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# The Novel And Highly Efficient P, O Chelated Pd(II) Complexes Catalyzed Suzuki Cross-Coupling Reaction At Room Temperature

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## ABSTRACT

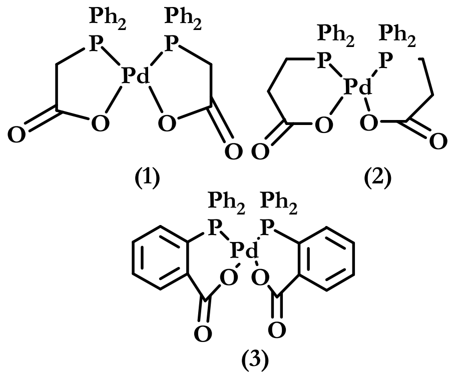
A novel class of air- and moisture- stable P, O chelated Pd(ll) complexes, found to be highly efficient catalysts for Suzuki reaction with generally low Pd-catalyst loading(0.01%) and low temperature, were synthesized and characterized by $^1$H-NMR, $^{31}$P-NMR, IR and single crystal X-ray. The crystal structures confirm that the Pd atom adopts a square-planar geometry with the $PdO_2P_2$ chromophore. Above complexes are all shown to catalyze the Suzuki-Miyaura coupling reaction of aryl boronic acids and aryl halides within aqueous solvents in good yield.

## KEYWORDS

Chelated Pd(ll) complexes;
Suzuki coupling;
Catalysis.

## INTRODUCTION

The palladium-catalyzed Suzuki-Miyaura coupling reaction is one of the most efficient methods for the construction of $C_{aryl}$-$C_{aryl}$ bonds and has found wide spread use in organic synthesis as well as in pharmaceutical and agricultural chemistry[1,2]. There has recently been considerable interest in the synthesis of new, high activity palladium-based catalysts that can be used in low concentration in the Suzuki reaction since such catalysts have the potential to be used in industrial systems[3]. In particular, palladacyclic catalysts in which a ligand coordinates to the metal center through both a donor atom and a metallated carbon have shown considerable promise. Beller and co-workers demonstrated that palladated phosphine complexes show good activity[4], and Milstein et al. have shown that a palladated imine complex shows excellent activity[5], whilst Zim et al. have shown that palladated thioether complexes can also be used[6]. Bedford and co-workers have also reported some palladated phosphate complexes and P, C-bidentate phosphio palladacycles as catalysts in the Suzuki reaction which show excellent activity[3,7]. To the best of our knowledge, the application of well-defined hemilabile P,O chelated palladium(II) complexes to Suzuki reaction in aqueous-phase coupling reactions has not been reported, only the reported palladium/P, O-ligand as catalyst was used in situ. In this paper, we report three new P, O che-



**SCHEME 1 : New P, O chelated palladium(II)complexes 1-3**

lated palladium(II) complexes, bis(diphenyl phosphine acetate) Pd(II)**(1)**, bis(diphenyl phosphine propionate) Pd(II)**(2)**, and bis[*o*-(diphenyl phosphine) benzoate] Pd(II)**(3)**, which all show remarkable activity in the Suzuki reaction at room temperature in aqueous solvents (SCHEME 1). Also, the crystal structure of bis(diphenyl phosphine acetate) Pd(II) is described.

The reaction of sodium diphenyl phosphine carboxylate with $Na_2PdCl_4$ as mole ratio 2:1 gives the complexes **(1-3)** in almost quantitative yield(>98%). Complexes **(1-3)**(solid powder) have all been characterized by satisfactory elemental analysis, infrared, $^1H$ and $^{31}P$-NMR spectroscopy. Single crystals(light yellow prism) of **(1)** suitable for X-ray measurements were obtained by recrystallization from dichloro methane. Complexes **(1-3)**all show remarkable stability to air and moisture-in solution they show no sign of decomposition after three months, whilst solid samples can be kept in air for at least one year. No decomposition is observed when complexes **(1-3)** are heated at 140$^0$C in air, demonstrating that the catalysts also show good thermal stability. All of the features of this new method, such as mild reaction conditions, high yield, simple separation, short reaction period and good stability of production would make the synthesis of the above catalysts a promising method in industrial applications.

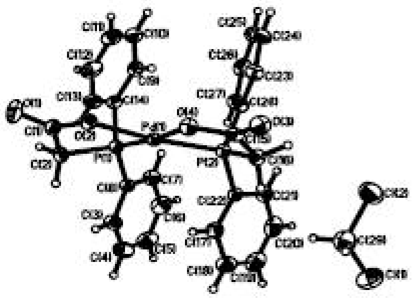
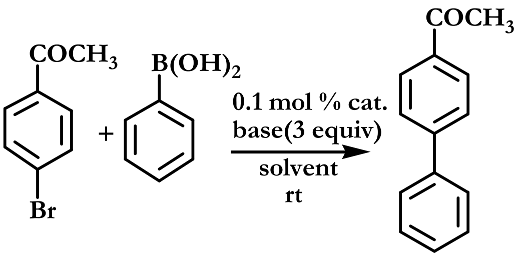


**Figure 1 : Molecular structure of $[(Ph_2PCH_2COO)_2Pd]\cdot CH_2Cl_2$ with the atomic numbering scheme**

**TABLE 1 : Chelated Pd(II) complexes catalyzed suzuki cross-coupling of 4-bromoacetophenone**[a]



| Entry | Catalyst | Base | Solvent | Pd % | Time[b] (h) | Yield[c] (%) |
|---|---|---|---|---|---|---|
| 1 | 1 | NaOH | $THF+H_2O$ | 1 | 8 | 72 |
| 2 | 1 | KOH | $THF+H_2O$ | 1 | 8 | 83 |
| 3 | 1 | $Na_2CO_3$ | $THF+H_2O$ | 1 | 8 | 43 |
| 4 | 1 | $K_3PO_4$ | $THF+H_2O$ | 1 | 6 | 99 |
| 5 | 1 | $NEt_3$ | $THF+H_2O$ | 1 | 10 | 29 |
| 6 | 1 | $KOBu^t$ | $THF+H_2O$ | 1 | 8 | 85 |
| 7 | 1 | NaAc | $THF+H_2O$ | 1 | 12 | 24 |
| 8 | 1 | KF | $THF+H_2O$ | 1 | 12 | 28 |
| 9 | 1 | $K_3PO_4$ | $CH_3CN+H_2O$ | 1 | 10 | 92 |
| 10 | 1 | $K_3PO_4$ | $EtOH+PhMe+H_2O$ | 1 | 10 | 95 |
| 11 | 1 | $K_3PO_4$ | $THF+H_2O$ | 0.5 | 6 | 98 |
| 12 | 1 | $K_3PO_4$ | $THF+H_2O$ | 0.1 | 6 | 97 |
| 13 | 1 | $K_3PO_4$ | $THF+H_2O$ | 0.01 | 6 | 97 |
| 14 | 2 | $K_3PO_4$ | $THF+H_2O$ | 0.01 | 6 | 95 |
| 15 | 3 | $K_3PO_4$ | $THF+H_2O$ | 0.01 | 6 | 97 |

[a] Reaction conditions: 1.0mmol of 4-bromoacetophenone, 1.5 mmol of aryl boronic acid, 3.0mmol of base, 4mL of solvents ; [b] Reaction time not optimized ; [c] Isolated yield

The X-ray structure of compound **(1)** shows that it is built up of mononuclear $[(Ph_2PCH_2COO)_2Pd]$ units and dichloromethane molecules in a 1:1 ratio(See figure 1). The two diphenyl phosphine acetate ligands are coordinated to the central Pd atom by their P and O atoms, forming five-membered chelate rings. The Pd(II) atom has a distorted square-planar configuration with the P-O bond lengths of

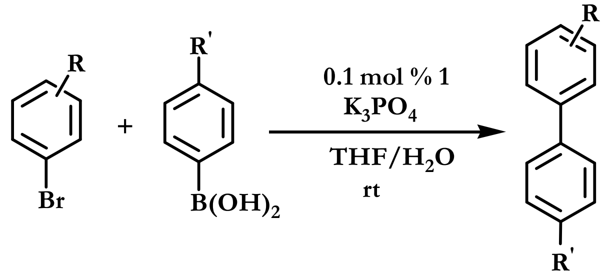
2.076(3) and 2.082(3) Å, which are slightly longer than those of the other Pd-O distance lengths of 2.214(1) and 2.216(1) Å are in accordance with the values usually encountered in related compounds[8a].

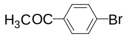
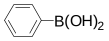
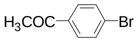
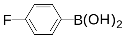
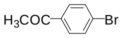
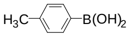
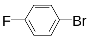
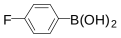
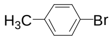
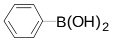
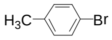
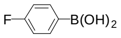
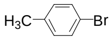
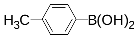
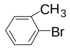
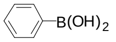
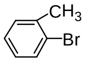
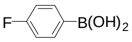
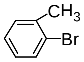
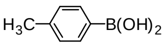
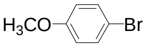
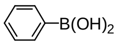
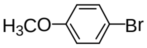
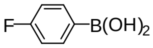
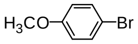
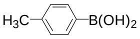
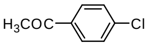
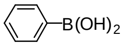
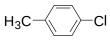
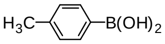
To begin to define the utility of these complexes as a useful catalysts, 4-bromoacetophenone was chosen as the main test substrate for the optimization studies. The results (TABLE 1) showed that the activity of the catalysts were profoundly affected by reaction conditions and demonstrated that THF/$H_2O/K_3PO_4$(entry 4, TABLE 1) mixtures gave the highest activity although good activity was also seen when $CH_3CN+H_2O$ or $EtOH+PhMe+H_2O$ was used as solvents. We were delighted to see that complex **(1)** gave turnover(TONs) of up to 9700 at 0.01 mol% loading at room temperature. No discernible influence was observed when chelated Pd(II) structure was changed(entry 13-15).

To evaluate the scope and limitations of this procedure, the reaction of a wide variety of aryl halides with phenylboronic acids was examined using complex**(1)** in $THF+H_2O$ and $K_3PO_4$ as a base. TABLE 2 summarizes our preliminary results for Suzuki coupling reactions. Complex**(1)**exhibits unusual catalytic activities toward the Suzuki coupling reaction of aryl bromides with a range of aryl boronic acids to give diaryl products in high yields in aqueous solvents at room temperature. Both electron-rich and electron-deficient aryl bromides were applicable for this reaction (entries 1-3, 11-13, TABLE 2). The catalyst system also tolerated sterically demanding aryl bromides(entries 8-10, TABLE 2) to give ortho-substituted biphenyl products in excellent yields with no change in the reaction time. No significant difference was observed in yield and in the reaction time, while the effect of varying the aryl boronic acids in the Suzuki cross-coupling reactions was investigated.

Complex **(1)** also efficiently promoted the cross-coupling of electron-poor aryl chlorides under the catalysis of 1.0mol% loading and gave excellent yields after 16h in DMF at 100$^0$C(entry 14, TABLE 2). Unfortunately, the Suzuki cross-coupling between para-chlorotoluene and tolylboronic acid proceeded sluggishly under the catalysis of 1.0mol% loading, only giving biaryls in 26% yield after 16 h in DMF at 100 $^0$C (entry 15, TABLE 2).

**TABLE 2 : Complex 1 catalyzed suzuki cross-coupling of aryl halides and phenylboronic acid**[a]



| Entry | Ar-Br | Ar'-B(OH)₂ | Time[b] (h) | Yield[c] (%) |
|---|---|---|---|---|
| 1 |  |  | 6 | 99 |
| 2 |  |  | 6 | 95 |
| 3 |  |  | 6 | 99 |
| 4 |  |  | 8 | 78 |
| 5 |  |  | 10 | 67 |
| 6 |  |  | 10 | 87 |
| 7 |  |  | 10 | 72 |
| 8 |  |  | 5 | 90 |
| 9 |  |  | 5 | 85 |
| 10 |  |  | 5 | 80 |
| 11 |  |  | 12 | 92 |
| 12 |  |  | 8 | 92 |
| 13 |  |  | 8 | 96 |
| 14 |  |  | 16 | 89[d] |
| 15 |  |  | 16 | 26[d] |

[a]Reaction conditions: 1.0mmol of aryl bromide, 1.5 mmol of aryl boronic acid, 3.0mmol of $K_3PO_4$, complex 1(0.001mmol), $THF+H_2O$= 4 mL (1:1) ; [b]Reaction time not optimized. ; [c]Isolated yield ; [d]The reaction was performed in DMF at 100$^0$C.

Interestingly, a dark red solution was always observed during the processes of the reactions. Upon completion of the reactions, extraction with ether drove the catalyst to partition predominately in the aqueous phase of the reaction mixture. The aqueous phase was dark red. Therefore, it was possible to recycle the catalyst. For example, the product resulting from the coupling of 4-bromoacetophenone and phenyl boronic acid in the presence of 1.0%mol catalyst was obtained in 99% yield after 6 h reaction in the aqueous phase at room temperature for the first cycle, 93% yield after 4h for the second cycle, and 90% yield after 4h for the third cycle. Soon afterwards, palladium deposition was observed. This indicated that the dark red species is likely the active species. This water-soluble active species is likely formed based on the hemilabile behaviour of the P, O chelated palladium(II) complexes, the opening of the Pd-O bond may be initiated under catalytic conditions, thus generating water-soluble active species and free coordination sites for catalysis[10]. Further investigations of the mechanism of this catalyst are underway in our laboratory.

In summary, we have developed a new class of simple and highly active P, O chelated Pd(II) complexes **(1-3)**for Suzuki cross coupling of aryl halides in low Pd-catalyst loading(0.01%). The high stability of the hemilabile P, O chelated Pd(II) complexes gave relatively high turnover numbers in Suzuki reaction in aqueous solvents at room temperature. The catalyst can be also recycled three times without degradation of catalyst active. The inexpensiveness of starting material, as well as the simplicity of the synthesis made this type of hemiabile P, O chelated Pd(II) complexes **(1-3)**highly attractive. In view of the extreme activity, comparably easy synthesis and excellent yield of the complexes **(1-3)**, we believe that they will be a good catalyst of choice in Suzuki reactions, and they will be commercially available on industrial-scale.

## ACKNOWLEDGMENTS

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