PEG-Supported Dipyridyl Ligand for Palladium-Catalyzed Suzuki and Suzuki-Type Reactions in PEG and Aqueous Media

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Abstract: An air- and water-stable PEG-supported bidentate nitrogen ligand is prepared and its applications in the palladium-catalyzed Suzuki reaction of aryl halides with arylboronic acids in PEG and Suzuki-type reaction of aryl halides with sodium tetraphenylborate in aqueous media are reported. The homogeneous catalyst system is environmentally friendly and offers the advantages of high activity, reusability and easy separation.

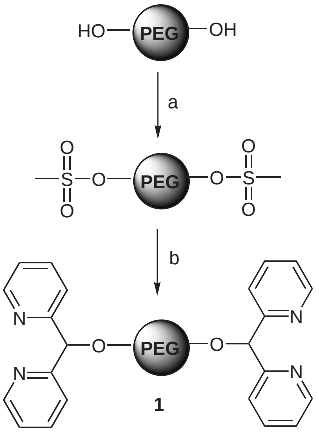
Key words: Suzuki reaction, ligand, reusability, PEG

The Suzuki–Miyaura cross-coupling reaction has emerged as an extremely powerful, attractive, and widely utilized method for the construction of carbon–carbon bonds.[1] The reaction has been applied to many areas,[2] including natural product synthesis.[3] A wide variety of palladium catalysts efficiently promote the couplings of aryl halides and other electrophiles with organoboron compounds, usually combinations of palladium salts or complexes with phosphorus ligands, such as phosphines,[4] phosphites,[5] and phosphine oxides.[6] However, phosphorus ligands, especially the electron-rich phosphine ligands, are often toxic, water-, and air-sensitive and therefore require water-, and air-free handling to minimize ligand oxidation. In such case, reuse of these catalysts is difficult.[7] Therefore, the development of phosphine-free recycling catalytic systems is focused in organic chemistry.[8]

In view of economical and environmental reasons, the development of recyclable catalytic systems is one of the most challenging fields in laboratory and industry. A more facile method is to immobilize the catalyst in a liquid phase such as ionic liquids (ILs).[9] Though ionic liquids have been adopted as a reaction media for the recycling of catalysts in a broad range of catalytic reactions,[10] they are very expensive and their toxicity and environmental burden data are for the most part unknown.

Poly(ethylene glycol) (PEG) and its monomethyl ethers are known to be inexpensive, thermally stable, recoverable, and non-toxic media for catalysts.[11] Furthermore, as a water-soluble polymer, it could be used to recover catalysts and ligands in organic synthesis.[12] More recently, PEG has been successfully used as an alternative solvent to replace ILs in catalytic systems.[13] Li and co-workers have reported $Pd(OAc)_2$/DABCO/PEG-400 system for Suzuki–Miyaura reaction recently.[14] Though the system could be recycled and reused five times without any loss of catalytic activity, it is difficult to avoid the leaching of DABCO every time. Corma et al reported an oxime carbapalladacycle that was covalently anchored on PEG for carbon–carbon coupling reactions.[15] The activity of their catalytic system was moderate. In view of our previous report on the synthesis of imidazolium ionic liquid grafted 2,2′-bipyridine,[16] herein, we report the synthesis of the PEG-supported dipyridyl ligand and its application in Suzuki and Suzuki-type reactions using PEG and PEG–water as solvents.

We selected PEG with a molecular weight of 2000 Da as the support. The preparation of ligand **1** was easily achieved by starting with mesylation of the PEG-2000's terminal alcohol groups. Mesylation of PEG proceeded in high yields (97%). The procedure commonly used[17] was modified by using trioctylamine (TOA) in place of triethylamine (TEA). The use of the less polar trioctylamine (TOA) was better because the by-product triethylamine hydrogen chloride was difficult to separate from PEG dimesylate. Replacement of TEA with the much more lipophilic TOA is an efficient solution to this problem, since TOA·HCl unlike TEA·HCl, is soluble in diethyl ether, the common solvent used for precipitating PEGs.



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Scheme 1 *Reagents and conditions*: a) PEG-2000, $MeSO_2Cl$, TOA, CH_2Cl_2, 0 °C, 97%; b) bis(2-pyridyl)methanol, NaH, THF, reflux, 61%.

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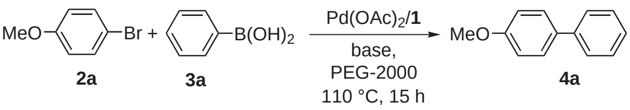
As shown in Scheme 1, the first step proceeded smoothly in 97% isolated yield. For the second step, the 61% yield of bis(2-pyridyl)methanol anchored on PEG was determined by ^{1}H NMR. Nevertheless, we found that the presence of incompletely functionalized PEG was not detrimental for the catalytic activity of the new ligand. In fact, we later used PEG as solvent for our reaction. Interestingly, though PEG is highly hygroscopic, the yellow solid **1** is air and moisture stable when left in air for three months.

With ligand **1** in hand, we first tested the catalytic activity of $Pd(OAc)_2$/**1** in PEG-2000 for the Suzuki–Miyaura reaction between 4-bromoanisole (**2a**) and phenylboronic acid (**3a**), and the results are summarized in Table 1. High yields were observed for the coupling reaction when **1** was used as the ligand. In the absence of **1**, only 44% yield of the coupling product **4a** was obtained (Table 1, entry 1), whereas in the presence of **1**, the yield of **4a** was increased to 91% (Table 1, entry 2). When Pd loading was decreased, the yield of **4a** also decreased (Table 1, entry 3 and 4). Other bases such as sodium carbonate, sodium acetate and sodium hydroxide were no better choices for this coupling reaction under the same conditions (Table 1, entry 6, 7 and 8). Ligand **1** is soluble in water, but when water was used as solvent, only 52% yield of **4a** was isolated after 24 hours (Table 1, entry 5), because the substrates were not well soluble in water.

Table 1 Pd-Catalyzed Suzuki–Miyaura Reaction of 4-Bromoanisole with Phenylboronic Acid in PEG[a]

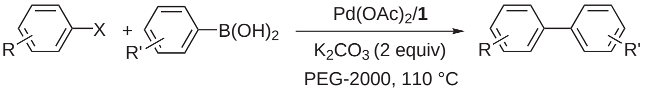


Entry	Pd(mol%)	Base	Solvent	Yield (%)[b]
1	0.2	K_2CO_3	PEG-2000	44[c]
2	0.2	K_2CO_3	PEG-2000	91
3	0.02	K_2CO_3	PEG-2000	70
4	0.1	K_2CO_3	PEG-2000	85
5	0.2	K_2CO_3	H_2O	52[d]
6	0.2	Na_2CO_3	PEG-2000	86
7	0.2	NaOAc	PEG-2000	74
8	0.2	NaOH	PEG-2000	68

[a] Reaction conditions: $Pd(OAc)_2$/**1** (1:1), 4-bromoanisole (2 mmol), phenylboronic acid (2.2 mmol), base (4 mmol), PEG (3 g), 110 °C, 15 h.
[b] Isolated yield.
[c] Prepared without **1**.
[d] Reaction time was 24 h.

Using the optimized reaction conditions, we next examined the application of $Pd(OAc)_2$/**1**/PEG system to the cross-coupling of a variety of aryl halides with several arylboronic acids and the results are summarized in Table 2. Under standard conditions, PEG-2000 as solvent, potassium carbonate as base, and $Pd(OAc)_2$/**1** at 110 °C, both electron-poor and electron-rich aryl bromides were cleanly coupled to give products in high yields (85–98%). Several arylboronic acids **3a**–**d** were tested and they all reacted with aryl bromides smoothly even with the sterically more hindered 2-methoxyphenylboronic acid (**3b**) (Table 2, entry 8 and 9). It was worth noting that this reaction was performed without the protection of an inert gas. It was interesting that Pd black emerged quickly after 2 hours in the absence of **1**, but it did not appear in the presence of **1**. It indicated that **1** could stabilize the metal during the reaction. Unfortunately, the $Pd(OAc)_2$/**1**/PEG catalytic system was less effective for the reaction of aryl chlorides. The reaction of activated aryl chloride **2j** with **3a** afforded 69% yield of corresponding coupled product **5** after 30 hours using $Pd(OAc)_2$ (3.0 mol%) (Table 2, entry 15). For the chlorobenzene, only 45% yield was obtained (Table 2, entry 14).

Table 2 $Pd(OAc)_2$/**1**/PEG-Catalyzed Cross-Coupling of Aryl Halides with Arylboronic Acids[a]



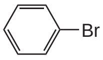
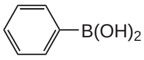
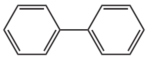
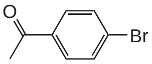
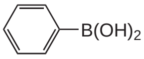
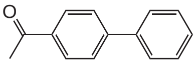
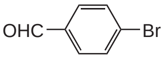
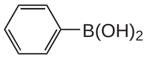
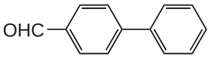
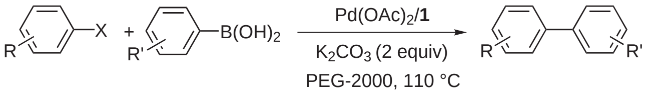
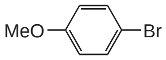
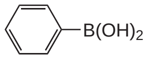
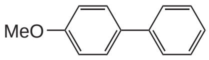
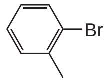
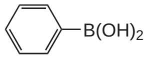
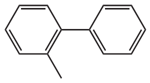
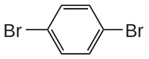
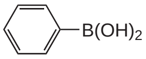
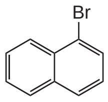
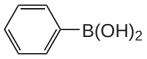
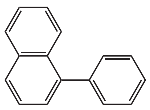
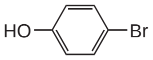
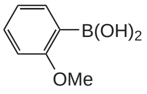
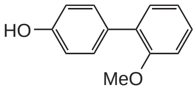
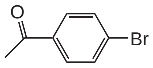
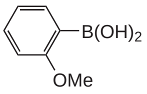
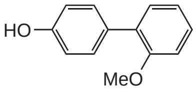
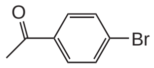
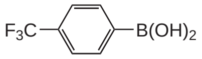
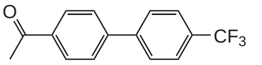
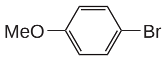
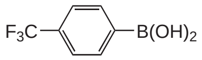
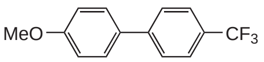
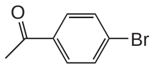
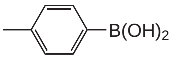
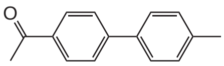
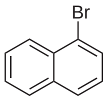
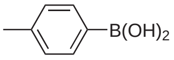
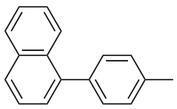
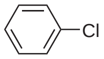
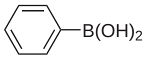
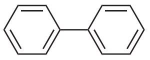
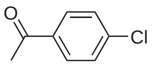
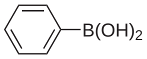
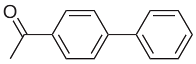
Entry	RArX	R′ArB(OH)$_2$	Time (h)	Products	Yield (%)[b]
1	 **2a**	 **3a**	15	 **4**	87
2	 **2b**	 **3a**	18	 **5**	98
3	 **2c**	 **3a**	15	 **6**	95

Table 2 Pd(OAc)$_2$/**1**/PEG-Catalyzed Cross-Coupling of Aryl Halides with Arylboronic Acids[a] (continued)



Entry	RArX	R′ArB(OH)$_2$	Time (h)	Products	Yield (%)[b]
4	 **2d**	 **3a**	18	 **7**	91
5	 **2e**	 **3a**	18	 **8**	92
6	 **2f**	 **3a**	24	 **9**	92
7	 **2g**	 **3a**	24	 **10**	98
8	 **2h**	 **3b**	24	 **11**	85
9	 **2b**	 **3b**	24	 **12**	90
10	 **2b**	 **3c**	15	 **13**	95
11	 **2d**	 **3c**	18	 **14**	89
12	 **2b**	 **3d**	15	 **15**	93
13	 **2g**	 **3d**	15	 **16**	97
14	 **2i**	 **3a**	30	 **4**	45[c]
15	 **2j**	 **3a**	30	 **5**	69[c]

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[a] Reaction conditions: ArX (2 mmol), ArB(OH)$_2$ (2.2 mmol), K_2CO_3 (4 mmol), PEG-2000 (3 g), Pd(OAc)$_2$ (0.004 mmol), 110 °C (bath temperature).

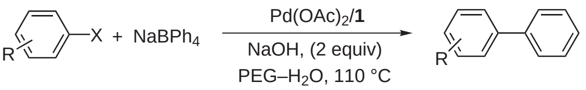
[b] Isolated yield.

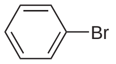
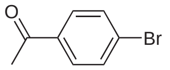
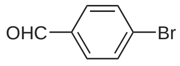
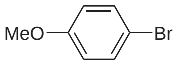
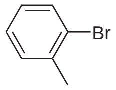
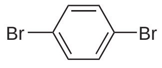
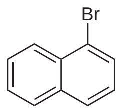
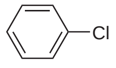
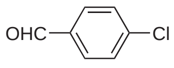
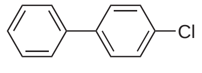
[c] Catalyst loading: 3.0 mmol% Pd.

To extend the application scope of the catalytic system, we carried out Suzuki-type reaction of aryl halides with sodium tetraphenylborate ($NaBPh_4$) in the system using water as co-solvent. As a new type of borate source, $NaBPh_4$ is a stable and commercially available reagent for the Suzuki reaction. Recently, Bumagin[18] and Xu[19] reported palladium-catalyzed Suzuki reaction by using $NaBPh_4$ in water. But the aryl halides they used had limited advantages; these aryl halides must be soluble or partly soluble in water. Herein, we used PEG–H_2O as solvent and many insoluble aryl halides could react with $NaBPh_4$ smoothly. Initially, we explored the conditions for the reaction by using $Pd(OAc)_2$–**1**–PEG–H_2O catalytic system. We found that sodium hydroxide as base was the best choice for the reaction and potassium carbonate, sodium acetate and sodium carbonate were less effective. In view of Zhang's report on Suzuki coupling in PEG–H_2O recently[20], we found that when the amount of PEG in water was 1.2 g/mL and Pd loading was 0.5 mol%, the reaction was the most efficient and the detailed results are summarized in Table 3. We found that the reaction proceeded much more smoothly when sodium tetraphenylborate was used instead of arylboronic acids. Many aryl bromides including electron-poor and electron–rich substrates **2a**–**g** could react with $NaBPh_4$ in the $Pd(OAc)_2$/**1**/PEG–H_2O catalytic system within two to five hours and the yields of corresponding coupling products **4**–**10** were higher than those shown in Table 2. It was worth noting that only 0.25 equivalent of $NaBPh_4$ was enough for this reaction. The concise mechanism had been reported in literature.[19] In order to test the activity of the catalytic system, we selected three aryl chlorides for the reaction. Unfortunately, the attempt to couple 4-chlorobiphenyl (**2l**) with $NaBPh_4$ was not successful even though extended reaction time and 3.0 mmol% Pd loading were employed (Table 3, entry 10). A moderate yield could be obtained with 4-chlorobenzaldehyde (**2k**) whereas the yield of the coupling product with chlorobenzene (**2i**) was just 14% (Table 3, entry 9 and 8).

Having established the scope of the new reaction system, our attention was focused on the recycling of the system. In order to evaluate the recycling potential of the catalytic system, we chose two methods (**A** and **B**). For method **A**, the coupling of 4-bromoacetophenone (**2b**) with phenylboronic acid (**3a**) was used as a model Suzuki reaction. For method **B**, different substrates including low activity substrates were tested in the same catalytic system. As shown in Table 4, we were gratified to observe that the $Pd(OAc)_2$/**1**/PEG-2000 system could be reused six times for Suzuki reaction (Table 4, method **A**). Furthermore, no Pd black emerged until the sixth run in method **A**. In method **B**, the system could be reused five times using different substrates without product contamination. In both methods, even though TON was similar, the TOF values decreased in the last two runs. It indicated that the catalytic efficiency of the system was decreased. Unfortunately, for Suzuki-type reaction, the system could be only reused for two runs with 99% and 93% yields using **1b** and $NaBPh_4$ as substrates because Pd black was observed in the second run.

Table 3 $Pd(OAc)_2$/**1**/PEG–H_2O-Catalyzed Suzuki-Type Reaction of Aryl Halides with Sodium Tetraphenylborate[a]



Entry	ArX	Time (h)	Product	Yield (%)[b]
1	 **2a**	2	**4**	99
2	 **2b**	2	**5**	99
3	 **2c**	2	**6**	99
4	 **2d**	5	**7**	93
5	 **2e**	5	**8**	90
6	 **2f**	5	**9**	95
7	 **2g**	2	**10**	98
8	 **2i**	15	**4**	14[c]
9	 **2k**	15	**6**	67[c]
10	 **2l**	15	**9**	–[c]

[a] Reaction conditions: ArX (2 mmol), $NaBPh_4$ (0.6 mmol), NaOH (4 mmol), $Pd(OAc)_2$ (0.01 mmol), PEG-2000–H_2O (3.5 g/3 mL), 110 °C (bath temperature).

[b] Isolated yield.

[c] Catalyst loading: 3.0 mmol%.

In summary, we have ligated a dipyridyl ligand to a PEG support and have demonstrated its utility in palladium-catalyzed Suzuki and Suzuki-type reactions in PEG and aqueous media. In combination with a palladium source, ligand **1** forms an active resin-bound catalyst for Suzuki and Suzuki-type reactions, allowing for simplified product separation and purification. A number of aryl halides, including aryl bromides and chlorides were coupled to arylboronic acids or sodium tetraphenylborate smoothly

Table 4 Reuse of the $Pd(OAc)_2$/**1**/PEG for the Suzuki Reaction[a]

Run	1	2	3	4	5	6
(**A**) Substrates	**2b** + **3a**	**2b** + **3a**	**2b** + **3a**	**2b** + **3a**	**2b** + **3a**	**2b** + **3a**
Yield (%)[c]	98	98	96	95	92[b]	95[b]
TON	490	490	480	475	460	475
TOF (h^{-1})	27	27	26.6	26	19	18
(**B**) Substrates	**2a** + **3a**	**2b** + **3d**	**2d** + **3d**	**2g** + **3a**	**2d** + **3a**	–
Yield (%)[c]	91[d]	96[d]	93[d]	94[b]	86[b]	–
TON	455	480	465	470	430	–
TOF (h^{-1})	30	32	31	20	18	–

[a] Unless otherwise indicated, the reaction conditions were as follows: **2** (2 mmol), **3** (2.2 mmol), $Pd(OAc)_2$/**1** (1:1, 0.004 mmol), K_2CO_3 (4 mmol) in PEG-2000 (3 g) at 110 °C for 18 h.

[b] Reaction time was 24 h.

[c] Isolated yield.

[d] Reaction time was 15 h.

and efficiently. Furthermore, the $Pd(OAc)_2$/**1**/PEG-2000 system could be recycled and reused five to six times without obvious loss of catalytic activity for Suzuki reaction. Further efforts to extend the application of the system in other Pd-catalyzed reactions are in progress in our laboratory.

Synthesis of Bis(2-pyridyl)methanol

To a stirred anhyd Et_2O (200 mL) solution of 2-bromopyridine (9.5 mL, 100 mmol) was added *n*-BuLi (62.5 mL, 100 mmol, 1.6 M in hexane) at –78 °C under a N_2 atmosphere. After being stirred for 20 min, the reaction was quenched with 2-pyridinecarboxaldehyde (9.5 mL, 100 mol) at the same temperature. The whole mixture was stirred for 30 min. After the cooling bath was removed, the mixture was diluted with 2 M HCl (160 mL) and then solid NaOH was added until a pH of ca. 8 was reached. The mixture was extracted with Et_2O (3 × 200 mL) and the organic layer was washed with brine and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residual mixture was purified by flash chromatography on silica gel (petroleum ether–EtOAc) to afford the product (14 g, 75%).

^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.56$ (d, $J = 4.8$ Hz, 2 H), 7.66 (td, $J = 1.8$, 6.0 Hz, 2 H), 7.54 (d, $J = 7.8$ Hz, 2 H), 7.19 (d, $J = 7.2$ Hz, 2 H), 5.90 (s, 1 H).

Mesylation of PEG-2000

PEG-2000 (4 g, 2 mmol) was dried under vacuum at 80 °C for 1 h and then dissolved in anhyd CH_2Cl_2 (100 mL). Trioctylamine (3.5 mL, 8 mmol) was added, and the mixture was cooled to 0 °C with stirring. Mesyl chloride (0.93 mL, 12 mmol) was added slowly, and the mixture was stirred for 24 h at r.t. The CH_2Cl_2 volume was then reduced by 95% under reduced pressure. The remaining CH_2Cl_2 was cooled to 0 °C, and anhyd Et_2O (100 mL) was slowly added with stirring. After 1 h a white solid (4.18 g, 97% yield) was obtained by filtration and washed with Et_2O (2 × 25 mL).

^1H NMR (600 MHz, $CDCl_3$): $\delta = 4.39$ (t, $J = 4.8$ Hz, 4 H), 3.63–3.77 (m, 184 H), 3.09 (s, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 70.51$, 69.24, 68.96, 37.68.

Preparation of PEG-Supported Dipyridyl Ligand (1)

Bis(2-pyridyl)methanol (0.518 g, 2.78 mmol) was dissolved in anhyd THF (50 mL). To this solution was added NaH (0.12 g, 5.0 mmol), and the resulting mixture was stirred for 1 h, after which dimesyl PEG (1 g, 0.464 mmol) was added. The solution was refluxed for 24 h, and THF was evaporated under reduced pressure. The brown residue was redissolved in a minimal amount of water and extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried over Na_2SO_4 and their volume was reduced by 95% under reduced pressure. The remaining CH_2Cl_2 was cooled to 0 °C, and anhyd Et_2O (100 mL) was slowly added with stirring. Yellow crystals were formed and filtered after 1 h. Yield: 0.66 g (61%) by ^1H NMR.

^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.55$ (d, $J = 4.8$ Hz, 4 H), 7.69 (m, 4 H), 7.60 (d, $J = 7.8$ Hz, 4 H), 7.18–7.16 (m, 4 H), 5.66 (s, 2 H), 3.60–3.73 (m, 302 H).

^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 160.31$, 149.18, 136.67, 122.49, 121.47, 85.95, 70.53, 68.93.

Suzuki Reaction; General Procedure

A mixture of aryl halides **2** (2 mmol), arylboronic acid **3** (2.2 mmol), $Pd(OAc)_2$/**1** (1:1, 0.004 mmol), K_2CO_3 (4 mmol), and PEG-2000 (3 g) was added to a flask and stirred at 110 °C in open air for the desired time until complete consumption of the starting substrates as judged by TLC. After the mixture was extracted with anhyd Et_2O (3 × 30 mL) and evaporated, the residue was purified by flash column chromatography (petroleum ether or petroleum ether–EtOAc) to afford the desired coupled products **4**–**16**.

Selected data for **5**: ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.04$ (d, $J = 8.4$ Hz, 2 H), 7.70 (d, $J = 8.4$ Hz, 2 H), 7.64 (d, $J = 7.2$ Hz, 2 H), 7.49 (t, $J = 7.2$ Hz, 2 H), 7.42 (t, $J = 7.2$ Hz, 1 H), 2.64 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 197.74$, 145.77, 139.86, 135.84, 128.94, 128.90, 128.22, 127.26, 127.21, 26.66.

Suzuki-Type Reaction; General Procedure

A mixture of aryl halides **2** (2 mmol), $NaBPh_4$ (0.6 mmol), $Pd(OAc)_2$/**1** (1:1, 0.01 mmol), NaOH (4 mmol), PEG-2000 (3.5 g), and H_2O (3 mL) was added to a flask and stirred at 110 °C in open air for the desired time until complete consumption of the starting substrates as judged by TLC. After the mixture was extracted with anhyd Et_2O (3×30 mL) and evaporated, the residue was purified by flash column chromatography (petroleum ether or petroleum ether–EtOAc) to afford the desired coupled products **4**–**10**.

Selected data for **6**: ^1H NMR (400 MHz, $CDCl_3$): $\delta = 10.06$ (s, 1 H), 7.96 (d, *J* = 8.4 Hz, 2 H), 7.76 (d, *J* = 8.4 Hz, 2 H), 7.65 (d, *J* = 7.2 Hz, 2 H), 7.49 (t, *J* = 7.2 Hz, 2 H), 7.41–7.44 (m, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 191.86$, 147.12, 139.65, 135.14, 130.21, 128.96, 128.42, 127.62, 127.31.

Recovery and Reuse of the System for the Suzuki or Suzuki-Type Reactions; General Procedure

After extracting with Et_2O, the mixture of $Pd(OAc)_2$/**1**/PEG-2000 or $Pd(OAc)_2$/**1**/PEG-2000–H_2O was cooled and then evaporated under reduced pressure and subjected to a second run of the Suzuki or Suzuki-type reactions by charging with the same substrates or different substrates.

References

(1) Selected recent reviews: (a) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11. (b) Kotha, S.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633. (c) Bellina, F.; Carpita, A.; Rossi, R. *Synthesis* **2004**, 2419. (d) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (e) Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176.

(2) (a) Wang, W.; Xiong, C.; Yang, J.; Hruby, V. J. *Tetrahedron Lett.* **2001**, *42*, 7717. (b) Vaz, B.; Rosana, R.; Nieto, M.; Paniello, A. I.; de Lera, A. R. *Tetrahedron Lett.* **2001**, *42*, 7409. (c) Schomaker, J. M.; Delia, T. J. *J. Org. Chem.* **2001**, *66*, 7125. (d) Wong, K.-T.; Huang, T. S.; Lin, Y.; Wu, C.-C.; Lee, G.-H.; Peng, S.-M.; Chou, C. H.; Su, Y. O. *Org. Lett.* **2002**, *4*, 513.

(3) (a) Hobbs, P. D.; Upender, V.; Dawson, M. I. *Synlett* **1997**, 965. (b) Nicolaou, K. C.; Li, H.; Boddy, C. N. C.; Ramanjulu, J. M.; Yue, T.-Y.; Natarajan, S.; Chu, X.-J.; Brase, S.; Rubsam, F. *Chem. Eur. J.* **1999**, *5*, 2584. (c) Nicolaou, K. C.; Koumbis, A. E.; Takayanagi, M.; Natarajan, S.; Jain, N. F.; Bando, T.; Li, H.; Hughes, R. *Chem. Eur. J.* **1999**, *5*, 2622. (d) Kamikawa, K.; Watanabe, T.; Daimon, A.; Uemura, M. *Tetrahedron* **2000**, *56*, 2325.

(4) (a) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550. (b) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S.; Petersen, J. L. *J. Org. Chem.* **1999**, *64*, 6797. (c) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem. Int. Ed.* **2000**, *22*, 4153. (d) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020. (e) Feuerstein, M.; Laurenti, D.; Bougeant, C.; Doucet, H.; Santelli, M. *Chem. Commun.* **2001**, 325. (f) Pickett, T. E.; Richards, C. J. *Tetrahedron Lett.* **2001**, *42*, 3767. (g) Feuerstein, M.; Doucet, H.; Santelli, M. *Synlett* **2001**, 1458. (h) Liu, S.-Y.; Choi, M. J.; Fu, G. C. *Chem. Commun.* **2001**, 2408. (i) Kudo, N.; Perseghini, M.; Fu, G. C. *Angew. Chem. Int. Ed.* **2006**, *45*, 1282. (j) Anderson, K.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2005**, *44*, 6173. (k) Willis, M. C.; Powell, L. H.; Claverie, C. K. *Angew. Chem. Int. Ed.* **2004**, *43*, 1249. (l) Colacot, T. J.; Shea, H. A. *Org. Lett.* **2004**, *6*, 3731. (m) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685.

(5) Zapf, A.; Beller, M. *Chem. Eur. J.* **2000**, *6*, 1830.

(6) Li, G. Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 1513.

(7) (a) *Homogeneous Catalysis with Metal Phosphine Complexes*; Pignolet, L. H., Ed.; Plenum: New York, **1983**. (b) Parshall, G. W.; Ittel, S. *Homogeneous Catalysis*; Wiley and Sons: New York, **1992**.

(8) (a) Okamoto, K.; Akiyama, R.; Kobayashi, S. *Org. Lett.* **2004**, *6*, 1987. (b) an der Heiden, M.; Plenio, H. *Chem. Eur. J.* **2004**, *10*, 1789. (c) Kim, N.; Kwon, M. S.; Park, C. M.; Park, J. *Tetrahedron Lett.* **2004**, *45*, 7057.

(9) (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071. (b) Wasserscheid, P.; Keim, W. *Angew. Chem. Int. Ed.* **2000**, *39*, 3772. (c) Sheldon, R. *Chem. Commun.* **2001**, 2399. (d) Earle, M. J.; Seddon, K. R. *Pure Appl. Chem.* **2000**, *72*, 1391.

(10) (a) Boon, J. A.; Levisky, J. A.; Pflug, J. L.; Wilkes, J. S. *J. Org. Chem.* **1986**, *51*, 480. (b) Brown, R. A.; Pollet, P.; McKoon, E.; Eckert, C. A.; Liotta, C. L.; Jessop, P. G. *J. Am. Chem. Soc.* **2001**, *123*, 1254. (c) Chauvin, Y.; Mussmann, L.; Olivier, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2698. (d) Favre, F.; Olivier-Bourbigou, H.; Commereuc, D.; Saussine, L. *Chem. Commun.* **2001**, 1360. (e) Adams, C. J.; Earle, M. J.; Roberts, G.; Seddon, K. R. *Chem. Commun.* **1998**, 2097. (f) Song, C. E.; Shim, W. H.; Roh, E. J.; Lee, S.; Choi, J. H. *Chem. Commun.* **2001**, 1122. (g) Xu, L.; Chen, W.; Xiao, J. *Organometallics* **2000**, *19*, 1123. (h) Handy, S. T.; Zhang, X. L. *Org. Lett.* **2001**, *3*, 233. (i) Adams, C. J.; Earle, M. J.; Seddon, K. R. *Chem. Commun.* **1999**, 1043. (j) Jiang, T.; Gao, H. X.; Han, B. X.; Zhao, G. Y.; Chang, Y. H.; Wu, W. Z.; Gao, L.; Yang, G. Y. *Tetrahedron Lett.* **2004**, *45*, 2699.

(11) *Polyethylene Glycol Chemistry: Biotechnological and Biomedical Applications*; Harris, J. M., Ed.; Plenum: New York, **1992**.

(12) (a) Bergbreiter, D. E. *Chem. Rev.* **2002**, *102*, 3345. (b) Bergbreiter, D. E.; Li, C. *Org Lett.* **2003**, *5*, 2445. (c) Dickerson, T. J.; Need, N. N.; Janda, K. D. *Chem. Rev.* **2002**, *102*, 3325. (d) Gravert, D. J.; Janda, K. D. *Chem. Rev.* **1997**, *97*, 489.

(13) (a) Chandrasehar, S.; Narsihmulu, C.; Sultana, S. S.; Reddy, N. R. *Org. Lett.* **2002**, *4*, 4399. (b) Wang, L.; Zhang, Y. H.; Liu, L. F.; Wang, Y. G. *J. Org. Chem.* **2006**, *71*, 1284. (c) Heldebrant, D. J.; Jessop, P. G. *J. Am. Chem. Soc.* **2003**, *125*, 5600. (d) Li, J. H.; Zhu, Q. M.; Liang, Y.; Yang, D. *J. Org. Chem.* **2005**, *70*, 5347. (e) Chandrasekhar, S.; Sultana, S. S.; Yaragorla, S. R.; Reddy, N. R. *Synthesis* **2006**, 839.

(14) Li, J. H.; Liu, W. J.; Xie, Y. X. *J. Org. Chem.* **2005**, *70*, 5409.

(15) Corma, A.; Carcía, H.; Leyva, A. *J. Catal.* **2006**, *240*, 87.

(16) Wu, X. E.; Ma, L.; Ding, M. X.; Gao, L. X. *Chem. Lett.* **2005**, *34*, 312.

(17) (a) Benaglia, M.; Cinquini, M.; Cozzi, F. *Tetrahedron Lett.* **1999**, *40*, 2019. (b) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F. *Chem. Eur. J.* **2000**, *6*, 133.

(18) Bumagin, N. A.; Bykov, V. V. *Tetrahedron* **1997**, *53*, 14437.

(19) Lu, G.; Franzén, R.; Zhang, Q.; Xu, Y. J. *Tetrahedron Lett.* **2005**, *46*, 4255.

(20) Liu, L. F.; Zhang, Y. H.; Wang, Y. G. *J. Org. Chem.* **2005**, *70*, 6122.