



C-C Cross-Coupling Reactions by Palladium on Barium and Potassium Polyoxotungstate Supports

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A heterogeneous catalyst system for Suzuki and Heck coupling reactions was developed using polyoxometalates as supports for palladium. The catalyst system was synthesized in a one step process using sodium phosphotungstate and palladium acetate. We used the supported catalyst in organic media without the need for special ligands. Substantial activity was observed after several recycles. The catalyst showed high product selectivity with yields up to > 95 % in both Suzuki and Heck reactions.

Keywords: Suzuki coupling, Heck coupling, Polyoxometalate, Heterogeneous, Palladium.

INTRODUCTION

The ongoing demand for greener approaches has revolutionized synthetic chemistry demanding efficient and environmentally friendly methodologies. The interest in C-C cross-coupling reactions was triggered by the high demand for biaryl intermediates in pharmaceuticals. Palladium catalyzed Suzuki cross-coupling of aryl and vinylboronic acids with aryl or vinyl halides [1,2] is being employed. However the reactions need exotic catalysts which are expensive and difficult to handle. Catalyst systems based on palladium ranging from simple salts like palladium acetate in the presence of quaternary ammonium salts [3] or water [4] to palladium nanoparticles (Pd-NPs) stabilized by ionic liquids [5], dendrimers [6], polyvinylpyridine (PVP) [7], fluoro ligands [8], phosphine ligands [9], aqueous solutions [10] as well as solid supports such as diatomite [11] and on polymer supports like poly(N,N-dihexylcarbodiimide) (PDHC) [12] have been employed. Most of the catalyst systems reported require sophisticated reaction setups in addition to homogeneity with the media making isolation of the product tedious. Ligand decomposition at higher temperatures has also been reported which tend to reduce the activity of Pd-catalyst systems employed so far [11,13] making the entire process very expensive. In the search for suitable supports, polyoxometalates (POMs), which possess excellent properties make POMs suitable supports. The chemical properties of POMs can be largely

controlled by transition metal substitution and the counterion used. They tolerate high temperatures, have versatile electronic properties that stabilize nanoparticles and can produce heterogeneous systems depending on the choice of counter ion used [14,15]. We sought a less sophisticated catalyst system that can be employed under ordinary conditions. A heterogeneous POM support for Pd provided a robust catalyst system that withstands high temperature conditions demanded by coupling reactions.

EXPERIMENTAL

Sodium phosphotungstate hydrate ($\text{Na}_3\text{PO}_4 \cdot 12\text{WO}_3 \cdot x\text{H}_2\text{O}$), $\text{Pd}(\text{OAc})_2$, aryl halides, inorganic bases and solvents were purchased from Sigma-Aldrich.

Gas chromatography (GC) analyses were performed using a Varian 3300 gas chromatograph with an FID and fitted with a 30 m Varian CP-Sil 5 CB capillary column. The following temperature program was used for the oven: 100 °C (initial, hold time 10 min) to 250 °C (final, hold time 12 min) at a rate of 20 °C/min. The injector temperature was 260 °C and the detector temperature was 320 °C. ICP analyses were performed on a Perkin-Elmer model OPTIMA 3000 DV instrument at the Department of Ecology in Lund University.

General procedure for synthesis of Pd/BaPOM and Pd/KPOM catalysts: $\text{Na}_3\text{PO}_4 \cdot 12\text{WO}_3$ (2.5 g) in a potassium acetate/acetic acid buffer solution (50 mL) was heated to 80 °C and

then adjusted to pH 7 by potassium carbonate. To the solution was added palladium acetate (0.19 g) solution and the mixture was refluxed at 95 °C for 2 h. Barium nitrate, (2.5 g) in minimum quantity of water was added to the refluxing mixture and the process continued for 1 h. The resulting mixture was evaporated to half the volume and then maintained at 40 °C for 1 h. The mixture was then filtered and the residue was kept at 10 °C overnight. The residue was then dried in air and at 120 °C for 12 h to yield the Pd/BaPOM catalyst. The procedure was modified by addition of ascorbic acid (0.43 g) during reflux but before precipitation of the POM to produce the reduced Pd/BaPOM catalyst. Synthesis of Pd/KPOM was similar to Pd/BaPOM but instead of barium nitrate, potassium chloride, KCl (1.0 g) was added as the precipitating agent. A portion of the synthesized Pd/BaPOM was heated at 400 °C for 2 h to yield calcined Pd/BaPOM catalyst.

General procedure for C-C cross-coupling reactions:

Suzuki reactions were performed using phenylboronic acid (1.2 mmol), aryl halide (0.8 mmol), base (0.8 mmol), catalyst (0.025 mg) and solvent (10 mL) under reflux. Heck reactions were performed using the same moles of the olefin and aryl halides as substrates. The reaction mixture was allowed to settle and a portion of the supernatant (0.5 mL) was shaken with mixture of diethyl ether (2.0 mL) and hydrochloric acid (1.0 mL, 2 M). The organic layer (2.0 µL) was analyzed by gas chromatography.

RESULTS AND DISCUSSION

Our initial step involved design and synthesis of POMs with inorganic counter ion where potassium and barium were used as counterions to precipitate the POM, forming KPOM and BaPOM, respectively on which the Pd gets adsorbed. We proceeded to determine the composition of the catalyst system using inductively coupled plasma atomic emission spectroscopy (Table-1). The results revealed a 6.7 times higher concentration of palladium in Pd/BaPOM (4.1 %) than Pd/KPOM (0.6 %).

TABLE-1
ELEMENTAL ANALYSIS OF PALLADIUM
SUPPORTED Ba AND K POLYOXOTUNGSTATE

Entry	Catalyst	Elemental comp (mg g ⁻¹)		Pd (%)
		Ba	K	
1	Pd/BaPOM	159	0	4.1
2	Pd/KPOM	0	151	0.6

This is attributed to the low solubility of barium in water allowing immediately precipitation forming the BaPOM and subsequent adsorption of more Pd on the precipitated support system. High solubility of potassium results to poor precipitation of the KPOM hence less amount of Pd adsorbed. We also generated a reduced Pd/BaPOM in which ascorbic acid was added in mild concentration to reduce some of the Pd²⁺ ions to Pd⁰ before adsorption. The Pd/KPOM and Pd/BaPOMs were compared in Suzuki coupling of phenylboronic acid and 4-bromoacetophenone (Table-2, entries 1 and 2). The Pd/BaPOM showed higher activity than Pd/KPOM attributed to the higher loading of Pd (4.1 %) in the former as observed from the elemental analysis (Table-1). The reduced Pd/BaPOM showed

the least activity likely because high formation of Pd back which lowers loading of Pd on the reduced Pd/BaPOM (Table-2, entry 3).

TABLE-2
EFFECT OF COUNTERION ON THE ACTIVITY
OF Pd/KPOM AND Pd/BaPOM CATALYSTS

Entry	Catalyst	Selectivity (%)	Yield (%)
1	Pd/KPOM	95	52
2	Pd/BaPOM	90	77
3	Reduced Pd/BaPOM	73	28

Unless stated, the reactions were performed using 4-bromoacetophenone (0.8 mmol), phenyl boronic acid (1.2 mmol), K₂CO₃ (1.6 mmol), catalyst (0.025 g, 3.6 % Pd) in toluene (10 mL), 140 °C, 24 h reflux.

The efficiency of bases in activating phenylboronic acid and the effect of temperature on the reaction was investigated using Pd/BaPOM in coupling of the acid with 4-bromoacetophenone. A significant increase in product yield and selectivity (69 to 97 % yield and 85 to 97 % selectivity) was observed when the temperature was increased from 120 to 150 °C (Table-3, entries 1-3). The presence of base was necessary for catalyst selectivity as no product was detectable in absence of the base. The conversion was 15 % in the absence of a base suggest very poor selectivity. The results clearly manifest increase in the product yield and selectivity with increase in base strength (Table-3, entries 3-7) and caesium carbonate emerged the best base (> 99 yield, > 99 % selectivity).

TABLE-3
EFFECT OF BASES ON THE ACTIVITY OF Pd/BaPOM
CATALYST IN SUZUKI COUPLING OF PHENYL
BORONIC ACID AND 4-BROMO-ACETOPHENONE

Entry	Base	Temp. (°C)	Selectivity (%)	Yield (%)
1	K ₂ CO ₃	120	85	69
2	K ₂ CO ₃	140	90	77
3	K ₂ CO ₃	150	97	97
4	Cs ₂ CO ₃	150	99	99
5	KHCO ₃	150	97	71
6	Na ₂ CO ₃	150	81	21
7	CH ₃ CO ₂ K	150	97	15
8	–	150	–	–

Unless stated, reactions were performed using 4-bromo-acetophenone (0.8 mmol), phenylboronic acid (1.2 mmol), base (1.6 mmol), Pd/BaPOM (0.025 g, 3.6 % Pd) in toluene (10 mL), 24 h.

The effect of the base on Heck reaction was investigated by coupling styrene with iodobenzene where caesium carbonate surpassed potassium carbonate giving yield of 61 % vs. 16 %, respectively with similar selectivity. We further proceeded to check the effect of selected organic on the reaction. Conversions (> 99 %) were recorded with dimethyl formamide and N-methyl-2-pyrrolidone. However, the former has a slight edge in selectivity (86 % vs. 84 %) (Table-4, entries 3 and 4). To the contrary toluene gave the least yield (44 %) in the Heck coupling (Table-4, entry 1).

Potassium carbonate and a temperature of 150 °C were chosen as the optimal conditions for the Pd/BaPOM in coupling of phenylboronic acid with selected aryl halides. The catalyst system gave > 95 % with 4-bromo-acetophenone and > 50 % yield with majority of the substrates. The low product yield by

TABLE-4
EFFECT OF ORGANIC SOLVENT ON THE
ACTIVITY OF Pd/BaPOM CATALYST SYSTEM IN
HECK COUPLING OF STYRENE AND IODOBENZENE

Entry	Solvent	Selectivity (%)	Yield (%)
1	Toluene	92	44
2	THF	87	61
3	DMF	86	86
4	NMP	84	84

Unless stated, reactions were performed using iodobenzene (0.8 mmol), styrene (1.2 mmol), Cs₂CO₃ (1.6 mmol), Pd/BaPOM (0.025 g, 3.6 % Pd) in solvent (10 mL), 150 °C, 24 h.

some substrates could be improved at extended reaction time (Table-5, entries 7 and 8). We were successful in coupling of the poorly reactive aryl chloride after extended hours (Table-5, entry 6).

TABLE-5
SUZUKI COUPLING OF PHENYLBORONIC ACID WITH
SELECTED ARYL HALIDES USING Pd/BaPOM

Entry	Aryl halide	Time (h)	Selectivity (%)	Yield (%)
1	C ₆ H ₅ -I	24	90	54
2	C ₆ H ₅ -Br	24	100	39
3	C ₆ H ₅ -Cl	24	–	–
4	<i>p</i> -Me-C ₆ H ₅ -Br	24	98	63
5	<i>p</i> -Me-C ₆ H ₅ -Cl	24	–	–
6	<i>p</i> -Me-C ₆ H ₅ -Cl	48	98	5
7	<i>o</i> -MeO-C ₆ H ₅ -Br	24	93	41
8	<i>o</i> -MeO-C ₆ H ₅ -Br	48	90	66
9	<i>p</i> -AcO-C ₆ H ₅ -Br	24	97	97

Unless stated, reactions were performed using aryl halide (0.8 mmol), phenylboronic acid (1.2 mmol), K₂CO₃ (1.6 mmol), Pd/BaPOM (0.025 g, 3.6 % Pd), toluene (10 mL), 150 °C, 24 h. ND = not detected.

The nature and position of the substituent on the aryl halide was found to greatly affect the reaction. Substituents with positive inductive effect enhanced the reaction. The reactivity of aryl halides increased in the order: bromobenzene < methylbenzene < acetylbenzene (Table-5, entries 2, 4 and 9). The methyl group in the *para* position activated bromobenzene significantly enhancing product yield. (Table-5, entries 2 vs. 4).

Caesium carbonate, DMF and temperature of 150 °C were taken as optimal conditions for the Pd/BaPOM catalyzed Heck coupling of selected olefins and aryl halides. Complete conversion with high selectivity (> 80 %) was observed with majority of the substrates except chlorobenzene where no yield was detectable within reaction time employed (Table-6, entries 1-10).

The recyclability of the Pd/BaPOM catalyst system was also investigated. It retained full activity after first recycle in coupling of phenylboronic acid with 4-bromoacetonephenone. Moderate yield (65 %) was obtained in the 3rd recycle (Fig. 1). Nevertheless, the Pd/BaPOM maintained full activity giving 100 % conversions up to the 4th cycle of reuse in the coupling of styrene with iodobenzene.

Leaching of Pd from BaPOM support was investigated by decanting a reaction mixture for 24 h. Fresh substrates were then coupled in the filtrate without addition of the catalyst. Very low yields were obtained in the absence of the catalysts in both Suzuki and Heck reactions of the same substrates compared to the same reaction with the catalyst added (Fig. 2).

TABLE-6
HECK COUPLING OF SELECTED OLEFINS
AND ARYL HALIDES USING Pd/BaPOM

Entry	Olefin	ArX	Selectivity (%)	Yield (%)
1		C ₆ H ₅ -I	> 99	> 99 ^a
2	CH ₂ =CHCO ₂ Me	C ₆ H ₅ -Cl	–	–
3		<i>p</i> -MeO-C ₆ H ₄ -I	90	90
4		C ₆ H ₅ -I	99	99 ^a
5	CH ₂ =CHCO ₂ Bu	C ₆ H ₅ -Cl	–	–
6		<i>p</i> -MeO-C ₆ H ₄ -I	99	99
7		<i>p</i> -AcO-C ₆ H ₄ -Br	> 99	> 99
8		C ₆ H ₅ -I	86	86 ^a
9	C ₆ H ₅ CH=CH ₂	C ₆ H ₅ -Cl	–	–
10		<i>p</i> -MeO-C ₆ H ₄ -I	81	81

Unless stated, reactions were performed using aryl halide (0.8 mmol), olefin (1.2 mmol), Cs₂CO₃ (1.6 mmol), Pd/BaPOM (0.025 g, 3.6 % Pd) in DMF (10 mL), 150 °C, 24 h; ^a 6 h.

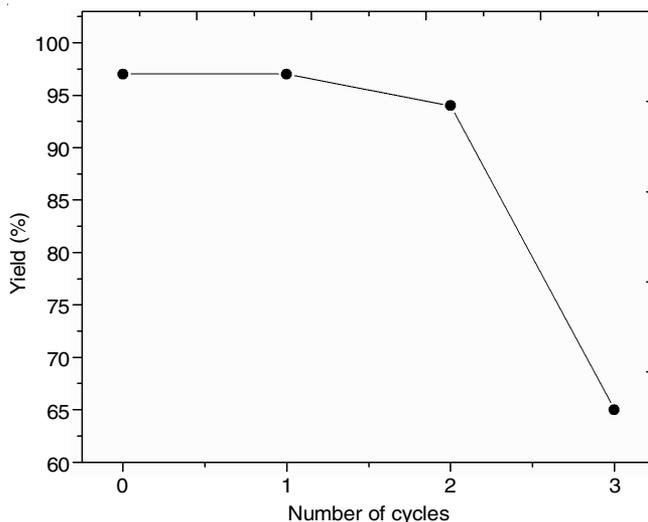


Fig. 1. Activity of Pd/BaPOM during recycling

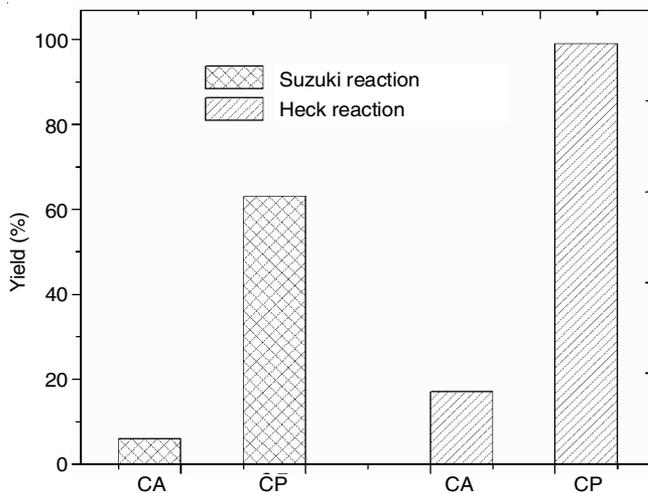


Fig. 2. Comparison leaching in the absence of catalyst (CA) and presence of catalyst (CP)

The low yields were probably due to minimal leaching of some Pd from the Pd/BaPOM in to the reaction solution used as the medium for the reaction where the catalyst was not added or more likely from the suspended Pd particles, which failed to settle during decanting of the reaction mixture [16].

Conclusion

Polyoxometalates with inorganic counterion provide heterogeneous supports with the ability to adsorb and stabilize palladium providing an excellent ligand-free catalyst system for organic media used in cross-coupling reactions. Our catalyst and reaction setup are less tedious and low-cost. The results obtained in this work compare well with work reported in literature using other Pd-catalyst systems. The robustness and excellent electronic of POMs make them suitable supports for other transition metal catalyst.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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