# Dinuclear Triphenylphosphine-Cyclopalladated 2,4-Dichloropyrimidine Complex with a Pd–Pd Bond: Synthesis, Crystal Structure, and Application in Suzuki Reaction of 3-(Hydroxymethyl)phenylboronic Acid in Water

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Cyclopalladated complexes have attracted considerable attention due to their high activity as effective precatalysts in coupling reactions.[1] Among several routes to palladacycle synthesis, the oxidative addition of Pd(0) to aryl halide species is a useful method for the generation of various palladacycles that cannot usually be obtained by direct C–H bond activation procedures. The most common palladacycles are halogen bridge dimers, phosphine-bound monomers, or pincer complexes and are usually five- or six-membered rings. However, a few examples of four-membered ring palladacycles have been reported.[2] For example, oxidative addition of 2-bromopyridine to [$Pd(PPh_3)_4$] results in a dinuclear pyridyl-bridged palladium complex with Pd–C and Pd–Pd bonds, which shows good catalytic activity for the Suzuki reaction.[3]

Recently, a part of our research effort has focused on the palladium-catalyzed coupling reactions.[4] In a preliminary study,[4d] we reported the convenient synthesis of substituted ferrocenylpyrimidines by coupling of 2,4,6-trichloro-pyrimidine (Scheme 1(a)). It was interesting that a red component as a side product was obtained from chromatography, which crystallized on evaporation to give suitable crystal for X-ray diffraction. The single-crystal X-ray analysis indicated that each Pd atom adopts a *trans* configuration of the phosphorus atom of $PPh_3$ to the nitrogen atom of pyrimidine (Figure 1). The two Pd centers are bridged by two pyrimidine ligands, and this arrangement leads to a short Pd–Pd contact (3.0972(5) Å), which is shorter than the sum of the van der Waals Pd radii (3.26 Å).[3,5] The four-membered [C,N,Pd,Pd] chelate ring and the pyrimidine ring are approximately coplanar (dihedral angles of 5.6° and 3.6°, respectively). These planes are inclined at an angle of 94.0°, forming a six-membered ring in a boat conformation.

Considering that pyrimidine chloride is very reactive, we speculated that the oxidative addition of 2,4,6-trichloropyrimidine to $Pd(PPh_3)_4$ could generate the dinuclear metallated palladium complex **1**. Thus, we investigated the above oxidative addition (Scheme 1(b)). As expected, 2,4,6-trichloropyrimidine reacted with [$Pd(PPh_3)_4$] and NaI, giving **1** in 52% yield. Complex **1** represented an intermediate catalyst in the coupling of chloromercuriferrocene and 2,4,6-trichloropyrimidine. In view of these findings and our continued interest in the synthesis of biarylmethanols,[6] we examined **1** as a precatalyst for the Suzuki reaction of 3-(hydroxymethyl)-phenylboronic acid.

The palladium-catalyzed Suzuki reaction is one of the most powerful methods of forming C–C bonds, and it is of particular interest to utilize water as a green solvent.[7] In the present study, our initial exploration of reaction conditions focused on the coupling of 3-(hydroxymethyl)phenylboronic acid with 4-bromotoluene using 0.2 mol % of **1** in water at 100 °C for 12 h, and the results are shown Table 1. The isolated yield of the coupled product **2a** was only 36% in presence of 3 equiv of $K_2CO_3$ (entry 1). However, the addition of $Bu_4NBr$ (TBAB) as a cocatalyst[8] gave a good yield (83%, entry 2). Under the same reaction conditions, $Pd(OAc)_2$ and $PdCl_2$ generated **2a** in low yields (entries 3, 4). We next investigated the effect of different bases, and $Cs_2CO_3$ was found to give the best result (86%, entry 6); $K_3PO_4 \cdot 3H_2O$ also afforded good yield (82% entry 7).

Suzuki reactions of 3-(hydroxymethyl)phenylboronic acid with a variety of electronically and structurally diverse aryl halides were carried out to explore the scope of this system (Table 2). Similar to the result of 4-bromotoluene, good yields were also obtained in the cases of bromobenzene and 4-bromoanisole (entries 1 and 2). For ortho-substituents with methyl and methoxy groups, the yields decreased slightly (entries 3 and 4). Excellent yields were also obtained with electron-deficient aryl bromides (92–94%, entries 5 and 6). In addition, the couplings of aryl chlorides were also examined (entries 7 and 9). In the case of chlorotoluene, **1** was almost inactive under the same reaction conditions. For electron-deficient aryl chlorides, the coupled products **2f** and **2g** were

Correction added on 01 October 2015, after first online publication: ISSN (Print) has been corrected.

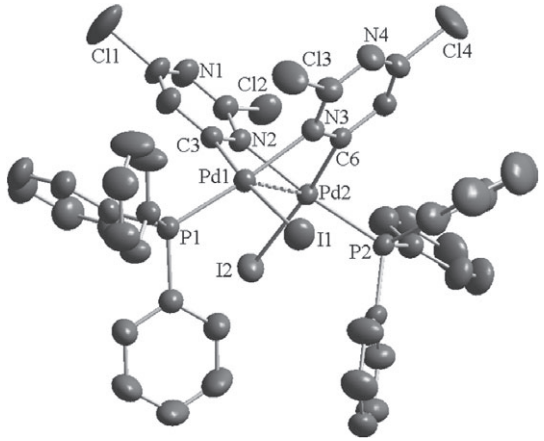
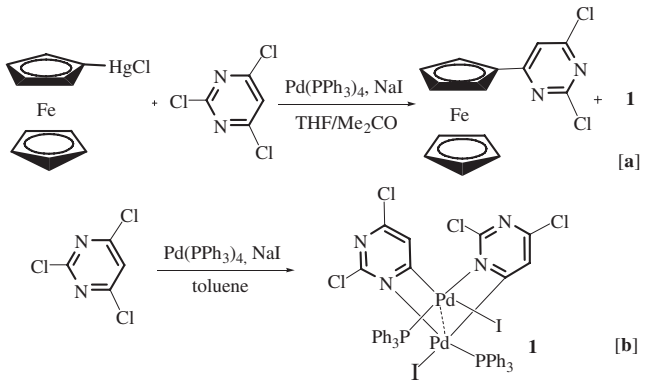



**Figure 1.** Molecular structure of complex **1**. H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Pd1–Pd2 3.0972(5), Pd1–C3 1.994(4), Pd1–P1 2.2637(11), Pd1–I1 2.6450(5), Pd1–N3 2.128(3), Pd2–C6 1.996(4), Pd2–P2 2.2640(10), Pd2–I2 2.6563 (5), Pd2–N2 2.135(3) and C3–Pd1–I1 173.33(11), P1–Pd1–N3 175.00(9), C6–Pd2–I2 172.03(11), P2–Pd2–N2 174.10(9).




**Scheme 1.** Synthesis of complex **1**.

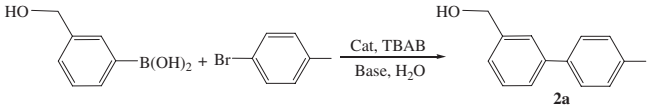
obtained in moderate yields. Finally, we also investigated the couplings of *N*-heteroaryl bromides. The couplings of *N*-heteroaryl bromides proceeded efficiently to form the expected products **2h–2o** in moderate to good yields (entries 10–17).

In conclusion, a dinuclear cyclopalladated palladium complex **1** has been synthesized and characterized. Its catalytic activity was evaluated in the Suzuki reaction of 3-(hydroxymethyl)phenylboronic acid in water. We have developed a practical method for the synthesis of biarylmethanol.

## Experimental

**Materials and Measurement.** All other chemicals were used as purchased. Elemental analyses were determined with a Thermo Flash EA 1112 elemental analyzer (Thermo, Waltham, USA). Mass spectra were measured on an LC-MSD-Trap-XCT instrument (Agilent, CA, USA). NMR spectra were recorded on a Bruker DPX-400 spectrometer

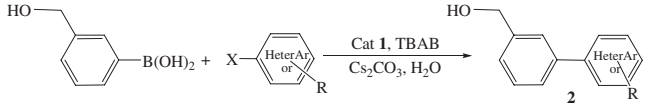
**Table 1.** Influence of base and catalyst on the Suzuki coupling of 3-$HOCH_2$-$PhB(OH)_2$.[a]




| Entry | Catalyst (mol %) | Base | Yield (%)[b] |
|---|---|---|---|
| 1[c] | **1**(0.2) | $K_2CO_3$ | 36 |
| 2 | **1**(0.2) | $K_2CO_3$ | 83 |
| 3 | $Pd(OAc)_2/PPh_3$ (0.5/1) | $K_2CO_3$ | 35 |
| 4 | $PdCl_2/PPh_3$ (0.5/1) | $K_2CO_3$ | 39 |
| 5 | **1**(0.2) | $Na_2CO_3$ | 77 |
| 6 | **1**(0.2) | $Cs_2CO_3$ | 86 |
| 7 | **1**(0.2) | $K_3PO_4$ | 82 |
| 8 | **1**(0.2) | KOAc | 67 |

[a] Reaction conditions: 4-bromotoluene (1 mmol), 3-$HOCH_2$–$PhB(OH)_2$ (1.5 mmol), TBAB (1 mmol), base (3 mmol), water (3 mL), 100 °C,12 h.
[b] Isolated yields.
[c] In absence of TBAB.

**Table 2.** Suzuki coupling of aryl halides with 3-$HOCH_2$–$PhB(OH)_2$ catalyzed by **1**.[a]




| Entry | X | R (or HeterAr) | Product no. Yield (%)[b] |
|---|---|---|---|
| 1 | Br | $H(C_6H_4)$ | **2b** 89 |
| 2 | Br | *p*-$OCH_3(C_6H_4)$ | **2c** 85 |
| 3 | Br | *o*-$CH_3(C_6H_4)$ | **2d** 78 |
| 4 | Br | *o*-$OCH_3(C_6H_4)$ | **2e** 73 |
| 5 | Br | *p*-$CH_3CO(C_6H_4)$ | **2f** 92 |
| 6 | Br | *p*-$NO_2(C_6H_4)$ | **2g** 94 |
| 7 | Cl | *p*-$CH_3(C_6H_4)$ | **2a** trace |
| 8 | Cl | *p*-$CH_3CO(C_6H_4)$ | **2f** 62 |
| 9 | Cl | *p*-$NO_2(C_6H_4)$ | **2g** 67 |
| 10 | Br | H(pyridin-2-yl) | **2h** 86 |
| 11 | Br | H(pyridin-3-yl) | **2i** 79 |
| 12 | Br | 4-$CH_3$(pyridin-3-yl) | **2j** 83 |
| 13 | Br | 5-$CH_3$(pyridin-3-yl) | **2k** 80 |
| 14 | Br | 6-$CH_3$(pyridin-3-yl) | **2l** 77 |
| 15 | Br | H(pyrazin-2-yl) | **2m** 85 |
| 16 | Br | H(pyrimidin-2-yl) | **2n** 88 |
| 17 | Br | 4,6-$2CH_3$(pyrimidin-2-yl) | **2o** 81 |

[a] Reaction conditions: aryl halides (1 mmol), 3-$HOCH_2$–$PhB(OH)_2$ (1.5 mmol), Cat **1** (0.02 mmol), TBAB (1 mmol), $Cs_2CO_3$ (3 mmol), water (3 mL), 100 °C, 12 h.
[b] Isolated yields.

in $CDCl_3$ with TMS as an internal standard. Crystallographic data were collected on a Bruker SMART APEX-II CCD diffractometer (Brucker, Ettlingen, Germany). CCDC reference number is 1037698 for **1**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/datarequest/cif.

**$[(C_4N_2HCl_2)_2Pd_2(PPh_3)_2I_2]$ (1).** A reaction mixture of $Pd(PPh_3)_4$ (0.2 mmol), 2,4,6-trichloropyrimidine (0.2 mmol), and NaI (0.3 mmol) in toluene (10 mL) was refluxed under nitrogen atmosphere for 3 h and then cooled to room temperature. Purification by flash chromatography gave the complex **1**. Red solid, 52% yield. Anal. Calcd. for $C_{44}H_{32}Cl_4I_2N_4P_2Pd_2$: C, 41.06; H, 2.51; N, 4.35. Found: C, 41.29; H, 2.33; N, 4.52. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.72–7.81 (12H, m, ArH), 7.28–7.42 (20H, m, PyH + ArH). MS-ESI$^+$ [*m/z*]: 1029.9 $(M - 2I)^{2+}$.

**General Procedure for the Suzuki Coupling.** A Schlenk tube was charged with the prescribed amount of catalyst, aryl halide (1.0 mmol), 3-(hydroxymethyl)phenylboronic acid (1.5 mmol), TBAB (1.0 mmol), the selected base (3.0 mmol), and water under nitrogen atmosphere. The reaction mixture was heated at 100 °C for 12 h. After cooling, the mixture was extracted with $CH_2Cl_2$, the solvent was evaporated, and the product was separated by passing through a silica gel column with $CH_2Cl_2$/ethyl acetate (5:1) as eluent. The products **2f, 2j, 2l,** and **2o** were new compounds and were determined by $^1$H and $C^{13}$ NMR. Other products were characterized by comparison with data in the literature.[9]

**4′-Acetyl-biphenyl-3-methanol (2f ):** Yield 92% (based on *p*-$CH_3CO(C_6H_4)Br$). Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.85; H, 6.09. MS-ESI$^+$ [*m/z*]: 226.1 ($M^+$). $^1$H NMR. (400 MHz, $CDCl_3$): δ 7.99 (d, $J$ = 6.8 Hz, 2H, ArH), 7.66 (d, $J$ = 6.8 Hz, 2H, ArH), 7.62 (s, 1H, ArH), 7.53 (d, $J$ = 6.0 Hz, 1H, ArH), 7.44 (t, $J$ = 6.0 Hz, 1H, ArH), 7.26 (s, 1H, ArH), 4.77 (s, 2H, $CH_2$), 3.16 (s, 1H, OH), 2.61 (s, 3H, $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): 198.1, 145.6, 141.9, 140.1, 135.8, 129.2, 128.9, 127.2, 126.8, 126.4, 125.8, 65.1, 26.7.

**[3-(4-Methylpyridin-2-yl)phenyl]methanol (2j):** Yield 83%. Anal. Calcd. for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.25; H, 6.47; N, 7.21. MS-ESI$^+$ [*m/z*]: 200.1 $(M + H)^+$. $^1$H NMR. (400 MHz, $CDCl_3$): δ 7.93 (s, 1H, ArH), 7.84 (m, 1H, ArH), 7.53 (s, 1H, ArH), 7.38–7.42 (m, 2H, ArH), 7.06 (s, 1H, ArH), 4.72 (s, 2H, $CH_2$), 2.82 (br, 1H, OH), 2.40 (s, 3H, $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): 157.2, 149.2, 148.0, 141.6, 139.7, 128.9, 127.4, 126.1, 125.8, 123.3, 121.8, 65.1, 21.2.

**[3-(6-Methylpyridin-2-yl)phenyl]methanol (2l):** Yield 77%. Anal. Calcd. for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.48; H, 6.43; N, 7.19. MS-ESI$^+$ [*m/z*]: 200.1 $(M + H)^+$. $^1$H NMR. (400 MHz, $CDCl_3$): δ 7.77 (s, 1H, ArH), 7.67 (d, $J$ = 6.0 Hz, 1H, ArH), 7.48 (t, $J$ = 6.0 Hz, 1H, ArH), 7.32 (d, $J$ = 6.0 Hz, 1H, ArH), 7.25 (t, $J$ = 6.0 Hz, 1H, ArH), 7.18 (t, $J$ = 6.0 Hz, 1H, ArH), 6.96 (t, $J$ = 6.0 Hz, 1H, ArH), 4.52 (s, 2H, $CH_2$), 3.70 (br, 1H, OH), 2.50 (s, 3H, $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): 158.3, 157.0, 141.8, 139.7, 137.1, 128.7, 127.3, 126.0, 125.6, 121.8, 118.1, 64.7, 24.5.

**[3-(4,6-Dimethylpyrimidin-2-yl)phenyl]methanol (2o):** Yield 81%. Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.07. Found: C, 72.98; H, 6.46; N, 13.21. MS-ESI$^+$ [*m/z*]: 215.1 $(M + H)^+$. $^1$H NMR. (400 MHz, $CDCl_3$): δ 8.18–8.22 (m, 2H, ArH), 7.30 (s, 2H, ArH), 6.80 (s, 1H, ArH), 4.59 (s, 2H, $CH_2$), 3.22 (s, 1H, OH), 2.41 (s, 6H, $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): 166.9, 164.1, 141.4, 138.1, 128.9, 128.7, 127.4, 126.7, 118.1, 65.0, 24.1.

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**Supporting Information.** Additional supporting information is available in the online version of this article.

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