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Reusable Palladium N-Heterocyclic Tetracarbene for Aqueous Suzuki−Miyaura Cross-Coupling Reaction: Homogeneous Catalysis and Heterogeneous Recovery

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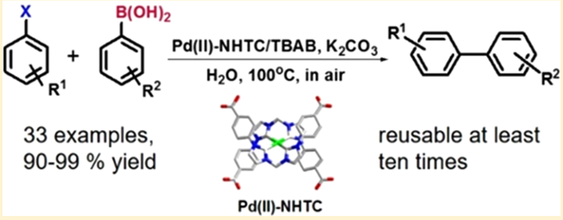
Supporting Information

ABSTRACT: A pH-responsive Pd(II) N-heterocyclic tetracarbene complex synthesized by a solvothermal method was reported. It can be a highly active reusable catalyst to homogeneously catalyze the Suzuki−Miyaura cross-coupling reaction in water and can be heterogeneously recovered by simply adjusting the pH value of the aqueous reaction media.



Palladium-catalyzed cross-coupling has provided a powerful tool in organic synthesis for C−C formation.[1] As palladium is a noble metal, its recovery and reuse are highly imperative. One useful way to address such an issue is to fabricate Pd-based heterogeneous catalysts. So far, various Pd heterogeneous catalysts of this type have been prepared by loading Pd species into porous supports such as polymers, silica, MOFs, COFs, and so on, which made Pd available for reuse.[2] The efficiency of heterogeneous catalysis, as is known, is generally lower than that of homogeneous catalysis due to its inherent nature. In addition, the Pd leaching from porous supports often occurs during heterogeneous catalytic processes. Thus, the most ideal case for a Pd-based catalytic procedure would be a homogeneous catalysis and a heterogeneous recovery.

On the other hand, water is a safe, abundant, eco-friendly, and low-cost solvent. The development of Pd-catalyzed cross-coupling reactions in neat water is significant. However, the limited stability and deactivation of Pd catalysts in aqueous media has largely impeded the practical application of Pd-based aqueous catalysis, although some remedies such as cosolvents/phase-transfer catalysts have been recently suggested.[3]

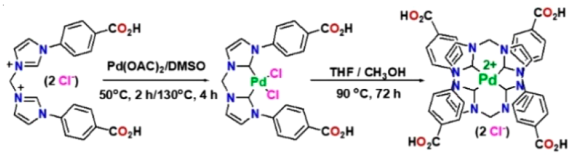
In addition, N-heterocyclic carbene (NHC) based Pd-NHC complexes are stable due to their high Pd−C dissociation energies. Moreover, they have exhibited remarkable catalytic performance in C−C coupling such as the Suzuki−Miyaura reaction.[4] To date, an increasing number of studies on aqueous metal NHC based catalysis have appeared in the literature.[5] However, reusable Pd-NHC catalysts for aqueous C−C cross-coupling have been very rarely reported.[6]

In principle, the water solubility of Pd-NHCs which contain a hydrophilic functional group such as carboxyl with active hydrogen atoms can be tuned by controlling the pH value of the aqueous phase. This provides a unique opportunity to design and prepare pH-driven Pd-NHCs for homogeneous aqueous catalysis and heterogeneous catalyst recovery. In this way, the requirements of highly efficient conversion, sustainability, and environmental friendliness for Pd-catalyzed C−C coupling would be met simultaneously.

In this contribution, we report for the first time the novel pH-responsive palladium N-heterocyclic tetracarbene complex Pd^{II}-NHTC (**3**), which was prepared under solvothermal conditions. The obtained Pd^{II}-NHTC (**3**) catalyst is air- and water-stable and can be reused to highly promote aqueous Suzuki−Miyaura cross-coupling in a homogeneous way on the basis of its unique pH-responsive aqueous solubility. By simply adjusting the pH value, the catalyst can be readily recovered heterogeneously from an aqueous reaction system and reused for the next catalytic run at least 10 times without loss of the catalytic activity.

As shown in Scheme 1, Pd^{II}-NHTC (**3**) was prepared via two steps. First, the palladium N-heterocyclic dicarbene Pd^{II}-NHDC (**2**) was synthesized as a light yellow solid by the

Scheme 1. Synthesis of the Multiple Carboxyl-Attached Pd N-Heterocyclic Tetracarbene Complex of 3



1 Pd(II)-NHDC (2) Pd(II)-NHTC (3)

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combination of Pd(OAc)$_2$ and a methylene-bridged bis(imidazolium) salt (**1**) with terminal carboxylate groups in 95% yield.[6,7] Second, the obtained **2** was heated under solvothermal conditions (THF/MeOH, 90 °C, 72 h) to generate the palladium N-heterocyclic tetracarbene **3** as colorless crystals with four terminal carboxylate groups in 50% yield (Supporting Information).

In comparison to **1**, the absence of a signal for the imidazolium methine protons at 10.65 ppm in the ^{1}H NMR spectra of **2** and **3** (Figure S1) indicated that the corresponding carbene species was successfully formed. Meanwhile, a single peak at 6.97 ppm for the methylene linkage in **1** was upshifted to 6.51−6.78 ppm as two doublets with geminal coupling signals in **2** and **3** (Figure 1). In the ^{13}C NMR spectra (Figures S2 and S3), the signals for carbene carbons appeared at 158.5 (**2**) and 168.7 ppm (**3**), respectively.[8] The IR spectra of **2** and **3** displayed strong carboxyl absorption bands at 1711−1715 cm^{-1} (Figure S4). The existence of a Pd species in **3** was further confirmed by inductively coupled plasma (ICP) analysis. The Pd amount in **3** was determined to be 11.21 wt % (calcd 11.81 wt %), which is quite consistent with its molecular formula of $C_{42}H_{32}N_8O_8PdCl_2$. The Pd valence was characterized by X-ray photoelectron spectroscopy (XPS). The main peaks at 337.9 and 343.1 eV could be assigned to the bivalent Pd binding energy (Figure S5).[9]

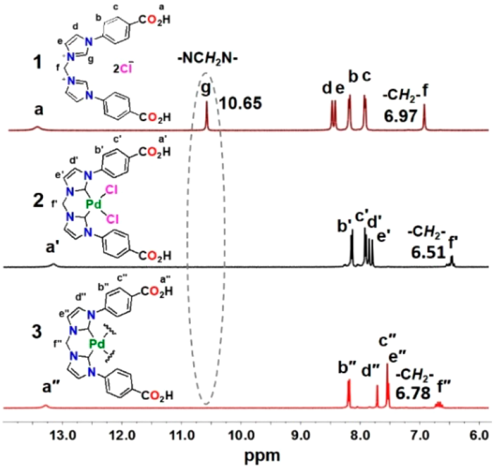


Figure 1. ^{1}H NMR spectra of **1**−**3**.

The structure of Pd^{II}-NHTC (**3**) was finally determined by a single-crystal analysis (CCDC 1815220, Table S1). As indicated in Figure 2, **3** crystallized in the triclinic space group $P\bar{1}$. The Pd(II) center was surrounded by two twisted carboxyl-attached and methylene-bridged bis(imidazolium) ligands to form a Pd(II)−tetracarbene complex. The Pd(II) center adopted a quasi-square-planar coordination sphere with Pd−C bond distances of 2.020(4) and 2.037(5) Å, respectively. The corresponding ∠C(10)−Pd(1)−C(10)#1 and ∠C(10)−Pd(1)−C(12) angles are 180.000 and 94.58(18)°, respectively (Table S2).[8]

As is known, Pd-NHC complexes are stable to air and moisture. For the application of **3** in aqueous homogeneous catalysis and heterogeneous recovery in the Suzuki−Miyaura coupling, its pH-driven aqueous solubility was tested. As shown in Figure 2b, with the aid of K$_2$CO$_3$ (pH 8), **3** readily dissolved in neat water due to the carboxyl−carboxylate conversion. However, it was easily precipitated out from aqueous solution once the pH value was adjusted to 5 with dilute HCl (Figure 2b). Such a phenomenon made the **3**-based aqueous homogeneous catalysis under alkaline conditions and heterogeneous catalyst recovery under acidic conditions feasible.

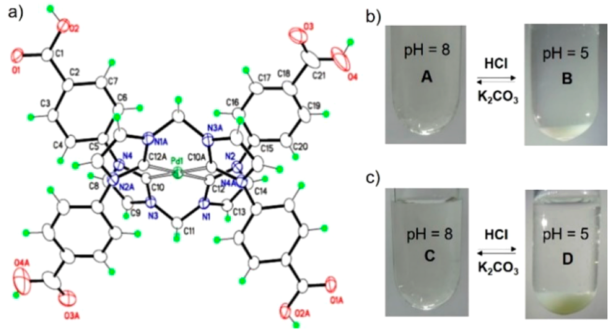
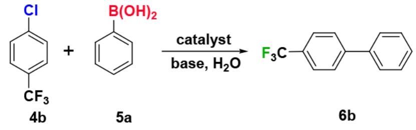


Figure 2. (a) ORTEP figure of **3**. (b) pH-driven solubility of **3** in neat water. (c) pH-induced aqueous solubility changes of **3** before and after the model coupling reaction of 4-chlorobenzotrifluoride (**4b**) with phenylboronic acid (**5a**).

Our initial Pd^{II}-NHTC (**3**) catalytic activity test for the Suzuki−Miyaura coupling started with 4-chlorobenzotrifluoride (**4b**) and phenylboronic acid (**5a**). Optimization of the reaction was first conducted at different temperatures such as 50, 80, and 100 °C to furnish the desired product **6b** under the given reaction conditions (Table 1, entries 1−3). The best result was observed when the reaction was performed at 100 °C to give **6b** in 99% yield (Table 1, entries 3 and 7), which placed **3** in a strong position among the reported Pd-NHC catalysts for aqueous Suzuki−Miyaura cross-coupling.[5] In addition, when the reaction was carried out in water with a lower catalyst loading, 0.5, 0.1, and 0.01 mol % instead of 1 mol %, the coupled product of **6b** was isolated in lower yields (Table 1,

Table 1. Optimization of the Model Suzuki−Miyaura Cross-Coupling Reaction of 4-Chlorobenzotrifluoride (4b) with Phenylboronic Acid (5a)[a]



entry	cat. (mol %)	t (h)	base	cocat. (1.0 equiv)	T (°C)	yield (%)[b]
1	1	1	K$_2$CO$_3$	TBAB	50	50
2	1	1	K$_2$CO$_3$	TBAB	80	74
3[c]	1	1	K$_2$CO$_3$	TBAB	100	99
4	0.5	1	K$_2$CO$_3$	TBAB	100	74
5	0.1	1	K$_2$CO$_3$	TBAB	100	56
6	0.01	1	K$_2$CO$_3$	TBAB	100	20
7	1	1	K$_3$PO$_4$	TBAB	100	99
8	1	1	Et$_3$N	TBAB	100	50
9	1	1	Cs$_2$CO$_3$	TBAB	100	59
10[d]	1	1	K$_2$CO$_3$		100	70
11	1	1	K$_2$CO$_3$	TBAB (0.8 equiv)	100	92
12	1	1	K$_2$CO$_3$	TBAB (0.5 equiv)	100	75

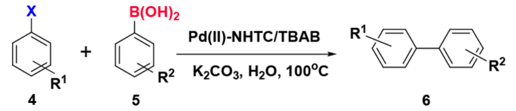
[a]Reaction conditions: 4-chlorobenzotrifluoride (**4b**, 1.0 mmol), phenylboronic acid (**5a**, 1.1 mmol), base (2.0 mmol), H$_2$O (2 mL), in air. [b]Isolated yield. [c]The TON and TOF values are 99 and 99 h^{-1}, respectively. [d]Pd black appeared during the reaction.

entries 4–6), but with improved TON values (i.e., TON values changed from 99 to 148, 560, and 2000, respectively). Furthermore, K_2CO_3 and K_3PO_4 were found to be superior over Cs_2CO_3 and Et_3N (Table 1, entries 7–9). Without the aid of tetra-*n*-butylammonium bromide (TBAB), **6b** was isolated in only 70% yield because TBAB can suppress Pd leaching[6] and the formed $Bu_4NPhB(OH)_3$ can facilitate the Suzuki–Miyaura cross-coupling reaction (Table 1, entry 10).[10] A lower amount of TBAB would also lead to lower yield (Table 1, entries 11 and 12).

Once the reaction was finished, the product was easily separated by ether extraction. Then, the pH value of the residual aqueous solution was tuned to 5 with dilute HCl. The regenerated **3** was obtained as a white solid (Figure 2c), and it could be reused for the next run after water washing. On the other hand, an aqueous solution containing deprotonated **3** could also be directly reused for the next run without isolation. Notably, **3** can be reused at least 10 times without loss of its catalytic activity under the optimized conditions (Figure S6). In addition, ^1H NMR (Figure S7), ^{13}C NMR (Figure S8), and IR spectra (Figure S9) demonstrated that **3** is stable after 10 catalytic runs. The Pd amount in **3** after 10 catalytic cycles was still up to 11.15 wt % (determined by ICP), indicating that no Pd species leaching occurred during the reuse process. On the other hand, no valence change for Pd(II) was detected on the basis of XPS measurements after 10 catalytic cycles (Figure S10). On the basis of the above observations, the Pd-based tetracarbene complex **3** herein is very stable (Figure S11) under the reaction conditions; moreover, it showed much better catalytic performance in comparison to that of a reported Pd-based dicarbene complex (Table S3).[6] The robust, highly active, and facile recyclable nature of **3** make it an important candidate for the practical applications in C–C cross-coupling. We distance ourselves from any type of explanation and frankly say that we do not know the detailed mechanism of **3** for this aqueous Suzuki–Miyaura cross-coupling at this stage, but we believe it might go through a catalytic pathway similar to those of reported palladium N-heterocyclic dicarbene catalysts.[4,5]

On the basis of the above optimized reaction conditions, the scope of the reaction was explored (Table 2). To our delight, **3** could tolerate various functional groups such as $-CF_3$, $-NO_2$, $-COCH_3$, $-CH_3$, $-OCH_3$, $-OH$, $-CO_2Me$, and $-CN$ at different substituent positions. As shown in Table 2, the electronic effect of the substituents appeared to be crucial. For aryl chlorides without substituents or with electron-withdrawing groups at different positions (Table 2, entries 1–11), the target cross-coupling products were obtained in excellent yields (93–99%) within 1 h. Meanwhile, the substituent groups on the aryl boric acids have no obvious effect on the coupling reactions under the reaction conditions (Table 2, entries 7–11). However, aryl chlorides with electron-donating groups, for example, 4-chloroanisole (**4h**) and phenylboronic acid (**5a**) coupling (Table 2, entry 12), gave an exceptionally low yield (56%) even at a prolonged reaction time (3 h). Further study indicated that Pd leaching occurred during this reaction (Figure S12), and the leaching amount in aqueous solution was 4.84 ppm (determined by ICP). This observation was further supported by high-resolution transmission electron microscopy measurements (Figure S13). The low reactivity of **4h** with an electron-donating $-OCH_3$ group in the reaction might be due to the reluctance of its C–Cl bond to oxidatively add to the Pd center, and Pd was likely to be reduced by boric acid.[11]

Table 2. Suzuki–Miyaura Cross-Coupling Reactions of Various Aryl Halides and Aryl Boric Acids Catalyzed by 3[a]



entry	substrate 4	substrate 5	t (h)	yield of 6 (%)[b]
1	**4a**: R^1 = H, X = Cl	**5a**: R^2 = H	1	**6a**: 99
2	**4b**: R^1 = 4-CF_3, X = Cl	**5a**: R^2 = H	1	**6b**: 99
3	**4c**: R^1 = 4-NO_2, X = Cl	**5a**: R^2 = H	1	**6c**: 99
4	**4d**: R^1 = 4-$COCH_3$, X = Cl	**5a**: R^2 = H	1	**6d**: 99
5	**4e**: R^1 = 2-CN, X = Cl	**5a**: R^2 = H	1	**6e**: 97
6	**4f**: R^1 = 2-CH_3, X = Cl	**5a**: R^2 = H	1	**6f**: 97
7	**4b**: R^1 = 4-CF_3, X = Cl	**5b**: R^2 = 3-CN	1	**6g**: 95
8	**4c**: R^1 = 4-NO_2, X = Cl	**5c**: R^2 = 4-F	1	**6h**: 94
9	**4g**: R^1 = 3-$COCH_3$, X = Cl	**5d**: R^2 = 4-OCH_3	1	**6i**: 93
10	**4e**: R^1 = 2-CN, X = Cl	**5e**: R^2 = 3-OCH_3	1	**6j**: 97
11	**4b**: R^1 = 4-CF_3, X = Cl	**5f**: R^2 = 2-OCH_3	1	**6k**: 96
12[c]	**4h**: R^1 = 4-OCH_3, X = Cl	**5a**: R^2 = H	3	**6l**: 56
13[d]	**4i**: R^1 = H, X = Br	**5a**: R^2 = H	0.5	**6a**: 99
14	**4j**: R^1 = 4-NO_2, X = Br	**5a**: R^2 = H	0.5	**6c**: 97
15	**4k**: R^1 = 4-$COCH_3$, X = Br	**5a**: R^2 = H	0.5	**6d**: 99
16	**4l**: R^1 = 4-OCH_3, X = Br	**5a**: R^2 = H	0.5	**6l**: 95
17	**4m**: R^1 = 4-CO_2CH_3, X = Br	**5a**: R^2 = H	0.5	**6m**: 99
18	**4n**: R^1 = 3-OH, X = Br	**5a**: R^2 = H	0.5	**6n**:90
19	**4o**: R^1 = 2-CH_3, X = Br	**5a**: R^2 = H	0.5	**6f**: 99
20	**4p**: R^1 = 3-NO_2, X = Br	**5a**: R^2 = H	0.5	**6o**: 99
21	**4q**: R^1 = 2-CN, X = Br	**5a**: R^2 = H	0.5	**6e**: 95
22	**4i**: R^1 = H, X = Br	**5g**: R^2 = 4-CN	0.5	**6p**: 95
23	**4i**: R^1 = H, X = Br	**5d**: R^2 = 4-OCH_3	0.5	**6l**: 99
24[d]	**4r**: R^1 = H, X = I	**5a**: R^2 = H	0.5	**6a**: 99
25	**4s**: R^1 = 2-OCH_3, X = I	**5a**: R^2 = H	0.5	**6q**: 95
26	**4t**: R^1 = 2-CF_3, X = I	**5a**: R^2 = H	0.5	**6r**: 99
27	**4u**: R^1 = 3-CH_3, X = I	**5a**: R^2 = H	0.5	**6s**: 98
28	**4v**: R^1 = 3-NO_2, X = I	**5a**: R^2 = H	0.5	**6o**: 97
29	**4w**: R^1 = 4-OCH_3, X = I	**5a**: R^2 = H	0.5	**6l**: 98
30	**4x**: R^1 = 4-CN, X = I	**5a**: R^2 = H	0.5	**6p**:99
31	**4y**: R^1 = 4-CO_2CH_3, X = I	**5a**: R^2 = H	0.5	**6m**:99
32	**4s**: R^1 = 2-OCH_3, X = I	**5a**: R^2 = H	0.5	**6q**: 95
33	**4r**: R^1 = H, X = I	**5g**: R^2 = 4-CN	0.5	**6p**: 93
34	**4r**: R^1 = H, X = I	**5d**: R^2 = 4-OCH_3	0.5	**6l**: 98

[a] Reaction conditions: aryl halide (1.0 mmol), boric acid (1.1 mmol), K_2CO_3 (2.0 mmol), **3** (1.0 mol %), TBAB (1.0 mmol), H_2O (2 mL), in air. [b] Isolated yield. [c] Pd black was found after the reaction (Supporting Information). [d] For PhBr and PhI with phenylboronic acid, a 99% yield could also be reached with 0.2 mol % of **3**, but lower catalyst loading (0.1 mol %) would decrease the yields within 0.5 h (Table S4). The characterization data for the coupled products are provided in the Supporting Information.

Aryl bromides were more active for the cross-coupling reaction. As shown in Table 2 (entries 13–23), the yields for the target coupled products were in the range of 90–99% within only 0.5 h. Similar to the case for aryl chlorides, lower yields were obtained for an electron-donating group attached to an aryl bromide (Table 2, entry 18). In addition, aryl iodides exhibited even higher reactivity, and all the aryl iodides employed under the optimized conditions furnished excellent coupling yields (93−99%) within 0.5 h (Table 2, entries 24−34). Again, electron-withdrawing or electron-donating groups on the arylboronic acid counterparts did not significantly affect the coupling yields between aryl bromides or aryl iodides with corresponding arylboronic acids.

In summary, we reported herein a novel Pd(II)−tetracarbene complex which was synthesized under solvothermal conditions. The obtained Pd^{II}-NHTC (**3**) is air- and water-stable and exhibits an interesting pH-responsive aqueous solubility. More importantly, it is able to highly promote the aqueous Suzuki−Miyaura cross-coupling homogeneously and can be readily recovered heterogeneously by simply adjusting the pH value of the aqueous reaction solution. We expect this approach to be viable for the construction of many more new and interesting metal-NHC-containing catalytic systems for organic transformations in this way.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.8b00195.

> Synthesis, characterization, catalytic activity, and catalytic cycle of **3**, single-crystal data of **3**, comparison of **3** with the reported N-heterocyclic dicarbene Pd(II) complex, and product characterization for the **3**-catalyzed cross-coupling reactions (PDF)

Accession Codes

CCDC 1815220 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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