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An inexpensive and highly stable palladium(II) complex for room temperature Suzuki coupling reactions under ambient atmosphere

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ABSTRACT

A new air- and moisture-stable Pd(II) complex **3**, which is a highly efficient catalyst for Suzuki reaction with low Pd-catalyst loading (0.01%), has been synthesized and characterized by single-crystal X-ray crystallography. The corresponding Suzuki coupling products were obtained in satisfactory to excellent yields at room temperature in aqueous media under ambient atmosphere.

Suzuki cross-coupling reaction has become one of the most powerful methods to construct C–C bonds.[1] The recent development of C–C bond formation methods involving aryl halides have largely focused on palladium catalysts containing electron-rich, sterically bulky phosphanes. In particular, tri-*tert*-butylphosphane, dialkyl(biphenyl)phosphanes, pentaarylferrocenylphosphane, and (2,2,2-triferrocenylethyl)diphenylphosphane have proved to be unique, highly efficient ligands for Suzuki cross-coupling reactions.[2] The extraordinary activity of these palladium catalysts in Suzuki cross-coupling reactions has been explained by an increased propensity of the more electron-rich catalyst to an oxidative addition of the aryl halide and an easier decomplexation of the catalytically active Pd(0)L species (L = phosphane).[3] Consequently, the development of structural diversity of electron-rich and sterically bulky phosphanes is still of considerable importance.[4] During our continuous research on Suzuki coupling reaction,[5] we have been interested in the development of new, high activity, air-stable palladium catalysts that can be used in room temperature Suzuki cross-coupling reaction in aqueous media under ambient atmosphere, since such catalysts have potential applications in industry. Recently, for the first time, we synthesized the palladium complex **3** with electron-rich, sterically bulky dibenzyl diisopropylphosphoramidite ligand for palladium-catalyzed Suzuki coupling reaction, and found that the cross-coupling reaction proceeded smoothly to provide the desired products in satisfactory to excellent yields.

Dibenzyl diisopropylphosphoramidite **2**, which contains one P–N bond and two P–O bonds, has not been used as ligand in transition-metal-catalyzed Suzuki cross-coupling reaction. Since ligand **2** exists as liquid and is moisture-sensitive at room temperature, it is not easy to handle. However, palladium complex **3**, achieved by

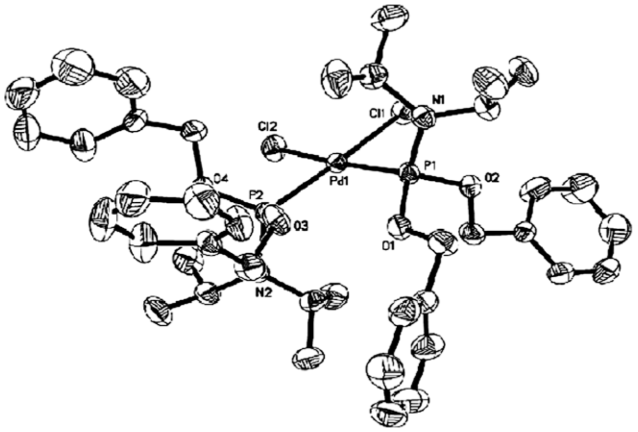

Figure 1. Molecular structure of the complex **3** with the atomic numbering scheme.

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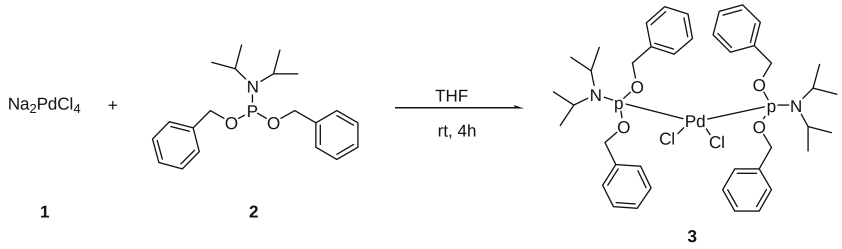


Scheme 1.

reacting Na_2PdCl_4 **1** with 2 equiv of the ligand **2** in THF at room temperature (Scheme 1), is insensitive to air and moisture. The X-ray crystal structure of **3** is shown in Figure 1. Single-crystal crystallographic analysis clearly shows that the unit cell of the complex **3** is built up of mononuclear $\{[(PhCH_2O)_2P(CH_3)_2CHNCH(CH_3)_2]_2PdCl_2\}$ units.[8] The Pd(II) ion has a square planar coordination geometry, which is coordinated by two chlorine atoms and two phosphorus atoms from two ligands of dibenzyl diisopropylphosphoramidite. Both chlorine atoms and both phosphorus atoms are in *cis*-position, with bond angles of Cl(2)–Pd(1)–Cl(1) being 89.42(4)° and P(1)–Pd(1)–P(2) being 98.90(3)°. Regarding the bond lengths of Pd(1)–Cl(1) [2.3659(9) Å] and Pd(1)–Cl(2) [2.3374(10) Å], the former is slightly longer and the latter is slightly shorter than those found in the similar structures, where the Pd–Cl bond lengths are in the range of [2.341(2)–2.353(3) Å][6] and [2.339(2)–2.349(2) Å].[7] Both the Pd–P bond distances 2.2515(9) Å and 2.2570(8) Å are longer than or in accordance with those in the above-cited structures [2.193(2)–2.207(2) Å][6] and [2.245(2)–2.257(2) Å].[7] All the bond lengths and bond angles in the ligand of dibenzyl diisopropylphosphoramidite are in the normal range.

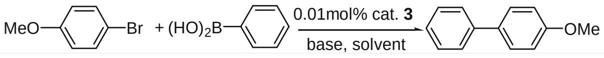
Initial catalytic studies with 0.01 mol % of complex **3** were performed on the Suzuki cross-coupling of 4-bromo anisole with phenylboronic acid in acetone/water (1:1) as a model reaction at room temperature in air and 2 equiv of various bases.[9] As shown in Table 1, the base additives strongly affected the coupling reaction. The common and inexpensive inorganic bases, such as Na_2CO_3 and K_2CO_3 or an organic base, Et_3 N, are more effective (entries 1–2 and 4), while Na_3PO_4 or Cs_2CO_3 (entries 3 and 9) gave slightly lower yields. In addition, the effect of solvents on the coupling reaction was also examined. CH_3COCH_3/H_2O (1:1) system afforded the highest yield (Table 1, entry 1) among the tested aqueous–organic solvents.

Under the optimized reaction conditions, a series of aryl bromides were coupled with phenylboronic acid with 0.01 mol % of catalyst, Na_2CO_3 as the base additive at room temperature in aqueous media under ambient atmosphere. As shown in Table 2, the cross-coupling reaction displayed remarkable tolerance toward the electronic properties of the substrates. For examples, electron-rich, as well as electron-deficient, aryl bromides coupled efficiently with phenylboronic acids to provide the desired products in satisfactory to excellent yields (entries 1–4). No significant difference was observed in yield or in the reaction time when the effect of various aryl boronic acids were investigated (entries 7–8 and 12). In particular, aryl bromides with sterically encumbering substituents such as *o*-methyl, 2,6-dimethyl also coupled effectively with phenylboronic acids to give the desired sterically demanding biaryl products in moderate to good yields (entries 5–6). We subsequently investigated the application of this catalytic system in the coupling reaction between hetero-aryl bromides and aryl boronic acids, but the results were disappointing (entries 15–16). It could be that hetero-aryl halides are less reactive in Suzuki cross-coupling reactions.[10] In addition, the coupling reaction of the relatively unactivated aryl chlorides with phenylboronic acid was also tested. Only moderate yields of 37–50% were achieved (entries 17–18).

In summary, we have synthesized and characterized an easily accessible palladium complex **3** for Suzuki cross-coupling of aryl halides in low Pd-catalyst loading (0.01 mol %). The advantages offered by this catalytic system are mild conditions, fast reactions at room temperature in aqueous media under ambient atmosphere, and excellent yields of products.

Table 1

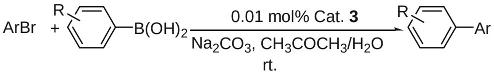
Screening of solvents and bases for Suzuki cross-coupling of 4-bromo anisole with phenylboronic acid using catalyst **3**

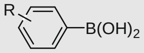
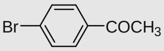
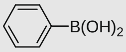
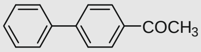
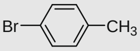
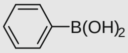
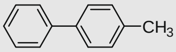
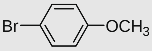
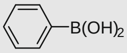
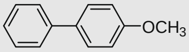
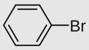
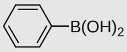
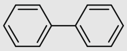
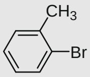
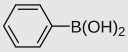
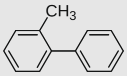
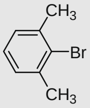
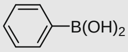
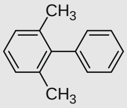
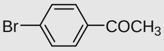
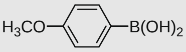
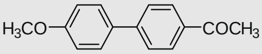
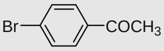
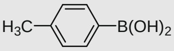
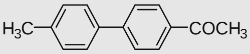
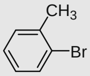
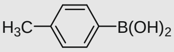
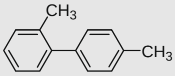
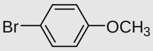
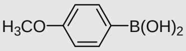
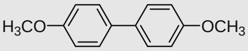
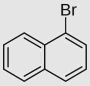
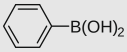
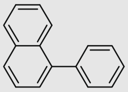
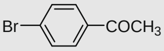
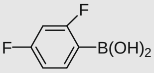
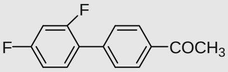
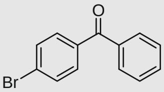
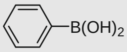
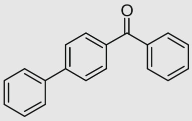
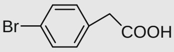
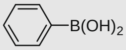
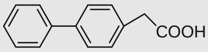
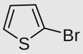
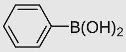
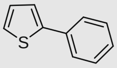
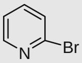
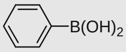
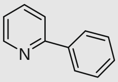
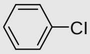
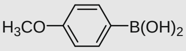
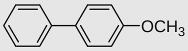
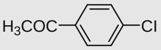
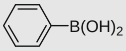
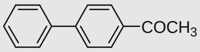


Entry	Base	Solvent (1:1)	Isolated yield[a] (%)
1	Na_2CO_3	CH_3COCH_3/H_2O	99
2	K_2CO_3	CH_3COCH_3/H_2O	99
3	$Na_3PO_4 \cdot 12H_2O$	CH_3COCH_3/H_2O	79
4	NEt_3	CH_3COCH_3/H_2O	98
5	$NaOAc \cdot 3H_2O$	CH_3COCH_3/H_2O	Trace
6	NaOH	CH_3COCH_3/H_2O	35
7	KOH	CH_3COCH_3/H_2O	52
8	NaF	CH_3COCH_3/H_2O	Trace
9	Cs_2CO_3	CH_3COCH_3/H_2O	73
10	Na_2CO_3	THF/H_2O	54
11	Na_2CO_3	DMF/H_2O	71
12	Na_2CO_3	$EtOH/H_2O$	94
13	Na_2CO_3	$PhMe/H_2O$	44
14	Na_2CO_3	CH_3OH/H_2O	91

[a] Reaction conditions: 4-bromo anisole (1.0 mmol), phenylboronic acid (1.2 mmol), base (2 equiv), solvent (4 ml), room temperature, 4 h.

Table 2
Complex **3** catalyzed Suzuki cross-coupling of aryl halides and phenylboronic acid[a]



Entry	ArBr		Product	Time (h)	Isolated yield (%)
1				2	99
2				2.5	99
3				4	99
4				3	99
5				4	89
6				4	72
7				2	92
8				2	95
9				4	90
10				4	93
11				4	95
12				4	92
13				4	87
14				4	92
15				8	Trace
16				8	Trace
17[b]				16	37
18[b]				16	50

[a] Reaction conditions:1.0 mmol of aryl bromide, 1.2 mmol of aryl boronic acid, 2.0 mmol of Na_2CO_3, complex **3** (0.0001 mmol), $CH_3COCH_3 + H_2O$ = 4 ml (1:1).

[b] Reaction conditions:1.0 mmol of aryl chloride, 1.2 mmol of aryl boronic acid, 2.0 mmol of Na_2CO_3, complex **3** (0.01 mmol), $CH_3COCH_3 + H_2O$ = 4 ml (1:1), 50 °C.

Acknowledgments

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8. *The complex* $\{[(PhCH_2O)_2P(CH_3)_2CHNCH(CH_3)_2]_2PdCl_2\}$ (**3**) *was prepared by the following procedure*: A solution of $(PhCH_2O)_2P(CH_3)_2CHNCH(CH_3)_2$ (0.345 g), 1 mmol in THF (2.0 ml) was added dropwise to a suspension of Na_2PdCl_4 of 0.147 g (0.5 mmol) in THF (20.0 ml) and the reaction mixture was stirred at ambient temperature for 4 h. The volume was reduced to ca. 5.0 ml and diethyl ether was added to precipitate a yellow powder which was then filtered off and washed with diethyl ether. The complex **3** was obtained in 92% yield. Single crystals of **3** were obtained by slow evaporation of a CH_2Cl_2 solution of **3** at ambient temperature. X-ray crystallographic analysis was carried out on a Bruker P4 diffractometer using a rotating anode with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). Crystal data for **3**: $C_{40}H_{56}Cl_2N_2O_4P_2Pd$, $M = 868.11$, space group: monoclinic, $P2(1)/c$, $a = 15.0614(15)$ Å, $b = 15.3221(13)$ Å, $c = 18.6924(17)$ Å, $\alpha = 90.00(0)°$ $\beta = 98.376(4)°$, $\gamma = 90.00(0)°$, $V = 4267.7(7)$ Å^3, $T = 153(2)$ K, $Z = 4$, $D_c = 1.351$ g cm^{-3}, $\mu = 0.675$ mm^{-1}, goodness of fit = 1.073, $R_1[I > 2\sigma(I)] = 0.0505$, $wR_2 = 0.1326$. Selected bond distances (Å) and angles (°) are shown as follows: Pd(1)–P(1) 2.2515(9), Pd(1)–P(2) 2.2570(8), Pd(1)–Cl(1) 2.3374(10), Pd(1)–Cl(1) 2.3659(9), P(1)–Pd(1)–P(2) 98.90(3), P(1)–Pd(1)–Cl(2) 174.00(4), P(2)–Pd(1)–Cl(2) 87.09(4), P(1)–Pd(1)–Cl(1) 84.59(3), P(2)–Pd(1)–Cl(1) 176.49(3), Cl(2)–Pd(1)–Cl(1) 89.42(4). Atomic coordinates, bond lengths, and angles and the other important parameters have been deposited to Cambridge Crystallographic Data Center as supplementary publication, CCDC No. 702614. Copies of this information can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1233 336033 or e-mail: deposit@ccdc.cam.ac.uk).
9. A mixture of aryl bromide (1.0 mmol), phenylboronic acid (1.2 mmol), Na_2CO_3 (2.0 mmol), CH_3COCH_3/H_2O (2 ml/2 ml), and catalyst **3** (0.01%) was stirred at room temperature under air. The reaction mixture was stirred for 4 h, and then quenched with water. The mixture was diluted with diethyl ether. The organic layer was separated, and the aqueous layer was extracted with diethyl ether for three times. The combined organic phase was dried with $MgSO_4$, filtrate, solvent was removed on a rotary evaporator, and the product was isolated by thin layer chromatography. The purfied products were identified by ^1H NMR, ^{13}C NMR spectroscopy and melting points with the literature data.
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