-	47
9:1	Na ₂ CO ₃ (2)	54
9:1	NaOAc (2)	50

^a Reactions were conducted in a DMF-H₂O mixture (4 mL) at room temperature for 24 h using p-IC₆H₄NO₂ (1 mmol), Ph₄BNa (1.1 mmol) and 1 mol% of PdCl₂ under argon. ^b GLC yields are based on the ArI employed.

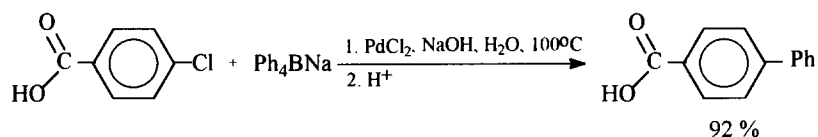
Palladium Catalyzed Phenylation of Chloroarenes by Tetraphenylborate Sodium. The ligandless palladium-catalyzed cross-coupling discussed above occurs readily in the presence of bases in aqueous solution under mild conditions (20-100°C, 10 min - 5 h, high yields) and exhibits broad functional group tolerance. Unfortunately, this efficient and convenient procedure for the synthesis of polyfunctional biaryls can't be used on large scale, because iodo- and bromo-arenes are expensive. Aryl chlorides are the most suitable aryl halides for applications in industrial synthesis, since they are inexpensive and readily available in bulk quantities. The attention of numerous research groups has been directed for many years in the catalytic activation, cleavage, and functionalization of the C-Cl bond in aryl chlorides.⁵ In most cases catalytic reactions of aryl chlorides require nickel complexes as the catalyst, because the metal center in Ni(0) compounds readily undergoes oxidative addition with aryl chlorides. Recently,⁵ high efficient palladium complexes containing Cy₃P, 1,3-bis(diisopropylphosphino)propane or other bidentate phosphines have been reported for various reactions of ArCl.

We have found that Ph₄BNa reacts with aryl chlorides in the presence of PdCl₂ and NaOH at 100°C in water.



We studied the influence of catalyst and base on the yield of cross-coupling product in the model reaction of Ph₄BNa with *p*-chlorobenzoic acid in water (Table 6).

The best conversion of *p*-ClC₆H₄COOH to *p*-phenylbenzoic acid was achieved in the presence of PdCl₂ (3 mol%) as catalyst and NaOH as a base.



Under these conditions (3 mol % PdCl₂, NaOH, H₂O, 100°) even chlorophenols react with Ph₄BNa to give hydroxybiphenyls in moderate yields (Table 7).

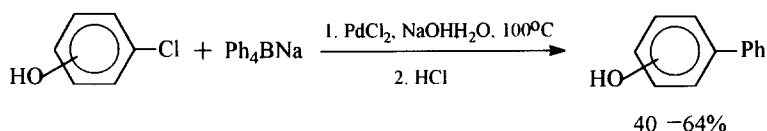


Table 6. Cross-Coupling of *p*-Chlorobenzoic Acid with Ph₄BNa under Various Reaction Conditions^a

Entry	Catalyst, (mol%)	Base (mmol)	Borane, (mmol)	t, h	Yield ^b , %
1	PdCl ₂ (1)	Na ₂ CO ₃ (2)	Ph ₄ BNa (0.27)	7	22
2	-, -	NaOH (2.1)	-, -	6	49
3	-, -	NaOH (4)	-, -	6	73
4	-, -	NaOH (8)	-, -		72
5	PdCl ₂ [PPh ₂ (<i>m</i> -C ₆ H ₄ SO ₃ Na)] ₂ (1)	NaOH (4)	-, -	5	26
6	Pd(acac) ₂ (1)	-, -	-, -	7	68
7	PdCl ₂ dppf (1)	-, -	-, -	3	0
8	PdCl ₂ (5)	-, -	-, -	7	75
9	PdCl ₂ (1)	-, -	Ph ₄ BNa (0.54)	5	81
10	PdCl ₂ (3)	-, -	Ph ₄ BNa (1)	3	92
11 ^c	-, -	-, -	Ph ₄ BNa (0.27)	7	59
12 ^d	-, -	-, -	Ph ₄ BNa (0.54)	5	95
13	PdCl ₂ (1)	-, -	PhB(OH) ₂ (1.3)	13	19
14	PdCl ₂ (1)	-, -	TolB(OH) ₂ (1.3)	5	trace

^a Reactions were carried out in water (10 mL) at 100°C by using ArX (1 mmol), Ph₄BNa or ArB(OH)₂, base, and catalyst, unless otherwise noted. ^b Yields (by TLC and UV spectroscopy) are based on ArCl. ^c 90°C. ^d 10 mol% of Na₂Cr₂O₇.

In the case of more reactive aryl chlorides such as 3-nitro-4-chlorobenzoic acid, the cross-coupling proceeds more smoothly in the presence of Na_2CO_3 as base.

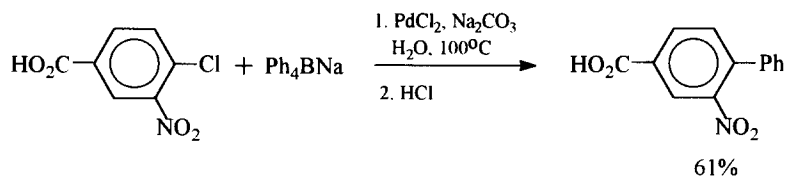
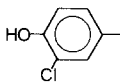
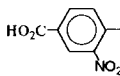
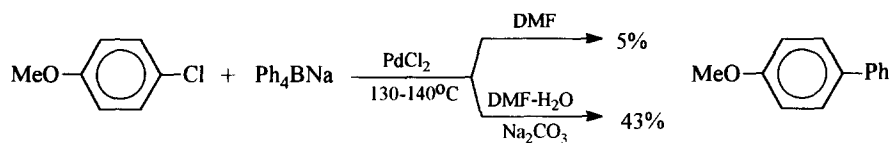


Table 7. Cross-Coupling Reactions of Ph_4BNa with Aryl Halides^a

Entry	Ar in ArCl	Base (mmol)	Solvent	T ($^\circ\text{C}$)	t, h	Yield ^b , %
1 ^c	<i>p</i> - HOC_6H_4	NaOH (4)	H_2O	100	3	(40)
2	<i>m</i> - HOC_6H_4	NaOH (4)	H_2O	100	3	64
3	<i>o</i> - HOC_6H_4	NaOH (4)	H_2O	100	3	55
4		NaOH (4)	H_2O	100	3	45
5 ^c		Na_2CO_3 (3)	H_2O	100	3	(61)
6	<i>p</i> - MeOC_6H_4	Na_2CO_3 (1)	$\text{HMPA-H}_2\text{O}$ (4:1)	130	3	36
7	— " —	Na_2CO_3 (1)	$\text{DMF-H}_2\text{O}$ (4:1)	130	4	34
8	— " —	Na_2CO_3 (1)	$\text{DMF-H}_2\text{O}$ (13:1)	140	4	43
9	— " —	Na_2CO_3 (1)	DMF	130	5	20
10	<i>p</i> - AcC_6H_4	Na_2CO_3 (1)	$\text{DMF-H}_2\text{O}$ (4:1)	130	2	78

^a Reactions were carried out in water (10 mL) or in mixture $\text{DMF(HMPA)-H}_2\text{O}$ (5 mL) by using ArCl (1 mmol), Ph_4BNa (1 mmol), base and 3 mol% of PdCl_2 (0.3 mL of 0.1 M PdCl_2), unless otherwise noted. ^b Yields (by TLC and UV spectroscopy) are based on ArCl and the isolated yields are in parentheses. ^c 0.54 mmol of Ph_4BNa .

Water-insoluble aryl chlorides react with Ph_4BNa in $\text{HMPA-H}_2\text{O}$ or $\text{DMF-H}_2\text{O}$ mixtures at high temperature. The yield of cross-coupling product decreases dramatically in the absence of water and bases.



There are the first examples of cross-coupling reactions between chloroarenes and organoboron compounds catalyzed with phosphine free palladium catalysts. These results demonstrate that palladium(0) complexes (which are generated from PdCl_2 in the presence of aqueous alkali) readily undergo oxidative addition of aryl chlorides under relatively mild conditions ($100-140^\circ\text{C}$) even in the absence of phosphine ligands.

EXPERIMENTAL

^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a VXR-400 Varian spectrometer and are referenced to residual protic solvents with chemical shifts being reported as δ (ppm) from TMS. The palladium complexes⁶, arylboronic acids⁷ and aryl iodides were prepared by standard procedures. Commercially available aryl bromides and Ph_4BNa were used without purification. A typical experimental procedure is given below.

Typical procedure for the reaction of $m\text{-IC}_6\text{H}_4\text{CO}_2\text{H}$ with PhB(OH)_2 (Table 1). 3-Iodobenzoic acid (124 mg, 0.5 mmol) and a base (1 mmol) was dissolved in H_2O (1-2 mL) under argon. Then, PhB(OH)_2 (98 mg, 0.55 mmol) and palladium salt (1 mol.%) were added. The mixture was stirred at room temperature and tested by GLC to check the completion of the reaction. When all the starting iodide was consumed, dilute HCl and an internal standard (p-aminobenzoic acid) were added and the mixture was extracted with ether. The product yield was determined by GLC analysis after methylation with diazomethane.

3-Phenylbenzoic acid (Table 2). 3-Iodobenzoic acid (248 mg, 1 mmol), Na_2CO_3 (318 mg, 3 mmol), PhB(OH)_2 (134 mg, 1.1 mmol) were dissolved in H_2O (4 mL) under argon. Then Pd(OAc)_2 (2.2 mg, 0.01 mmol) was added. The reaction mixture was stirred for 10 min at room temperature. Then Pd-black was filtered off. The filtrate was diluted with water (150 mL) and treated with HCl until it was acidic to litmus. The precipitate was filtered off, washed with water and dried over P_2O_5 under reduced pressure to give 185 mg (93%) of 3- $\text{PhC}_6\text{H}_4\text{CO}_2\text{H}$, mp. $165-166^\circ\text{C}$ (lit.⁸ mp 166°C).

3-(4-Fluorophenyl)benzoic acid (Table 2). A mixture of 3-iodobenzoic acid (248 mg, 1 mmol), H_2O (4 mL), 4- $\text{FC}_6\text{H}_4\text{B(OH)}_2$ (157 mg, 1.1 mmol) and 1.07 mL of 3.7 M NaOH (4 mmol) was stirred for 30 min under argon and then Pd(OAc)_2 (2.2 mg, 0.01 mmol) was added. The reaction mixture was stirred for 5 min at room temperature when Pd-black was filtered off. The filtrate was diluted with water (150 mL) and treated with HCl till it was acidic to litmus. The precipitate was filtered off, washed with water and dried over P_2O_5 under reduced pressure to give 207 mg (96%) of 3-(4- FC_6H_4) $\text{C}_6\text{H}_4\text{CO}_2\text{H}$ as a colourless solid, m.p. $183-185^\circ\text{C}$. ^1H NMR (CD_3COCD_3): 7.25 (t, $J = 8.6$ Hz, 2H), 7.59 (t, $J = 8.0$ Hz, 1H), 7.71-7.76 (m, 2H), 7.88 (d, $J = 7.6$ Hz, 1H), 8.03 (d, $J = 7.8$ Hz, 1H), 8.26 (s, 1H). Anal. Calcd for $\text{C}_{13}\text{H}_9\text{FO}_2$: C, 72.2; H, 4.15; F, 8.8. Found: C, 72.6; H, 4.1; F, 8.85.

5-(4-Fluorophenyl)salicylic acid (Table 2). 5-Bromosalicylic acid (217 mg, 1 mmol), Na_2CO_3 (318 mg, 3 mmol) and $\text{p-FC}_6\text{H}_4\text{B(OH)}_2$ (157 mg, 1.1 mmol) were dissolved in H_2O (5 mL) under argon and Pd(OAc)_2 (2.2 mg, 0.01 mmol) was added. The reaction mixture was stirred at room temperature. After 1 h the slurry was dissolved in water (300 mL) and filtered. The filtrate was treated with HCl until it was acidic to litmus. The precipitate was filtered off, dried and dissolved in acetone (15 mL). The acetone solution was filtered to remove a trace of Pd-black and diluted with water (150 mL). The precipitate was filtered off, washed with water and dried over P_2O_5 under reduced pressure to give 209 mg (90%) of 5-(4-fluorophenyl)salicylic acid as a colourless solid, m. p. 203-205°C. $^1\text{H NMR}$ (CD_3COCD_3): 6.20 (br. s, 1H, OH), 7.04 (d, $J = 8.4$ Hz, 1H), 7.20 (t, $J = 9.0$ Hz, 2H), 7.62-7.67 (m, 2H), 7.77-7.82 (dd, $J = 8.2$ Hz, 1H), 8.09-8.11 (d, 1H), 11.13 (s, 1H, COOH). Anal. Calcd for $\text{C}_{13}\text{H}_9\text{FO}_3$: C, 67.25, H, 3.9; F, 8.2. Found: C, 67.3; H, 3.7; F, 8.2.

5-Phenylsalicylic acid (Table 3). 5-Bromosalicylic acid (217 mg, 1 mmol), Na_2CO_3 (318 mg, 3 mmol) and Ph_4BNa (89.4 mg, 0.26 mmol) were dissolved in H_2O (10 mL) under argon and Pd(OAc)_2 (2.2 mg, 0.01 mmol) was added. The reaction mixture was stirred at the room temperature. After 1 h the slurry was treated with HCl until it was acidic to litmus. The precipitate was filtered off and dissolved in ether (30 mL). The ether solution was filtered to remove Pd-black. The residue, after evaporation of the ether, was dissolved in aqueous 0.01 M NaOH (300 mL) and filtered. The filtrate was treated with HCl. The precipitate was filtered off, washed with water and dried over P_2O_5 under reduced pressure to afford 177 mg (79%) of 5-phenylsalicylic acid, m. p. = 212-214°C (lit.⁹ mp 213-214°C). $^1\text{H NMR}$ (CD_3COCD_3): 5.90 (br. s, 1H, OH), 7.03-7.06 (m, 1H, ArH), 7.30-7.35 (m, 1H, PhH), 7.42-7.46 (m, 2H, PhH), 7.60-7.63 (m, 2H, PhH), 7.81-7.83 (m, 1H, ArH), 8.13-8.14 (1H, ArH).

4-Nitrobiphenyl (Table 4). Pd(OAc)_2 (2.2 mg, 0.01 mmol) was added to p-iodonitrobenzene (249 mg, 1 mmol), H_2O (5.3 mL), 0.67 mL of 1.5 M Na_2CO_3 (1 mmol) and Ph_4BNa (91.2 mg, 0.267 mmol) under argon. The reaction mixture was boiled under reflux for 2 h under vigorously stirring. After being cooled to room temperature, the mixture was treated with HCl and extracted with ether. GLC analyses of this material revealed the formation of 4-nitrobiphenyl in a yield of 96%.

4-Fluorobiphenyl (Table 4). The mixture of iodobenzene (816 mg, 4 mmol), 4-fluorophenylboronic acid (616 mg, 4.4 mmol), 5.34 mL of 1.5 M Na_2CO_3 (8 mmol) and aqueous 0.1 M PdCl_2 (0.4 mL, 0.04 mmol) in H_2O (10 mL) was vigorously stirred at 100°C for 2 h. After cooling, the resulting mixture was extracted with ether. The residue after evaporation of ether was dissolved in EtOH and precipitated with water. The precipitate was washed with water and dried over P_2O_5 under reduced pressure to afford 585 mg (85%) of 4- $\text{FC}_6\text{H}_4\text{Ph}$, m. p. = 74-76°C (lit.¹⁰ mp 74.2°C). $^1\text{H NMR}$ (CD_2Cl_2): 7.12-7.19 (m, 2H), 7.33-7.39 (m, 1H, Ph), 7.42-7.48 (m, 2H), 7.55-7.64 (m, 4H, Ph). $^{13}\text{C NMR}$ (CD_2Cl_2): 115.77 (d, $J_{\text{C-F}} = 21.3$ Hz), 127.28 (s), 127.64 (s), 129.03 (d, $J_{\text{C-F}} = 8.2$ Hz), 129.17 (s), 137.68 (d, $J_{\text{C-F}} = 3.2$ Hz), 140.45 (s), 162.81 (d, $J_{\text{C-F}} = 244$ Hz).

4-[4-(4-trans-n-Amylcyclohexyl)phenyl]phenol (Table 4). H_2O (0.8 mL), Na_2CO_3 (318 mg, 3 mmol) and Pd(OAc)_2 (2.2 mg, 0.01 mmol) were added to a stirred solution of 4-(4-trans-n-amylcyclohexyl)phenylboronic acid (274 mg, 1 mmol) and 4-iodophenol (220 mg, 1 mmol) in DMF (3.2 mL). The reaction mixture was stirred under argon at 50°C. After 4 h the mixture was diluted with water (100 mL). The precipitate was filtered off, washed with water and extracted with ether. The ether extract was filtered, diluted hexane and evaporated until it started to precipitate. The precipitate was filtered off and dried over P_2O_5 under reduced pressure to afford 206 mg (64%) of 4-[4-(4-trans-n-amylcyclohexyl)phenyl]phenol as a

colourless solid, m. p. 208-210°C. ^1H NMR (CD_3COCD_3): 0.87-0.93 (t, 3H, CH_3), 1.04-1.15 (m, 2H), 1.22-1.40 (m, 9H), 1.46-1.58 (m, 2H), 1.85-1.92 (brd, 4H), 2.47-5.56 (m, 1H), 6.91 (d, $J = 8.4$ Hz, 2H), 7.27 (d, $J = 8.4$ Hz, 2H), 7.43-7.50 (m, 4H), 8.83 (s, 1H, OH). Anal. Calcd for $\text{C}_{23}\text{H}_{30}\text{O}$: C, 85.7; H, 9.3. Found: C, 85.5; H, 9.3.

4-(4-trans-n-Amylcyclohexyl)-4'-difluoromethylthiobiphenyl (Table 4). H_2O (21.6 mL), 28.8 mL of 1.6M Na_2CO_3 (45 mmol) and $\text{Pd}(\text{OAc})_2$ (0.0238 g, 0.108 mmol, 0.5 mol.%) were added to a stirred solution of $p\text{-IC}_6\text{H}_4\text{SCHF}_2$ (6.19 g, 21.64 mmol) and 4-(4-trans-n-amylcyclohexyl)phenylboronic acid (6.52 g, 21.66 mmol) in DMF (58.5 mL). The reaction mixture was vigorously stirred at 80°C for 2 h, then diluted with water (150 mL) and extracted with hexane. The crude product, after evaporation of the hexane, was chromatographed on SiO_2 with hexane as the eluent. Yield 90% of a colourless solid, m. p. 93-94°C. ^1H NMR (CD_3COCD_3): 0.87-0.91 (t, 3H, CH_3), 1.04-1.15 (m, 2H), 1.21-1.39 (m, 9H), 1.46-1.58 (m, 2H), 1.85-1.93 (brd, 4H), 2.50-2.59 (m, 1H), 7.28 (t, $J_{\text{H-F}} = 56$ Hz, 1H), 7.35 (d, $J = 8.4$ Hz, 2H), 7.60 (d, $J = 8.4$ Hz, 2H), 7.67 (d, $J = 8.4$ Hz, 2H), 7.72 (d, $J = 8.4$ Hz, 2H). Anal. Calcd for $\text{C}_{24}\text{H}_{30}\text{F}_2\text{S}$: C, 74.2; H, 7.7; S, 8.25. Found: C, 74.5; H, 7.9; S, 8.6.

Reaction of 3-bromobenzoic acid with Ph_4BNa catalyzed of 0.0004 mol.% PdCl_2 . H_2O (2.56 mL), an aqueous 1.5 M Na_2CO_3 (1.34 mL, 2 mmol), Ph_4BNa (92.4 mg, 0.27 mmol) and aqueous 0.00004 M PdCl_2 (0.1 mL, $4 \cdot 10^{-6}$ mmol) were added to 3-bromobenzoic acid (201 mg, 1 mmol) under argon. The reaction mixture was stirred at 100°C for 4 h. After being cooled to room temperature, the mixture was treated with dilute HCl, extracted with ether (25 mL \times 4) and analysed by TLC and UV spectroscopy.¹¹ The analysis revealed the formation of 3-phenylbenzoic acid in a yield of 100%.

4-(4-Tolyl)benzoic acid. A solution of 4-TolMgBr obtained from Mg (0.389 g, 16 mmol) and 4-bromotoluene (2.736 g, 16 mmol) in ether (11 mL) was added dropwise to a vigorously stirred solution of $\text{B}(\text{OMe})_3$ (0.416 g, 4 mmol) in ether (5 mL) and the mixture then was boiled under reflux for 15 min. A solution of NaOH (2 g, 50 mmol), 4-iodobenzoic acid (2.48 g, 10 mmol) and 1 mL of 0.1 M PdCl_2 (0.0177 g, 0.1 mmol) in water (70 mL) was added dropwise to the resulting mixture. After being boiled under reflux for 1 h the mixture was extracted with ether. The ether extracted was diluted by hexane and evaporated until it started to precipitate. The precipitate was filtered off, washed with hexane and dried over P_2O_5 under reduced pressure to give 1.27 g (60%) of 4-(4-MeC₆H₄)C₆H₄CO₂H, m. p. 250-252°C (lit.¹² mp 243-244°C). ^1H NMR ((CD_3)₂SO): 2.34 (s, 3H, CH_3), 7.30 (d, $J = 8.2$ Hz), 7.62 (d, $J = 8.2$ Hz), 7.76 (d, $J = 8.4$ Hz), 8.00 (d, $J = 8.4$ Hz). ^{13}C NMR ((CD_3)₂SO): 20.83 (CH_3), 126.58, 126.90, 129.49, 129.51, 130.08, 136.22, 137.93, 144.33, 167.38 (CO_2H).

Benzophenone. To stirred aqueous 1.6 M Na_2CO_3 (1 mL, 1.6 mmol) was added Ph_4BNa (92.2 mg, 0.27 mmol), acetone (2 mL), benzoyl chloride (140 mg, 1 mmol) and 0.1 mL of 0.1 M PdCl_2 (0.01 mmol) in H_2O . The reaction mixture was vigorously stirred at 20°C for 3 h. Then, the mixture was diluted with water (10 mL) and extracted with ether (25 mL \times 4). Analysis (by TLC and UV spectroscopy) of this stage revealed the formation of PhCOPh in yield of 94%.

4-Phenylphenol (Table 7). H_2O (9 mL), 0.74 mL of 5.4 M NaOH (4 mmol), 0.3 mL of 0.1 M PdCl_2 (3 mol%) and Ph_4BNa (185 mg, 0.54 mmol) were added to 4-chlorophenol (129 mg, 1 mmol) under argon. The reaction mixture was boiled under reflux for 5 h. After being cooled to room temperature, Pd-black was filtered

off. The filtrate was treated with HCl until it was acidic to litmus. The precipitate was filtered off and crystallised from ethanol-water. Yield 40% of a colourless solid, m. p. 165-166°C (lit.¹³ mp 166).

3-Nitro-4-phenylbenzoic acid (Table 7). 1.92 mL of 1.6 M Na₂CO₃ (3 mmol), 3-nitro-4-chlorobenzoic acid (202 mg, 1 mmol) and 7.8 mL of H₂O and Ph₄BNa (1.85 mg, 0.54 mmol) were added to 0.3 mL of 0.1 M PdCl₂ (0.03 mmol) in H₂O (0.03 mmol). The reaction mixture was boiled under reflux for 3h, cooled and 0.5 mL of 29% H₂O₂ added. After being stirred for 1 h at room temperature, the mixture was filtered from Pd-black and treated with HCl. The precipitate was filtered off, dried and dissolved in ether/hexane (1:4). Resulting solution was filtered to remove the Pd-black traces. The solvent was evaporated, the residue dissolved in *i*-PrOH and precipitated with water. The precipitate was filtered off washed with water and dried over P₂O₅ under reduced pressure to give 148 mg (61%) of 3-nitro-4-phenylbenzoic acid, m.p. 189-191°C (lit.¹⁴ mp 191°C). ¹H NMR (CD₃COCD₃): 7.30-7.32 (m, 2H, Ph), 7.39-7.44 (m, 3H, Ph), 7.53 (d, 1H, Ar, J= 8.0), 8.26 (dd, 1H, Ar, J=8.0, J=1.6), 8.46 (d, 1H, Ar, J=1.6).

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