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Pd(II)-Catalyzed Synthesis of Unsymmetrical Biaryls from Tetraphenylborate and Aryl Halides Under Microwave Activation

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ABSTRACT

A rapid and efficient method for synthesis of unsymmetrical biaryls under microwave irradiation conditions is described. The process involves the reactions of sodium tetraphenylborate with aryl halides in the presence of catalytic amount [$PdCl_2(PPh_3)_2$] with KF/Al_2O_3 under microwave irradiation to afford the unsymmetrical biaryls in good to excellent isolated yields.

Key Words: Palladium-catalyzed; Suzuki reaction; Microwave irradiation; Cross-coupling reactions.

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INTRODUCTION

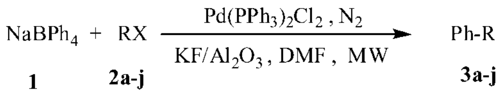
The palladium-catalyzed Suzuki cross-coupling[1] reaction of organoborate compounds with organic electrophiles is one of the most-efficient methods for the construction of carbon–carbon bonds. Indeed, in recent years, various efficient Pd catalyst precursors have been developed that allow aryl iodides, bromides, triflates, and chlorides to be effectively coupled with aryl boronic acids under mild reaction conditions.[2–4] Recently, Bumagin[2a] reported that the cross-coupling reaction of $NaBPh_4$ with acyl chlorides in the presence of $Pd(OAc)_2$ and Na_2CO_3 in dry or aqueous acetone gives high yields of unsymmetric ketones.

Microwave irradiation is known to accelerate many organic reactions in polar solvents or in the absence of solvent, and some important reviews on its application have been published.[5] Recently, we have reported the synthesis of unsymmetrical ketones[6] and conjugated acetylenic ketones[7] catalyzed by palladium(II) complex or copper(I) under microwave irradiation conditions. Several microwave assisted palladium-catalyzed cross-coupling reactions have been reported.[8]

In this paper, we wish to report a very simple, fast, economically viable and general method for palladium-catalyzed cross-coupling reactions of sodium tetraphenylborate with aryl halides in the presence of KF/Al_2O_3 under microwave irradiation conditions. The reactions are shown in Sch. 1, and results are summarized in Table 1. The results in Table 1 showed that the activities of aryl halides are in the following order: iodides > bromides > chlorides.

Using the reaction of sodium tetraphenylborate with bromobenzene as an example, we investigated the effects of the power and time of microwave irradiation for the formation of **3a**. The results are summarized in Tables 2 and 3. It was found that the high yield unsymmetric biaryls could be obtained at 675 W for 10 min under microwave irradiation conditions.

The amount of $[PdCl_2(PPh_3)_2]$ affected the yield, and the use of 5 mol% of the catalyst gives the best result. We investigated the effect of bases on the reaction of sodium tetraphenylborate with bromobenzene. It was found that the activity of bases is in the following sequence: $KF/Al_2O_3 > NaOH/Al_2O_3 > KF > Na_3PO_4/Al_2O_3 > Na_2CO_3/Al_2O_3 > Al_2O_3$.



$$\underset{\mathbf{1}}{NaBPh_4} + \underset{\mathbf{2a\text{-}j}}{RX} \xrightarrow[KF/Al_2O_3,\ DMF,\ MW]{Pd(PPh_3)_2Cl_2,\ N_2} \underset{\mathbf{3a\text{-}j}}{Ph\text{-}R}$$

Scheme 1.

Table 1. Preparation of unsymmetric biaryls **3a–j**.

Entry[a]	R (Ar)	X	Product[b]	Yield (%)[c]
1	Ph	I	**3a**	97
2	Ph	Br	**3a**	88
3	Ph	Cl	**3a**	78
4	4-$CH_3C_6H_4$	Br	**3b**	82
5	4-BrC_6H_4	Br	**3c**	84[d]
6	2-$C_{10}H_7$	Br	**3d**	86
7	1-$C_{10}H_7$	Br	**3e**	80
8	3-$CH_3C_6H_4$	I	**3f**	90
9	4-$O_2NC_6H_4$	I	**3g**	92
10	4-$O_2NC_6H_4$	Cl	**3g**	87
11	2-$O_2NC_6H_4$	I	**3h**	88
12	4-$CH_3OC_6H_4$	I	**3i**	89
13	2,5-Dimethylphenyl	Br	**3j**	79

[a] Mole ratio: $NaBPh_4$: aryl halide : $[PdCl_2(PPh_3)_2]$: KF/Al_2O_3 = 1 : 1.7 : 0.05 : 3.2.
[b] All products were determined by IR, ^1H NMR, and MS.
[c] Isolated yield.
[d] The product is 4-biphenylyl benzene.

The effectiveness of the microwave irradiation and conventional heating for the formation of compounds **3a–j** has been compared, and the results showed that the synthesis of compounds **3a–j** under microwave irradiation were 144 times faster than under conventional heating. This ratio between the reaction time using conventional reflux and microwave irradiation (t_c/t_{mw}) under same condition, quantifies the microwave heating effect.

EXPERIMENTAL

Microwave irradiation was carried out with a commercial microwave oven Glanz WP 750B at 2450 Hz. ^1H NMR spectra were recorded at

Table 2. Effect of the power of microwave irradiation on the formation of **3a**.[a]

Power (W)	375	450	525	600	675	750
Yield (%)[b]	31	46	57	69	88	83

[a] The reaction was carried out in the presence of KF/Al_2O_3 using $[PdCl_2(PPh_3)_2]$ as catalyst in DMF under nitrogen. Mole ratio: $NaBPh_4$: bromobenzene : $[PdCl_2(PPh_3)_2]$ = 1 : 1.4 : 0.05.
[b] Isolated yield.

Table 3. Effect of the time of microwave irradiation on the formation of **3a**.[a]

Time (min)	3	5	7	8	9	10	11	11	13
Yield (%)[b]	33	48	65	80	84	88	88	50[c]	88

[a] The reaction was carried out in the presence of KF/Al_2O_3 using $[PdCl_2(PPh_3)_2]$ as catalyst in DMF under nitrogen. Mole ratio: $NaBPh_4$: bromobenzene : $[PdCl_2(PPh_3)_2] = 1:1.4:0.05$.

[b] Isolated yield.

[c] None supported reagents (KF/Al_2O_3).

200 MHz on a Bruker PT 200A spectrometer in $CDCl_3$ with tetramethylsilane as internal standard. Chemical shifts were reported as δ in ppm. IR spectra were measured with an Alpha Centauri FI-IR spectrometer as KBr discs. Mass spectra were recorded on a QP-1000A GC-MS using the electron ionization mode (70 eV). Melting points were determined with an electrothermal micromelting point apparatus and are uncorrected. All solvents were used without further purification. The $[PdCl_2(PPh_3)_2]$ was prepared according to Ref.[9]

General Procedure for the Preparation of Compounds 3a–j

A mixture of sodium tetraphenylborate (1 mmol), aryl halide (1.7 mmol), $[PdCl_2(PPh_3)_2]$ (0.05 mmol), KF/Al_2O_3 (3.2 mmol), and DMF (15 mL) was irradiated at 675 W for 10 min by microwaves under a nitrogen atmosphere. The precipitate was filtrated, and the filtrate was poured into a saturated aqueous sodium chloride (50 mL) and extracted with diethyl ether (3 × 20 mL). The extracts were washed with water (3 × 20 mL) and then dried over with magnesium sulfate. The dried diethyl ether solution was concentrated to yield crude product, which was purified by column chromatography on silica gel (200–300 mesh) using petroleum/ethyl acetate (v/v, 20 : 1) as eluant or recrystallized **3a–j** in 78–90% yield. The following compounds were obtained:

Biphenyl (3a). M.p.: 68–69°C (Lit.[10]: 70°C). IR (KBr): 13,033, 1943, 1597, 1569, 1479, 1429, 1344, 1170, 1006, 983, 729, 696. ^1H NMR (200 MHz, $CDCl_3$): 7.67–7.25 (m, 10H). EI-MS (*m/z*, %): 154 (M^+, 100).

4-Methylbiphenyl (3b). M.p.: 44–46°C (Lit.[11]: 47.5°C). IR (KBr): 3038, 2932, 2876, 1608, 1568, 1516, 1486, 1444, 1403, 1376, 1129, 1006, 910, 822, 755, 609. ^1H NMR (200 MHz, $CDCl_3$): 7.60–7.22 (m, 9H), 2.39 (s, 3H). EI-MS (*m/z* %): 168 (M^+), 77 (100%).

4-Bromobiphenyl (3c). M.p.: 212–213°C (Lit.[12]: 208–210°C). IR (KBr): 3033, 1595, 1576, 1480, 1454, 1404, 1160, 910, 839, 746, 600. ^1H

NMR (200 MHz, $CDCl_3$): 7.69–7.37 (m, 14H); EI-MS (m/z, %): 220 (M^+), 77 (100).

2-Phenylnaphthalene (3d). M.p.: 97–98°C (Lit.[13]: 95–96°C); IR (KBr): 13,053, 1947, 1597, 1494, 1453, 1361, 1130, 893, 860, 821, 771, 680. ^{1}H NMR (200 MHz, $CDCl_3$): 8.07–7.25 (m, 12H). EI-MS (m/z, %): 204 (M^+, 100).

1-Phenylnaphthalene (3e). Oil: (Lit.[14]: 191–199°C/5 mmHg). IR (neat): 3056, 1592, 1597, 1494, 1395, 802, 779, 761, 617. ^{1}H NMR (200 MHz, $CDCl_3$): 7.91–7.76 (m, 3H), 7.48–7.30 (m, 9H). EI-MS (m/z, %): 204 (M^+, 100).

3-Methylbiphenyl (3f). M.p.: 42–43°C (Lit.[15]: 110–115°C/2 mmHg). IR (KBr): 3032, 1980, 1600, 1567, 1520, 1486, 1406, 1377, 1129, 1026, 1006, 823, 756, 609. ^{1}H NMR (200 MHz, $CDCl_3$): 8.58–7.20 (m, 9H), 2.37 (s, 3H); EI-MS (m/z, %): 168 (M^+, 100).

4-Nitrobiphenyl (3g). M.p.: 112–113°C (Lit.[16]: 113°C). IR (KBr): 1576, 1513, 1345, 1206, 1006, 853, 748, 693; ^{1}H NMR (200 MHz, $CDCl_3$): 8.32–8.28 (m, 2H), 7.75–7.25 (m, 7H). EI-MS (m/z, %): 199 (M^+, 100).

2-Nitrobiphenyl (3h). Oil: (Lit.:[15] 142–147°C/2 mmHg). IR (neat): 3063, 1601, 1570, 1525, 1354, 1076, 853, 783, 740, 699. ^{1}H NMR (200 MHz, $CDCl_3$): 7.77–7.14 (m, 9H). EI-MS (m/z, %): 199 (M^+, 100).

4-Methoxybiphenyl (3i). M.p.: 88–89°C (Lit.[17]: 90–91°C). IR (KBr): 3034, 2908, 2843, 1604, 1592, 1486, 1437, 1343, 1138, 918, 823, 756. ^{1}H NMR (200 MHz, $CDCl_3$): 7.55–6.96 (m, 9H), 3.86 (s, 3H). EI-MS (m/z, %): 184 (M^+, 100).

2,5-Dimethylbiphenyl (3j). Oil: (Lit.[18]: 107–109°C/2 mmHg). IR (KBr): 3036, 2960, 2820, 1600, 1550, 1520, 1486, 1440, 1380, 1123, 1015, 890, 810, 760, 600. ^{1}H NMR (200 MHz, $CDCl_3$): 7.43–7.16 (m, 8H), 2.43 (s, 3H), 2.08 (s, 3H). EI-MS (m/z, %): 182 (M^+, 100).

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