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# Polymer-supported DABCO–palladium complex as a stable and reusable catalyst for room temperature Suzuki–Miyaura cross-couplings of aryl bromides

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**Abstract**—Polymer-supported DABCO–palladium complex was observed as to be efficient and reusable catalytic system for the Suzuki–Miyaura cross-coupling reaction. In the presence of 0.25 mol % of the polymer-supported DABCO–palladium complex, a variety of aryl bromides were coupled with arylboronic acids efficiently in an aqueous ethanol at room temperature under air. Moreover, the reaction was very rapid, and the catalyst could be recovered readily from the reaction by simple filtration and could be reused at least five times.

The Suzuki–Miyaura cross-coupling reaction has become a common transformation for the formation of carbon–carbon bonds because their products,[1] in particular biaryls, are recurring functional groups in many natural products and biologically active compounds as well as useful blocks in organic synthesis.[2–8] Consequently, extensive efforts have been made to develop many efficient and selective catalytic systems for the reaction. Among these efficient and selective catalytic systems, the most common catalytic system is a palladium combined with a ligand (often a phosphine ligand). However, the cost of the palladium system is considerably expensive. In view of economy and environment, the development of a recoverable and reusable palladium catalytic system is still interesting. An effective route is to immobilize palladium onto a polymer to obtain a heterogenous polymer-supported palladium complex. In recent years, many efficient polymer-supported palladium complexes have been developed for the purpose.[2–6] However, almost all attention had been focused on the polymer-supported phosphine–palladium complexes and the polymer-supported carbene–palladium complexes. Although these complexes exhibited highly catalytic activity and could be recycled, many were still expensive besides the requirement of higher reaction temperatures, long reaction times and inert gas conditions. Recently, we found that DABCO was an effective and inexpensive ligand for the $Pd(OAc)_2$-catalyzed Suzuki–Miyaura cross-coupling reaction under aerobic conditions.[8] Among these methods, we have immobilized the $Pd(OAc)_2$/DABCO catalytic system in PEG-400 to realize the recovery and reuse of the $Pd(OAc)_2$/DABCO system as well as the medium successfully. However, the catalytic system could not be separated from the media. In addition, the products were also difficult to be isolated from the reaction in the reused procedures.[8b] Very recently, we also found that the $Pd(OAc)_2$/DABCO-catalyzed Suzuki–Miyaura cross-coupling could be conducted smoothly in $H_2O$ using PEG-400 as a phase-transfer catalyst.[8c] Thus, we expected to immobilize the $Pd(OAc)_2$/DABCO catalytic system onto a polymer to form an ammonium salt, another type of effective phase-transfer catalyst, which may improve the reaction and realize the catalyst recycle. Indeed, the polymer-supported DABCO–palladium complex from the $Pd(OAc)_2$/DABCO catalytic system immobilized onto Merrifield resin displayed high catalytic activity. The reactions of aryl bromides were performed rapidly at a loading of 0.25 mol % polymer-supported DABCO–palladium complex in air to afford excellent yields of the desired products in the first run.

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*Keywords*: Polymer-supported DABCO–palladium complex; Suzuki–Miyaura cross-coupling reaction; Aryl bromide; Arylboronic acid.

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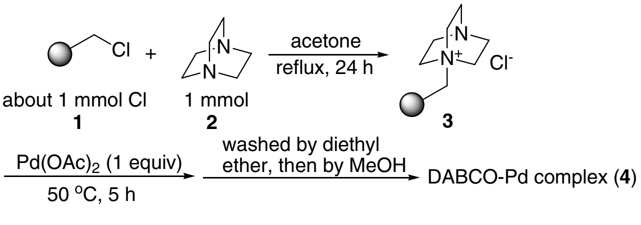
Furthermore, the complex could be recovered readily and be reused at least five times. Here, we report our primary results (Eq. 1):

$$\mathrm{ArBr} + \mathrm{Ar'B(OH)_2} \xrightarrow[\mathrm{K_2CO_3,\ rt}]{\text{DABCO–Pd complex}} \mathrm{Ar{-}Ar'} \qquad (1)$$

As shown in Scheme 1, 0.5 g of Merrifield resin (**1**, 2.0–2.2 mmol Cl/g) reacted with DABCO (**2**) (1 mmol) in acetone reflux for 24 h. The mixture was then cooled to room temperature. After 1 equiv of $Pd(OAc)_2$ was added, the mixture was stirred again at 50 °C for 5 h. The mixture was then filtered and washed with diethyl ether and MeOH, respectively, to provide the polymer-supported DABCO–palladium complex (**4**).[2,9]

Subsequently, we employed the polymer-supported DABCO–palladium complex (**4**) in the Suzuki–Miyaura cross-coupling of *p*-bromoanisol (**5a**) with phenylboronic acid (**6a**), and the results are summarized in Table 1.[10] The results indicated that the solvent had a fundamental influence on the reaction (entries 1–5). In DMF, treatment of substrate **5a** with **6a**, the polymer-supported DABCO–palladium complex **4** (0.25 mol %; 20 mg) and $K_2CO_3$ (2.5 equiv) at room temperature after 12 h afforded only 20% yield of the corresponding coupled product **7** (entry 1), whereas the yield of **7** was enhanced sharply to 98% in 1 h when ethanol was used as the solvent (entry 3). We were happy to find that substrate **5a** was consumed completely in 0.2 h to offer the desired product **7** in 98% yield using a mixture of ethanol/$H_2O$ (1:1) as the solvent (entry 5). However, a moderate yield of the target product **7** was isolated in $H_2O$ alone (entry 4). It was noteworthy that the polymer-supported DABCO–palladium complex (**4**) could be reused at least four times after simple filtration when the reaction was performed in either ethanol or ethanol/$H_2O$ as the solvent (entries 3 and 5). After initial experimentation the reaction mixture was filtered to give a solution and a solid. The solution was evaporated, then extracted by diethyl ether, evaporated in vacuum and purified by flash column chromatography to give the target product **7**. After being washed by diethyl ether and dried, the solid was subjected to a second run of the coupling by charging with the same substrates, base and solvent. The results of the reused runs showed that they were almost consistent in yields, but rates of the reaction were reduced to some extent and prolonged reaction times were required to provide high yields (entries 3 and 5). This may be due to the loss of some active Pd species during the reaction and recovered processes.[11] We also found that excellent yield of **7** could be achieved in DMF when the reaction temperature was increased to 80 °C (entries 1 and 2). Although the polymer-supported DABCO–palladium complex (**4**) could be reused in DMF at 80 °C, the catalytic activity of **4** was decreased dramatically after the third run in terms of yield and rate (entry 2). The reaction catalyzed by the $Pd(OAc)_2$/DABCO catalytic system was also evaluated, and the results indicated that its catalytic activity was inferior to the polymer-supported DABCO–palladium complex (**4**) (entries 5 and 6). It was pleased to find that substrate **5a** was coupled with the other boronic acids **6b** or **6c** efficiently to afford good yields of the corresponding products in 0.3 h under the optimized reaction conditions (entries 7 and 8).



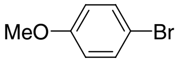
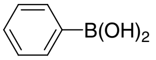
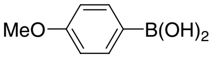
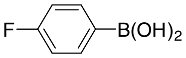
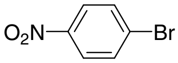
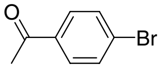
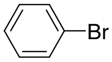
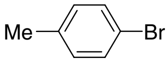
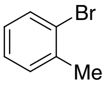
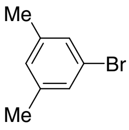
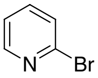
**Scheme 1.** Synthesis of the polymer-supported DABCO–palladium complex (**4**).

With the optimized reaction conditions in hand, the couplings of a number of other aryl bromides including heteroaryl bromides were then conducted (entries 9–21 in Table 1). To our delight, the rates of the first runs were also rapid for all bromides **5b–g** including two sterically hindered substrates **5f** and **5g**, and excellent yields were still obtained after prolonging the reaction times in the reused runs (entries 9–16). For example, the complex **4** could be reused seven times in the coupling of substrate **5b** with **6a** to give the target product **10** in identical yields, but the rate was decreased after the second reused run (entry 9). Thus, the reaction temperature was elevated from the fifth runs to shorten the reaction times. As expected, substrate **5b** was consumed completely in 12 h when the fifth run of the reaction was performed at 40 °C (14 h in the sixth run and 18 h in the seventh run; entry 9). It is interesting to discover that the present conditions also allowed for the coupling of heteroaryl bromides **5h–k**, but the catalytic efficiency of the complex **4** was reduced based on the reaction rate (entries 17–20). Only 73% yield of **18** was obtained in 12 h when 2-bromopyridine **5h** was treated with **6a**, the complex **4** and $K_2CO_3$ in $H_2O/CH_3CH_2OH$ at room temperature (entry 17). It was happy to observe that the other heteroaryl bromides **5i–k** underwent the coupling with **6a** smoothly in good yields including the reused procedures (entries18–20). However, higher reaction temperature was required to improve the reaction among the reused couplings. Unfortunately, the complex **4** was less effective for the reaction of 4-nitro-1-chlorobenzene (**5l**) with **6a** under the same conditions (entry 21). Gratifyingly, we found that the reaction of substrate **5l** with **6a**, the complex **4** and $K_2CO_3$ in DMF at 80 °C could provide the corresponding product **10** in good yield, but the complex **4** could not be reused (entry 22). Noteworthy is that an 86% yield of the target product **22** could be obtained in the coupling between the deactivated bulky chloride **5m** and **6a** in the presence of 1 mol % of the complex **4** (entry 23).

In summary, we have demonstrated that a new air-stable polymer-supported DABCO–palladium complex is readily available from simple inexpensive reagents, which represents an efficient and general catalyst for the Suzuki–Miyaura cross-coupling reaction. The current reaction was conducted rapidly under mild conditions providing moderate to excellent yields. It is noted that the catalytic activity of the polymer-sup-

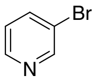
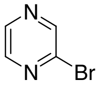
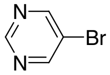
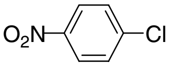
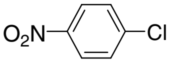
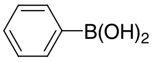
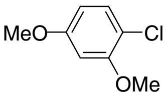
**Table 1.** The polymer-supported DABCO–palladium complex-catalyzed Suzuki–Miyaura cross-couplings of aryl halides (**5**) with arylboronic acids (**6**)[a]

$$\underset{\mathbf{5}}{\mathrm{ArX}} + \underset{\mathbf{6}}{\mathrm{Ar'B(OH)_2}} \xrightarrow[\mathrm{K_2CO_3,\ rt\ -\ 80\ ^{o}C}]{\text{DABCO-Pd complex}} \underset{\mathbf{7\text{-}22}}{\mathrm{Ar\text{-}Ar'}}$$

| Entry | ArX | Ar′B(OH)$_2$ | Recycle no. | Time (h) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1[c] |  (**5a**) |  (**6a**) | | 12 | 20 (**7**) |
| 2[d] | (**5a**) | (**6a**) | 1 | 2 | 100 (**7**) |
| | | | 2 | 10 | 95 (**7**) |
| | | | 3 | 15 | 83 (**7**) |
| | | | 4 | 30 | 75 (**7**) |
| 3[e] | (**5a**) | (**6a**) | 1 | 1 | 98 (**7**) |
| | | | 2 | 6 | 93 (**7**) |
| | | | 3 | 16 | 94 (**7**) |
| | | | 4 | 24 | 93 (**7**) |
| 4[f] | (**5a**) | (**6a**) | | 8 | 56 (**7**) |
| 5 | (**5a**) | (**6a**) | 1 | 0.2 | 98 (**7**) |
| | | | 2 | 3 | 97 (**7**) |
| | | | 3 | 10 | 94 (**7**) |
| | | | 4 | 15 | 95 (**7**) |
| | | | 5 | 18 | 95 (**7**) |
| 6[g] | (**5a**) | (**6a**) | | 8 | 86 (**7**) |
| 7 | (**5a**) |  (**6b**) | | 0.3 | 85 (**8**) |
| 8 | (**5a**) |  (**6c**) | | 0.2 | 96 (**9**) |
| 9 |  (**5b**) | (**6a**) | 1 | 0.3 | 98 (**10**) |
| | | | 2 | 12 | 99 (**10**) |
| | | | 3 | 30 | 97 (**10**) |
| | | | 4 | 48 | 91 (**10**) |
| | | | 5[h] | 12 | 96 (**10**) |
| | | | 6[h] | 14 | 95 (**10**) |
| | | | 7[h] | 18 | 99 (**10**) |
| 10 |  (**5c**) | (**6a**) | | 0.2 | 97 (**11**) |
| 11 |  (**5d**) | (**6a**) | | 0.2 | 109 (**12**) |
| 12 |  (**5e**) | (**6a**) | | 0.2 | 98 (**13**) |
| 13 | (**5e**) | (**6b**) | | 0.3 | 88 (**14**) |
| 14 | (**5e**) | (**6c**) | | 0.2 | 99 (**15**) |
| 15 |  (**5f**) | (**6a**) | | 1 | 90 (**16**) |
| 16 |  (**5g**) | (**6a**) | 1 | 1 | 96 (**17**) |
| | | | 2 | 6 | 96 (**17**) |
| | | | 3 | 10 | 95 (**17**) |
| | | | 4 | 15 | 95 (**17**) |
| | | | 5 | 22 | 98 (**17**) |
| 17 |  (**5h**) | (**6a**) | | 12 | 73 (**18**) |

(*continued on next page*)

**Table 1** (*continued*)

| Entry | ArX | Ar′B(OH)$_2$ | Recycle no. | Time (h) | Yield (%)[b] |
|---|---|---|---|---|---|
| 18 |  (**1i**) | (**6a**) |  | 6 | 93 (**19**) |
| 19 |  (**5j**) | (**6a**) | 1 | 4 | 94 (**20**) |
|  |  |  | 2 | 28 | 96 (**20**) |
|  |  |  | 3 | 30 | 91 (**20**) |
|  |  |  | 4[h] | 12 | 93 (**20**) |
|  |  |  | 5[h] | 15 | 92 (**20**) |
| 20 |  (**5k**) | (**6a**) | 1 | 4 | 96 (**21**) |
|  |  |  | 2 | 18 | 94 (**21**) |
|  |  |  | 3 | 28 | 93 (**21**) |
|  |  |  | 4[h] | 10 | 97 (**21**) |
|  |  |  | 5[h] | 12 | 95 (**21**) |
| 21 |  (**5l**) | (**6a**) |  | 18 | Trace (**10**) |
| 22[d] |  (**5l**) |  (**6a**) | 1 | 12 | 95 (**10**) |
|  |  |  | 2 | 26 | 30 (**10**) |
| 23[d,i] |  (**5m**) | (**6a**) |  | 22 | 86 (**22**) |

[a] Reaction conditions: **5** (0.5 mmol), **6** (0.6 mmol), [Pd] **4** (0.25 mol %) and $K_2CO_3$ (2.5 equiv) in $H_2O/CH_3CH_2OH$ (1:1; 4 mL) at room temperature.
[b] Isolated yield.
[c] DMF (4 mL) as the solvent. 70% of **5a** was recovered.
[d] DMF (4 mL) as the solvent at 80 °C.
[e] $CH_3CH_2OH$ (4 mL) as the solvent.
[f] $H_2O$ (4 mL) as the solvent. 38% of **5a** was recovered.
[g] $Pd(OAc)_2$ (0.25 mol %) combined with DABCO (0.50 mol %) instead of the polymer-supported DABCO–palladium complex at 40 °C. 8% of **5a** was recovered.
[h] At 40 °C.
[i] [Pd] **4** (1 mol %).

ported DABCO–palladium complex is even higher than those of the homogeneous palladium catalytic systems. Importantly, the complex could be recovered readily and still displayed high efficiency in the reused procedures. Efforts to extend the polymer-supported DABCO–palladium complex in other palladium-catalyzed transformations are underway in our laboratory.

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.10.148.

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9. The loading level of Pd is 0.063 mmol/g, which was determined by means of a inductively coupled plasma-atomic emission spectrometer (ICP-AES). The loading level of DABCO is about 1.720 mmol/g on the base of nitrogen content by elemental analysis (Anal. Calcd for $C_{15n}H_{22n}N_{2n}Cl_n$ including 2% of $C_{10m}H_{12m}$: C, 81.02; H, 8.18; N, 4.76. Found: C, 81.58; H, 7.82; N, 4.48). We also determined the loading level of DABCO (about 1.658 mmol/g) based on the chlorine content by titrimetric analysis [primary standard: $C_{NaCl} = 0.02$ M; titrant (standard solution): $C_{AgNO_3} = 0.0204$ M; indicator: $K_2CrO_4$; titrate: the polymer-supported DABCO–palladium complex **4** (129.2 mg), deionized water (25 mL) and $K_2CrO_4$ (0.25 mL)].
10. *Typical experimental procedure for the palladium-catalyzed Suzuki–Miyaura cross-coupling reaction.* A mixture of aryl halide **5** (0.5 mmol), arylboronic acid **6** (0.7 mmol), the polymer-supported DABCO–palladium complex (**4**) (0.25 mol %), $K_2CO_3$ (2.5 equiv) and $H_2O/CH_3CH_2OH$ (1:1; 4 mL) was stirred at room temperature for desired time until complete consumption of starting material as monitored by TLC. The reaction mixture was filtered to give a solution and a solid. The solution was evaporated, then extracted by diethyl ether, evaporated in vacuum and purified by flash column chromatography (hexane or hexane/ethyl acetate) to give the target product. After being washed by diethyl ether and dried, the solid was subjected to a second run of the coupling by charging with the same substrates, base and solvent (**5**, **6**, $K_2CO_3$ and $H_2O/CH_3CH_2OH$).
11. The loading level of Pd was decreased to 0.039 mmol/g after the fifth run, which was calculated by ICP-AES.