Phosphine ligand and base-free, Pd- catalyzed oxidative cross-coupling reaction of arylboronic acids with arylmercuric acetates

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Abstract
Arylmercuric acetates have been found to undergo Suzuki type cross coupling reactions with arylboronic acids catalyzed by palladium salts in non-polar solvents under ambient conditions to give biaryl derivatives in high yields. The reaction is mild and does not require any organic or inorganic base nor a phosphine ligand.

Keywords: Arylmercuric acetate, Suzuki coupling, palladium salts, arylboronic acid

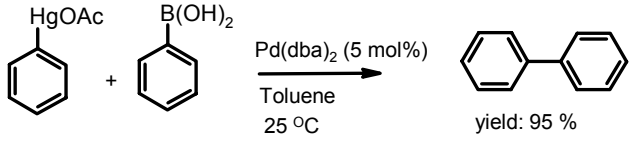
Introduction

The palladium-catalyzed Suzuki-Miyaura coupling of aryl halides with arylboronic acids or esters is one of the most powerful and versatile methods for the formation of C-C bonds, in particular for the preparation of biaryl compounds.[1] In recent years, this reaction has been successfully applied for the synthesis of natural products, [2] drugs[3] and conducting polymers.[4] The massive interest for the Suzuki reaction can be explained by the impressively wide range of substrates' tolerance, relatively higher stability and less toxicity of boronic acids. The development of improved conditions for the Suzuki reaction has received much recent attention due to the importance of biaryls that find applications in a range of pharmaceuticals, herbicides, as well as in conducting polymers and liquid crystalline materials. In addition to a wide range of metal complexes including palladacycles that have been employed,[5] several new coupling partners such as aryl iodonium salts, [6] aryl sulfonyl chlorides, [7] diazonium salts,[8] aryltrimethylammonium salts,[9] aryltellurides,[10] benzylic phosphates and carbonates[11] etc. were successfully coupled with arylboronic acid to afford biaryls.

Organomercuric compounds are an important class of organometallic compounds and a number of methods are available for their synthesis.[12] The ability of arylmercuric compounds to undergo oxidative addition with palladium was first reported by Heck.[13]

Results and discussion

In this communication we wish to report the use of arylmercuric acetates, prepared following the known electrophilic mercuration methods,[12b] as the coupling partner with the boronic acid in non-polar solvents to get biaryl compounds under ambient temperature. It has been reported that the reaction of arylboronic acids with mercuric salts in polar solvent such as methanol led to the isolation of diarylmercury.[14] We found that when the same reaction was carried out in non-polar solvents like toluene in the presence of palladium salts as catalyst, it took a different course to give the cross coupled biaryls in good yield (Scheme 1).



Scheme 1. Pd-Catalyzed Suzuki-type coupling reaction of arylmercuric acetate.

In order to study this catalytic system in a systematic manner, several metal salts and solvents have been screened and the results are shown in the Table 1. Remarkably, palladium salts were found to be extremely active and gave excellent yield of biphenyl over other metal complexes. The maximum yield of biphenyl was obtained with $Pd(dba)_2$ whereas Pd/C gave a poor yield. Other metals like Cu, Ni and Ru were found to be inactive. Among the solvents screened, toluene gave excellent yields while the more polar solvents like MeOH, CH_3CN, H_2O and dioxane resulted in diphenyl mercury as the major product. Another interesting feature of this reaction is that the base, which is typically an important requirement in palladium-catalyzed coupling reactions, was not required. On the contrary, addition of organic bases increases the polarity of the system and thus resulted in the formation of diphenyl mercury in considerable amounts.

With the optimized conditions in hand we subjected a variety of boronic acids with phenylmercuric acetate and the results are given in the Table 2. In all the cases a <5% of homo-coupled product was isolated. Attempts to avoid the homo-coupled product by reducing the reaction temperature (up to 15 ºC) had no considerable effect. The cross coupling reaction was successful only in the case of arylmercuric acetate and failed in the case of arylmercuric bromide or chloride. In the case of 4-chlorophenylmercuric acetate the boronic acid replaced only the mercuric acetate while the chlorine was unaffected. The easily oxidizable aldehyde group was found to be unaffected under these reaction conditions. After the reaction, the Pd-catalyst was deposited as a black colored particle and mercury (II) as mercury metal.

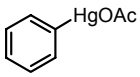
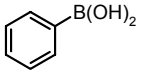
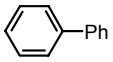
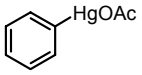
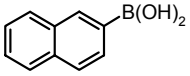
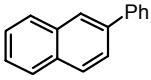
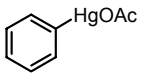
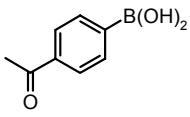
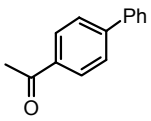
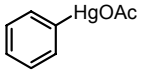
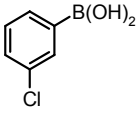
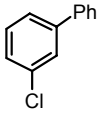
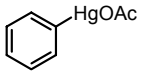
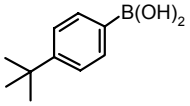
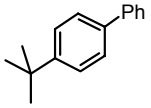
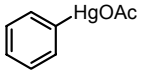
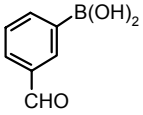
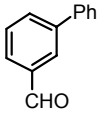
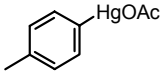
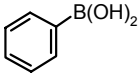
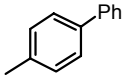
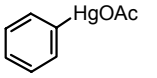
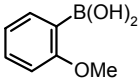
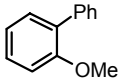
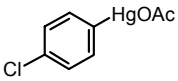
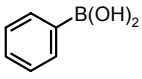
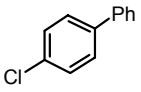
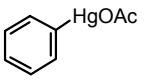
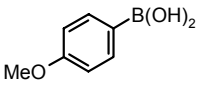
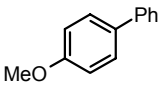
Table 1. Effect of the catalyst and solvent on the coupling reaction of phenylboronic acid with phenyl mercuric acetate[a]

Entry	Catalyst	Solvent	Yield (%)[b]
1	$PdCl_2$	toluene	82
2	$Pd(OAc)_2$	toluene	90
3	$Pd(dba)_2$	toluene	95
4	$Pd(PPh_3)_4$	toluene	93
5	$RuCl_3.3H_2O$	toluene	trace
6	$RuH_2CO(PPh_3)_3$	toluene	0
7	5% Pd/C	toluene	11c
8	$Pd(dba)_2$	DMF	14
9	$Pd(dba)_2$	CH_2Cl_2	87
10	$Pd(dba)_2$	$CHCl_3$	78
11	$Pd(dba)_2$	CCl_4	53
12	$Pd(dba)_2$	dioxane	20
13	$Pd(dba)_2$	CH_3CN	trace

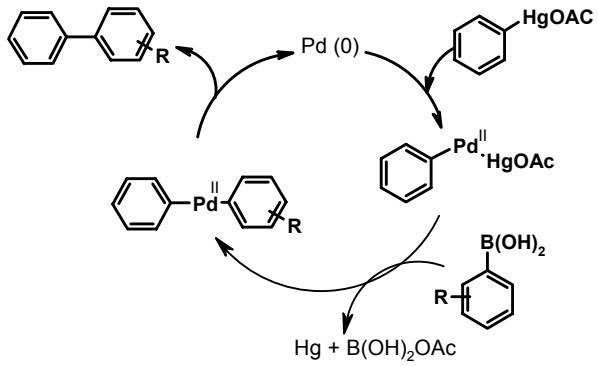
[a] Reaction conditions. Phenylmercuric acetate (3 mmol), phenylboronic acid (3 mmol), catalyst (5 mol %), solvent (5 ml), 25 ºC, 3 h.
[b] Isolated yield by column chromatography.

One may expect the reaction to proceed through two different routes, i.e. i) normal Suzuki coupling mechanism of oxidative addition followed by aryl transfer and reductive elimination (Scheme 2) ii) initial formation of a diarylmercury followed by its dimerization[15] catalyzed by palladium. Since dimerization requires high temperatures and highly polar solvents like HMPA, MeOH, CH_3CN, etc. we presume the reaction to follow the Suzuki coupling pathway. The non-requirement of base may be ascribed to the acetate anion liberated from the phenylmercuric acetate acting as base and increasing the nucleophilicity of the neutral boronic acid and thereby facilitating the transmetallation from boron to organopalladium. This assumption also explains the inactivity of arylmercuric halides towards arylboronic acid under these reaction conditions.

Table 2. Pd- Catalyzed Suzuki-type cross coupling reaction[a] between arylmercuric acetate and arylboronic acid

Entry	Substrate	Boronic acid	Product	Yield (%)[b]
1				95
2				92
3				71
4				77
5				89
6				75
7				85
8				82
9				74
10				78

[a] Reaction conditions: arylmercuric acetate (3 mmol), aryl boronic acid (3 mmol) $Pd(dba)_2$ (5 mol%), toluene (5 mL), 25 °C , 3 h.
[b] isolated yield by column chromatography.



Scheme 2. Proposed mechanistic pathway.

In conclusion, we have described that arylmercuric acetates underwent smooth coupling with arylboronic acids in a non-polar solvent in the presence of palladium as catalyst under ambient conditions to give the corresponding biaryl compound. A remarkable feature of this system is that neither a base nor a phosphine ligand was required.

Experimental Section

General procedure for the Pd- catalyzed coupling of arylmercuric acetates with boronic acids:

To a mixture of arylmercuric acetate (3 mmol) and $Pd(dba)_2$ (5 mol%) in toluene (10 ml) was added arylboronic acid (3 mmol) and the reaction mixture was stirred at 25 °C. The reaction was monitored periodically by TLC. After the completion of the reaction, the reaction mixture was extracted with ethyl acetate washed twice with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was purified by column chromatography.

Biphenyl: Yield: 78%; Colorless solid, mp: 68–71 °C; IR ($CHCl_3$, cm^{-1}) 3008, 2986, 1602, 1424; ^1H NMR ($CDCl_3$): δ 7.18–7.65 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 127.23, 127.31, 128.81, 141.32; Elemental analysis calculated for $C_{12}H_{10}$: required C, 93.46; H, 6.54. Found: C, 93.51; H 6.60.
2-Phenylnaphthalene: Yield: 89%; Colorless solid, mp: 105 °C; IR ($CHCl_3$, cm^{-1}): 668, 688, 758, 770, 820, 860, 892, 1076, 1216, 1452, 1496, 1598, 1948, 3106, 3058; ^1H NMR (200 MHz, $CDCl_3$): δ 7.40-8.27 (m, 12H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 125.32, 125.70, 125.98, 126.06, 126.90, 127.19, 127.65, 128.24, 130.05, 131.67, 133.84, 140.27, 140.80; Elemental analysis calculated for $C_{16}H_{12}$: C, 94.08; H, 5.92. Found: C, 94.29; H, 5.70.
1-Biphenyl-4-yl-ethanone: Yield: 78%; Colorless solid, mp: 118 °C; IR ($CHCl_3$, cm^{-1}): 595, 668, 697, 756, 1007, 1216, 1267, 1358, 1604, 1680, 3019; ^1H NMR (200 MHz, $CDCl_3$): δ 2.59 (s, 3H), 7.40-7.47 (m, 3H), 7.56-7.65 (m, 4H), 7.97-8.01 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ

26.35, 127.06, 128.06, 128.79, 135.67, 139.67, 145.48, 196.87; Elemental analysis calculated for $C_{14}H_{12}O$: required C, 85.68; H, 6.16. Found: C, 85.59; H, 6.42.

3-Chlorobiphenyl: Yield: 86%; viscous liquid, IR ($CHCl_3$, cm^{-1}): 523, 624, 766, 803, 892, 1014, 1061, 1114, 1420, 1604, 1694, 1766, 1810, 1884, 1957, 3033, 3086; ^1H NMR (200 MHz, $CDCl_3$): δ 7.16-7.44 (m, 9H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 125.25, 127.12, 127.27,127.36, 127.86, 128.89, 129.94, 134.76, 139.85, 143.14; Elemental analysis calculated for $C_{12}H_9Cl$: C, 76.4; H, 4.81; Cl, 18.79. Found: C, 76.12; H, 4.95; Cl, 18.54.

4-t Butylbiphenyl: Yield: 89%; Colorless solid; mp 48 °C; IR ($CHCl_3$) 2962, 1486, 1179, 836, 766; ^1H NMR ($CDCl_3$) δ 1.41 (s, 9H), 7.3-7.64 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 150.5, 141.3, 138.6, 129, 127.3, 127.2, 127, 126, 34.8, 31.7; Elemental analysis calculated for $C_{16}H_{18}$: required C, 91.38; H, 8.62. Found: C, 90.23; H, 9.5.

Biphenyl-3-carbaldehyde: Yield: 75%; Colorless solid, mp 53–54 °C; IR ($CHCl_3$, cm^{-1}) 2982, 2832, 1690, 1592, 1200, 720; ^1H NMR ($CDCl_3$) δ 9.9 (s, 1H), 8.01 (m, 1H) 7.78 (m, 2H), 7.49 (m, 3H), 7.32 (m, 2H), 7.21(m, 1H); ^{13}C NMR ($CDCl_3$) δ 191.2, 137.2, 137.1, 136.6, 133.34, 129.8, 129.3, 129.2, 128.5, 127.9,127.8, 127.3, Elemental analysis calculated for $C_{13}H_{10}O$: required C, 85.69; H, 5.53. Found: C, 85.72; H, 5.55.

4-Methylbiphenyl: Yield: 95%; viscous liquid; IR ($CHCl_3$, cm^{-1}): 546, 667, 760, 822, 1038, 1352, 1598, 1907, 2589, 2583, 3065; ^1H NMR (200 MHz, $CDCl_3$): δ 2.36 (s, 3H), δ 7.20-7.57 (m, 9H); ^{13}C NMR (50MHz, $CDCl_3$): δ 21.15, 126.82, 126.99, 127.17, 128.70, 129.47, 136.80, 138.43, 141.21; Elemental analysis calculated for $C_{13}H_{12}$: C, 92.81; H, 7.19. Found: C, 92.64; H, 7.40.

2-Methoxybiphenyl: Yield: 82%; viscous liquid; IR ($CHCl_3$, cm^{-1}): 565, 612, 667, 698, 732, 753, 800, 1028, 1055, 1122, 1236, 1259, 1463, 1504, 1597, 2834, 2956, 3011, 3061; ^1H NMR (200 MHz, $CDCl_3$): δ 3.71 (s, 3H), 6.75-7.49 (m, 9H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.30, 111.34, 120.80, 121.62, 126.66, 127.76, 128.43, 128.52, 129.44, 130.72, 133.25, 138.66, 156.48; Elemental analysis calculated for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.85; H, 6.49.

4-Chlorobiphenyl: Yield: 74%; viscous liquid; IR ($CHCl_3$, cm^{-1}): 803, 892, 1061, 1114, 1420, 1604, 1694, 1766, 1810, 1884, 1957, 2983, 3033; ^1H NMR ($CDCl_3$) δ 7.52 (m, 4H), 7.4 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 140, 139.6, 133.3, 129, 128.9, 128.4, 127.6, 127; Elemental analysis calculated for $C_{12}H_9Cl$: C, 76.4; H, 4.81; Cl, 18.79. Found: C, 76.01; H, 4.23.

4-Methoxybiphenyl: Yield: 81%; Colorless solid, mp: 87 °C ; IR ($CHCl_3$, cm^{-1}): 566, 703, 776, 845, 1051, 1130, 1198, 1304, 1414, 1462, 1530, 1615, 2917, 2970, 3065; ^1H NMR (200 MHz, $CDCl_3$): δ 3.72 (s, 3H), 6.85-7.46 (m, 9H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.11, 114.18, 126.65, 128.06, 128.67, 133.7, 140.8, 159.15; Elemental analysis calculated for $C_{13}H_{12}O$: C, 84.75; H, 6.56. Found: C, 84.55; H, 6.81.

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