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Synthesis, crystal structures and catalytic activity of three cyclopalladated 6-bromo-2-ferrocenylquinoline complexes with *N*-heterocyclic carbenes (NHCs) and triphenylphosphine

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ABSTRACT

Three cyclopalladated 6-bromo-2-ferrocenylquinoline complexes with NHCs and PPh_3 **1**–**3** have been synthesized and characterized by elemental analysis, IR, NMR and single-crystal X-ray diffraction. Their application to Suzuki coupling of phenylboronic acid containing hydroxymethyl was also investigated. An efficient **3**/Cu cocatalyzed oxidation/Suzuki coupling of aryl chlorides with phenylboronic acids containing hydroxymethyl in air has been developed.

1. Introduction

Cyclopalladated complexes have attracted a great deal of attention due to their high activity as precatalysts in coupling reactions [1]. In general, adducts of palladacycles combine the stability induced by the presence of a palladacycle framework with phosphine ligands or NHCs, and were far more active than the corresponding dimeric palladacycles. For example, Buchwald [2], Nolan [3] groups have reported the use of dialkylbiaryl phosphine-palladacycles and NHC-palladacycles as highly efficient catalysts for Suzuki reaction of unactivated aryl chlorides. In addition, palladium-catalyzed alcohol oxidation to carbonyl compounds is one of the most fundamental and widely utilized transformations in organic synthesis [4]. Great recent progress has been obtained for the palladium-catalyzed oxidation by using NHC ligands or nitrogen donor ligands reported by Sigman and co-workers [5]. Recently, we have also developed NHC-palladacycles/Cu cocatalyzed oxidation/Suzuki reaction for the synthesis of biarylaldehydes from chlorophenylmethanol and arylboronic acids [6]. As a continuation of our interest in the synthesis and application of cyclopalladated ferrocene complexes [7], we prepared three adducts of palladacycle **1**–**3** (Scheme 1) and examined their catalytic activity in Suzuki reaction and described **3**/$Cu(OAc)_2$-cocatalyzed one-pot reaction for the synthesis of biarylaldehydes from aryl chlorides and arylboronic acids containing hydroxymethyl.

2. Experimental

2.1. General procedures

Solvents were dried and freshly distilled prior to use. All other chemicals were commercially available except for the 6-bromo-2-ferrocenylquinoline which was prepared according to the published procedure [8]. Elemental analyses were determined with a Carlo Erba 1160 Elemental Analyzer. IR spectra were collected on a Bruker VECTOR22 spectrophotometer in KBr pellets. NMR spectra were recorded on a Bruker DPX-400 spectrometer in $CDCl_3$ with TMS as an internal standard. Crystallographic data for **1** and **2**, **3** were measured on a Bruker SMART APEX-II CCD diffractometer and a Xcalibur, Eos, Gemini diffractometer, respectively. The data were corrected for Lorentz polarization factors as well as for absorption. Structures were solved by direct methods and refined by full-matrix least-squares methods on F^2 with the SHELX-97 program. All non-hydrogen atoms were refined anisotropically.

2.2. The synthesis of cyclopalladated complex *1*

A mixture of 6-bromo-2-ferrocenylquinoline (1 mmol), Li_2PdCl_4 (1 mmol) and NaOAc (1.1 mmol) in 10 mL of dry methanol was

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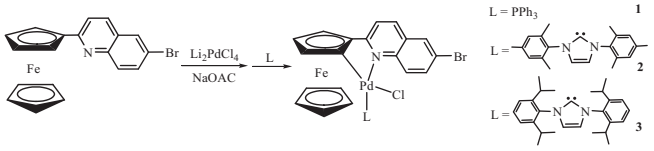
0020-1693/



Scheme 1. Synthesis of **1**–**3**.

stirred for 12 h at rt. The formed red solid (yield: 92%) were collected by filtration, and can be assigned as a chloride-bridged palladacyclic dimer [6,7]. Without further purification, the above dimer was treated with PPh_3 (1.1 mmol) in CH_2Cl_2 at rt for 1 h. The product **1** was separated by passing through a short silica gel column with CH_2Cl_2 as eluent. Red solid, yield: 93%. *Anal.* Calc. for $C_{37}H_{28}BrClFeNPPd$: C, 55.88; H, 3.55; N, 1.76. Found: C, 55.99; H, 3.41; N, 1.93%. IR (KBr, cm^{-1}): 2918, 1595, 1506, 1462, 1372, 1260, 1187, 1068, 1018, 918, 806,774. ^1H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H, ArH), 7.73–7.99 (m, 9H, ArH), 7.41–7.43 (m, 10H, ArH), 4.68 (s, 1H, C_5H_3), 4.15 (s, 1H, C_5H_3), 3.74 (s, 5H, C_5H_5), 3.67 (s, 1H, C_5H_3).

2.3. General procedure for the synthesis of cyclopalladated complexes *2* and *3*

A Schlenk tube was charged with the above dimer (0.5 mmol), the corresponding imidazolium salt (1.2 mmol) and K^{t}OBu (2.0 mmol) under nitrogen. Dry THF was added by a cannula and the solution was stirred for 3 h at rt. The product was separated by passing through a short silica gel column with CH_2Cl_2 as eluent, the second band was collected and afforded the corresponding NHC-palladacycles **2** and **3**. (**2**): Red solid, yield 89%. *Anal.* Calc. for $C_{40}H_{37}BrClFeN_3Pd$: C, 57.37; H, 4.45; N, 5.02. Found: C, 57.52; H, 4.26; N, 5.15%. IR (KBr, cm^{-1}): 2916, 1592, 1548, 1480, 1402, 1321, 1103, 1018, 920, 731. ^1H NMR (400 MHz, $CDCl_3$): δ 9.36 (s, 1H, ArH), 7.79 (d, 1H, ArH), 7.66 (s, 1H, ArH), 7.59 (m, 1H, ArH), 7.07–7.22 (m, 5H, ArH), 6.85 (s, 1H, ArH), 6.71 (s, 1H, ArH), 4.59 (s, 1H, C_5H_3), 4.20 (s, 1H, C_5H_3), 3.97 (s, 1H, C_5H_3), 3.43 (s, 5H, C_5H_5), 2.91 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 2.35 (s, 6H, CH_3), 2.17 (s, 3H, CH_3), 1.92 (s, 3H, CH_3). (**3**): Red solid, yield 88%. *Anal.* Calc. for $C_{46}H_{49}BrClFeN_3Pd$: C, 59.95; H, 5.36; N, 4.56. Found: C, 60.12; H, 5.18; N, 4.73%. IR (KBr, cm^{-1}): 2957, 1589, 1547, 1462, 1361, 1329, 1259, 1103, 1040, 920, 819, 810, 699. ^1H NMR (400 MHz, $CDCl_3$): δ 9.51 (s, 1H, ArH), 7.79 (d, 1H, ArH), 7.68 (s, 1H, ArH), 7.47–7.55 (m, 4H, ArH), 7.18–7.26 (m, 5H, ArH), 7.15 (d, 1H, ArH), 4.95–5.02 (m, 1H, CH), 4.56 (s, 1H, C_5H_3), 4.25 (s, 1H, C_5H_3), 3.89 (s, 1H, C_5H_3), 3.27 (m, 6H, C_5H_5+CH), 2.87–2.98 (m, 2H, CH), 1.84 (d, 3H, CH_3), 1.61 (d, 3H, CH_3), 1.52 (d, 3H, CH_3), 1.45 (d, 3H, CH_3), 1.25 (d, 3H, CH_3), 1.08 (d, 3H, CH_3), 0.83 (s, 3H, CH_3), 0.62 (s, 3H, CH_3).

2.4. General procedure for the one-pot oxidation/Suzuki coupling

A 10 mL round-bottom flask was charged with the prescribed amount of catalyst Pd/Cu, aryl chlorides (0.5 mmol), phenylboronic acids containing hydroxymethyl (0.75 mmol), Cs_2CO_3 (1.0 mmol) and dioxane (5 mL) in air. The reaction mixture was then placed in an oil bath and heated at 110 °C for 24 h. After removal of the solvent, the resulting residue was purified by flash chromatography on silica gel using CH_2Cl_2 as eluent. The products **4a**–**k**, and **4m** are known compounds [6,9] except for **4l** and **4n**.

2-(4-Methylpyridin-2-yl)benzaldehyde (**4l**). *Anal.* Calc. for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found: C, 79.38; H, 5.43; N, 7.26%. IR (KBr, cm^{-1}): 3056, 1681, 1603, 1556, 1446, 1440, 1295, 1071, 1029, 825, 734. ^1H NMR (400 MHz, $CDCl_3$): δ 9.91 (s, 1H, CHO), 7.97 (d, 2H, ArH), 7.55 (s, 1H, ArH), 7.38–7.48. (m, 3H, ArH), 7.05 (d, 1H, ArH), 2.41 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 196.7, 157.6, 149.6, 147.9, 139.7, 129.0, 128.8, 127.1, 123.3, 121.7, 21.4.

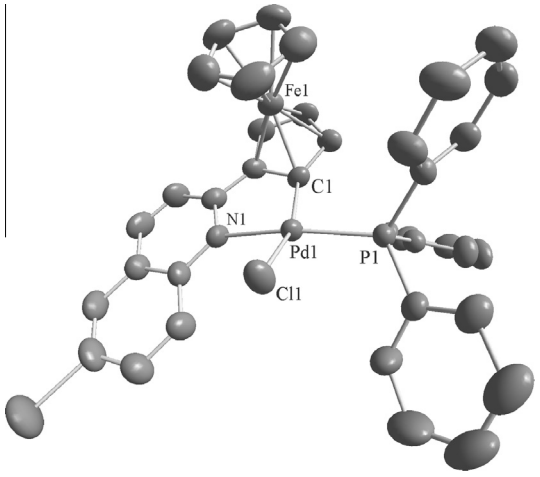


Fig. 1. Molecular structure of complex **1**. CH_2Cl_2 and H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Pd(1)–C(1) 1.977(3), Pd(1)–P(1) 2.2361(9), Pd(1)–N(1) 2.193(3), Pd(1)–Cl(1) 2.4233(9), and C(1)–Pd(1)–N(1) 80.95(13), C(1)–Pd(1)–P(1) 93.55(11), N(1)–Pd(1)–Cl(1) 97.51(8), P(1)–Pd(1)–Cl(1) 94.65(3).

2-(Pyrazin-2-yl)benzaldehyde (**4n**). *Anal.* Calc. for $C_{11}H_8N_2O$: C, 71.73; H, 4.38; N, 15.21. Found: C, 71.88; H, 4.26; N, 15.34%. IR (KBr, cm^{-1}): 3063, 1687, 1656, 1446, 1348, 1295, 1194, 1102, 1027, 837, 738. ^1H NMR (400 MHz, $CDCl_3$): δ 9.94 (s, 1H, CHO), 8.31 (s, 1H, ArH), 7.92 (d, 1H, ArH), 7.65–7.72 (m, 5H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): 198.7, 140.1, 138.7, 138.2, 134.4, 131.2.

3. Results and discussion

3.1. Synthesis and structures of complexes *1–3*

The synthetic route for three adducts of palladacycle **1**–**3** is shown in Scheme 1. These complexes have been easily prepared from the bridge-splitting reaction and characterized by elemental

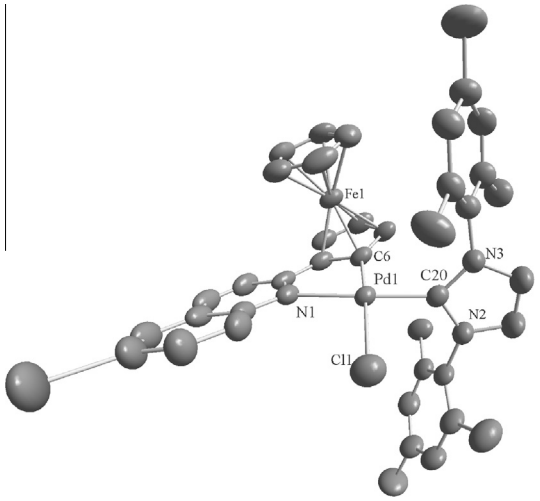


Fig. 2. Molecular structure of complex **2**. CH_2Cl_2 and H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Pd(1)–C(6) 1.975(4), Pd(1)–C(20) 1.990(4), Pd(1)–N(1) 2.190(3), Pd(1)–Cl(1) 2.438(5), and C(6)–Pd(1)–N(1) 80.66(14), C(6)–Pd(1)–C(20) 92.77(15), N(1)–Pd(1)–Cl(1) 96.90(14), C(20)–Pd(1)–Cl(1) 89.09(15).

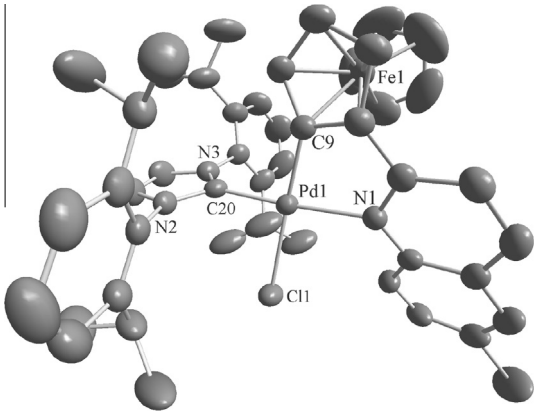


Fig. 3. Molecular structure of complex **3**. CH_2Cl_2 and H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Pd(1)–C(9) 1.983(4), Pd(1)–C(20) 1.993(4), Pd(1)–N(1) 2.151(3), Pd(1)–Cl(1) 2.4201(10), and C(9)–Pd(1)–N(1) 80.19(14), C(9)–Pd(1)–C(20) 95.22(15), N(1)–Pd(1)–Cl(1) 95.11(9), C(20)–Pd(1)–Cl(1) 89.19(10).

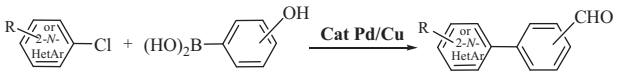
analysis, IR and ^1H NMR. Their crystals were obtained by recrystallization from CH_2Cl_2–petroleum ether solution at rt. The molecules are shown in Fig. 1–3. CH_2Cl_2 molecule in **1** is disordered, bromine atom and CH_2Cl_2 molecule in **2** are also disordered. The molecule of **1**–**3** adopts a *trans* configuration of the coordinated PPh_3 and NHCs to the quinoline nitrogen. The bicyclic system formed by the palladacycle and the C_5H_3 moiety is approximately coplanar (dihedral angles of 9.1, 10.8, and 14.4° for **1**–**3**, respectively). The Pd–C_{carb} [1.990(4) and 1.993(4) Å] bond lengths of complexes **2** and **3** are similar to those of related carbene adducts [6,7c,10], while they are evidently shorter than Pd–P bond length of **1** [2.2361(9) Å].

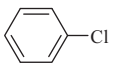
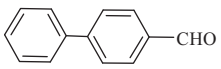
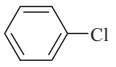
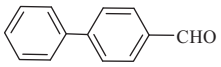
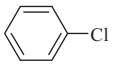
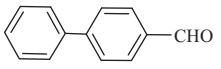
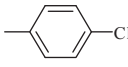
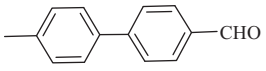
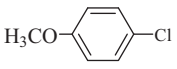
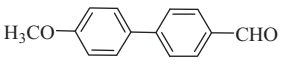
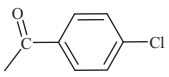
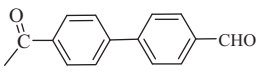
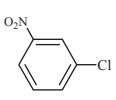
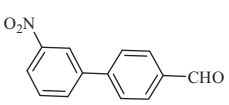
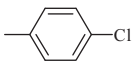
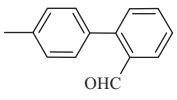
3.2. Pd/Cu cocatalyzed oxidation/Suzuki reaction

The palladium-catalyzed Suzuki reaction is an extremely powerful approach to generate biaryl compounds. Generally, Suzuki reaction of aryl halides with arylboronic acids containing hydroxymethyl produces the corresponding biarylalcohols [7b,11]. Recently, we have found NHC-palladacycles/Cu cocatalyzed reaction involving oxidation and Suzuki reaction of aryl chlorides containing hydroxymethyl [6]. One possible reaction mechanism is via Pd/Cu cocatalyzed alcohol oxidation and Pd catalyzed Suzuki reaction. In order to extend the scope of this method, we performed the coupling of 4-hydroxymethylphenylboronic acid with chlorobenzene to evaluate the effectiveness of the new palladacycles **1**–**3** (Table 1, entries 1–3). **3** was the most efficient among these palladacycles (entry 3), however, **1** was inactive under the same reaction conditions (Cs_2CO_3, dioxane, air). Additionally, the relative catalyst [Pd(bpp)(IMes)Cl] [6] in comparison with **3** showed slightly lower activity for the above reaction, producing the coupled product in 71% yield. The coupling reactions of 4-hydroxymethyl-phenylboronic acid with a variety of electronically and structurally diverse aryl chlorides were investigated (entries 4–7). Electron-withdrawing substrates reacted to give the corresponding products **4d** and **4e**, the yields (93% and 91%) are higher than the yields of electron-donating substrates containing $-CH_3$ and $-OCH_3$ groups. This protocol was also successfully applied to synthesis of 2-biarylcarboxaldehydes via oxidation and Suzuki reaction of 2-hydroxymethylphenylboronic acid (entries 8–10). An obvious decrease in the yield (51%) of *meta*-substitution product **4g** was observed (entry 9).

The Suzuki reactions of heteroarylboronic acids serve as important building blocks for the construction of biologically active compounds [12]. However, the Suzuki reactions of 2-pyridyl boronic

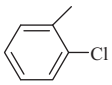
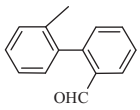
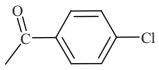
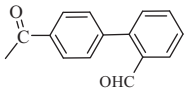
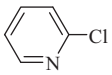
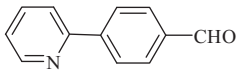
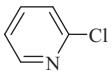
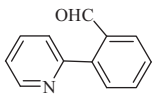
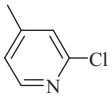
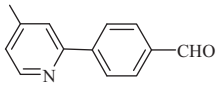
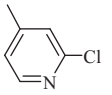
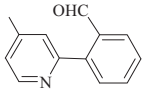
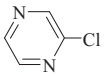
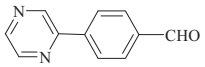
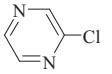
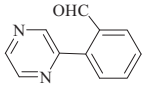
Table 1
Reaction of aryl chlorides with phenylboronic acid containing hydroxymethyl catalyzed by Pd/Cu(OAc)$_2$.[a]



Entry	Aryl halide	Product		Yield(%)[b]
1[c]			**4a**	0
2[d]			**4a**	75
3			**4a**	86
4			**4b**	83
5			**4c**	80
6			**4d**	93
7			**4e**	91
8			**4f**	72

(*continued on next page*)

Table 1 (*continued*)

Entry	Aryl halide	Product		Yield(%)[b]
9			**4g**	51
10			**4h**	84
11			**4i**	88
12			**4j**	79
13			**4k**	82
14			**4l**	71
15			**4m**	90
16			**4n**	78

[a] Reaction conditions: aryl chloride (0.5 mmol), phenylboronic acid containing hydroxymethyl (0.75 mmol), **3**/$Cu(OAc)_2$ (1/5 mol%), Cs_2CO_3 (1.0 mmol), dioxane (5 mL), 110 °C, 24 h, air atmosphere.
[b] Isolated yield.
[c] Catalyst **1** (1 mol%).
[d] Catalyst **2** (1 mol%).

acids have been relatively less reported [13]. The difficulty may be attributed to its instability [13b,c]. So, the coupling of 2-*N*-heteroaryl halides with arylboronic acid provided a valuable complement the preparation of the corresponding 2-aryl-*N*-heterocycles. In the following experiments, the Suzuki coupling of a variety of 2-*N*-heteroaryl chlorides with phenylboronic acids containing hydroxymethyl was investigated under the same reaction conditions. Similar to the results of chlorobenzene, good yields (79–88%) were obtained in the case of 2-chloropyridine (entries 11 and 12). For 2-chloro-4-methylpyridine, the yields of the coupled products **4k** and **4l** could be reached 71–82% (entries 13 and 14). Finally, the couplings of 2-chloropyrazine with phenylboronic acids containing hydroxymethyl also gave good yields (entries 15 and 16).

4. Conclusions

Three cyclopalladated 6-bromo-2-ferrocenylquinoline complexes have been synthesized and characterized. Their catalytic activity was evaluated in the coupling reactions of phenylboronic acid containing hydroxymethyl. We have developed an efficient NHC- palladacycle/Cu cocatalyzed oxidation and Suzuki reaction for the synthesis of biarylaldehydes from phenylboronic acids containing hydroxymethyl in air.

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Appendix A. Supplementary material

CCDC 1001676–1001678 contain the supplementary crystallographic data for complexes **1**–**3**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ica.2014.07.037.

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