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Suzuki coupling with ligandless palladium and potassium fluoride

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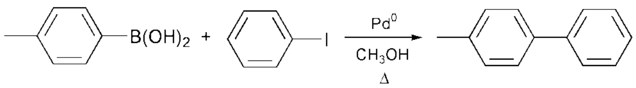
A ligandless palladium catalyzed Suzuki coupling reaction is described.

The palladium catalyzed carbon–carbon cross-couplings of organometallics with organoelectrophiles is an important synthetic reaction.[1] Most organometallic compounds are sensitive to air, moisture or are toxic and often will not tolerate functional groups which may be important in complex syntheses. Boronic acids constitute one of the few organometallic reagents that tolerate a wide range of functional groups, are available and generally environmentally benign. In addition, they are inert to air, resistant to heat, and can be recrystallized from water or alcohol.

The Suzuki reaction[2] which uses boron-containing precursors has gained considerable attention in recent years because a large number of functionally substituted boron-containing reagents are commercially available. The Suzuki reaction generally employs expensive organic solvents such as tetrahydrofuran as well as expensive complex palladium catalysts. These palladium reagents tend to be difficult to manipulate and recover. We recently reported an energy efficient modification of the Suzuki reaction using an alumina surface and palladium powder which solved some of these problems.[3,4]

Earlier studies revealed that potassium fluoride was an effective Suzuki base.[5] Therefore we selected KF as the base for the current study. We found that aromatic iodides readily couple with arylboronic acids in the presence of palladium powder when the reactions are carried out in methanol, Scheme 1. The initial results are summarized in Table 1. The reaction can be utilized to couple benzyl bromides with arylboronic acids but aryl bromides and aryl chlorides are ineffective substrates. Aliphatic boronic acids are also not reactive.



Scheme 1

Table 1 Suzuki coupling of tolylboronic acid with aryl iodides[a]

Boronic acid	Aryl iodide	Yield[b] (%)
4-Methylphenyl	1-Fluoro-2-iodobenzene	91
4-Methylphenyl	1-Iodo-4-nitrobenzene	94
4-Methylphenyl	2-Iodoaniline	77
4-Methylphenyl	4-Iodoacetophenone	93
4-Methylphenyl	4-Iodoanisole	83
4-Methylphenyl	2-Iodothiophene	93
4-Methylphenyl	2-Iodophenol	76
4-Methylphenyl	1-Fluoro-3-iodobenzene	98
4-Methylphenyl	4-Iodotoluene	89

[a] Reactions carried out utilizing 1.0 mmol of aryl iodide and 1.1 mmol of tolylboronic acid in refluxing methanol (5 mL) for 4 h in the presence of palladium powder. [b] Isolated yields.

Table 2 Suzuki coupling of arylboronic acids with aryl iodides[a]

Boronic acid	Aryl iodide	Yield[b] (%)
Naphthyl	Iodobenzene	90
Naphthyl	1-Iodo-4-nitrobenzene	89
Naphthyl	2-Iodoaniline	74
2-Methylphenyl	2-Iodothiophene	90
2-Methylphenyl	1-Iodo-4-nitrobenzene	93
2-Methylphenyl	Iodobenzene	97
3-Formylphenyl	2-Iodothiophene	98
3-Formylphenyl	1-Iodo-4-nitrobenzene	98

[a] Reactions carried out utilizing 1.0 mmol of aryl iodide and 1.1 mmol of arylboronic acid in refluxing methanol (5 mL) for 4 h in the presence of palladium powder. [b] Isolated yields.

From the data in Tables 1 and 2, it would appear that the reaction is relatively insensitive to the electronic nature of substituents on the aromatic ring.

The synthesis of 4-methylbiphenyl is representative: palladium black (0.050 g), KF (0.380 g), *p*-methylphenylboronic acid (0.150 g, 1.10 mmol) and iodobenzene (0.204 g, 1.0 mmol) were added to a clean, dry, 50 mL round bottomed flask. Methanol (5 mL) was added to the mixture and the solution was refluxed for 4 h in the open air. After decanting the solution, the product was isolated *via* flash chromatography to yield 4-methylbiphenyl (92.2%); m.p. 44.0–45.5 °C, ^{1}H NMR ($CDCl_3$; δ ppm): 7.40 (m, 9 H), 2.37 (s, 3H).

It is important to note that the palladium metal can be recovered and recycled by a simple decantation of the reaction solution. In one series of experiments, we carried out eight consecutive preparations of 4-methylbiphenyl with no significant loss in product yields. In each case, the palladium powder was recovered by decantation, washed with methanol, and the experiment repeated. We made no effort to rigorously exclude water from the reactions. In fact, successful syntheses were achieved in 20% aqueous methanol.

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Notes and references

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