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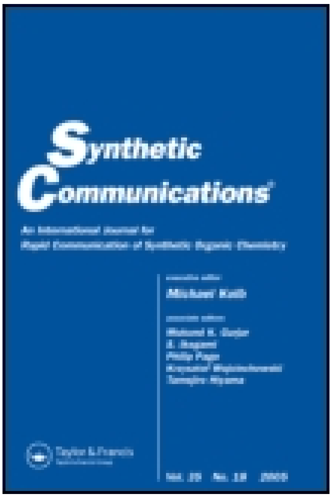

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GREENER ULLMANN-TYPE COUPLING OF ARYL HALIDES FOR PREPARING BIARYLS USING REUSABLE Pd/ZrO$_2$ CATALYST

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Biaryls with excellent yields can be prepared by the Ullmann-type coupling of aryl halides in the presence of potassium carbonate (as a base) and dimethylformamide (as a solvent), at 140°C, using a reusable Pd (2.5 wt%)/ZrO$_2$ catalyst. The product yield of 4-iodoanisole coupling is strongly influenced by the catalyst preparation method, solvent, and base.

Keywords: Aryl halides; biaryls; Pd/ZrO$_2$; Ullmann coupling reaction

INTRODUCTION

Biaryls play an important role in modern organic chemistry. Ullmann coupling of two aryl halide molecules with the elimination of two halogen atoms is considered one of the most important methods for the formation of the C–C bond, particularly in the synthesis of biaryls.

In the Ullmann reaction, two molecular equivalents of aryl halide are reacted with one equivalent of finely divided copper at high temperature (>200 °C) to form a biaryl and a copper halide. This reaction with different variants has been thoroughly reviewed by Fanta.[1–3] Recently, Hassan et al.[4] have reviewed comprehensively aryl–aryl bond formation one century after the discovery of the Ullmann reaction. A large number of studies have been reported for aryl–aryl bond formation using copper as a reagent (in stoichiometric amounts) or catalyst and also using nickel as a promoter. Use of the reagent or catalyst, however, produced lot of waste, and these cannot be reused. Hence, there is a need to develop an environmentally friendly catalyst that can be easily separated and reused for the reaction.

Pd-containing complex catalyst systems, such as Pd/C with zinc in the presence of water and liquid carbon dioxide[5] and Pd (OCOCF$_3$)/P(2-furyl) in supercritical carbon dioxide,[6] have been reported for the Ullmann-type coupling reactions.

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Palladium-catalyzed coupling of Grignard reagents or metal (viz., zinc, mercury, silicium, germanium, lead, bismuth, antimony, copper, zirconium, indium, tin, etc.) derivatives have also been employed extensively for aryl–aryl bond formation.[4] However, these palladium-catalyzed reactions are complex, require expensive reagents, and are difficult to perform. Moreover, because they create a lot of waste, these are also not environmentally friendly reactions. It would therefore be very interesting if a simple but easily separable and reusable palladium catalyst could be developed for the Ullmann-type coupling reaction. This has been achieved in the present investigation. In this communication, we report a greener process for the Ullmann-type aryl–aryl coupling of aryl iodides or bromides, forming biaryls with excellent yields at low temperature (140 °C) in the presence of potassium carbonate and dimethylformamide (DMF), using easily separable and reusable zirconia-supported palladium catalyst.

RESULTS AND DISCUSSION

The performance of Pd/ZrO_2 catalysts [prepared by different methods, viz. impregnation, coprecipitation, deposit precipitation (DP), and homogenous deposit precipitation (HDP)] in the Ullmann-type coupling of 4-iodoanisole is shown in Table 1.

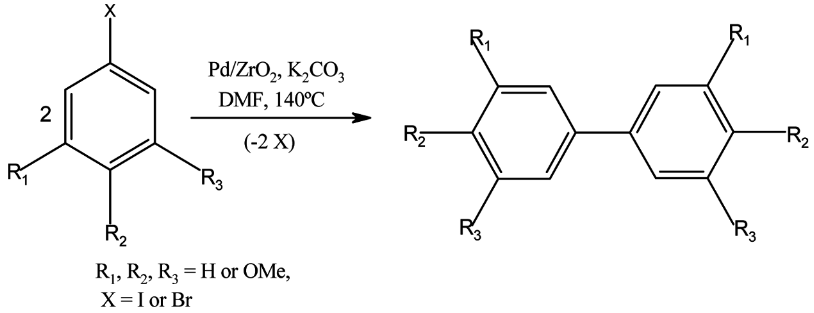
The results (Table 1) show a strong influence of the catalyst preparation method on the product yield in the Ullmann-type coupling reaction. The catalyst prepared by the impregnation technique showed the best performance (85% product yield). The poorest performance was shown by the catalyst prepared by the coprecipitation method, which is most probably because a large part of the Pd (which is buried in the bulk of the catalyst) is not available for the reaction. The catalysts prepared by the DP and HDP methods show intermediate activity in the reaction, even though their Pd particles are smaller in size. Their lesser activity is therefore expected, mostly because of the lower Pd loading in these catalysts (Table 1).

Results showing the Ullmann-type coupling of different aryl halides to corresponding biaryls (Scheme 1) over the Pd/ZrO_2 catalyst (prepared by the impregnation technique) in the presence of DMF (as a solvent) and K_2CO_3 (as a base) are presented in Table 2. In the absence of any catalyst, the product yield in the coupling of 4-iodoanisole for 15 h was quite small (<5%).

The results (Table 2) show that the product yield in the Ullmann-type coupling of aryl iodides is quite high (>80%). As expected, the product yield in the case of

Table 1. Ullmann-type coupling of 4-iodoanisole to 4,4′-dimethoxy biphenyl over Pd/ZrO_2 catalyst prepared by different methods

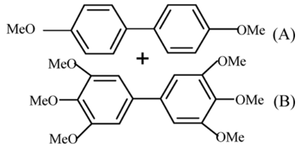
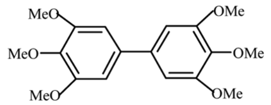
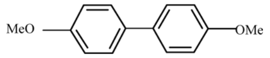
Catalyst preparation method	Pd loading in catalyst (wt%)	Pd particle size (nm)	Reaction time (h)	Isolated product yield (%)
Impregnation	2.5	16	5	85
Coprecipitation	2.5	—	10	16
DP	1.2	9	12	37
HDP	1.5	8	8	43



Scheme 1. Ullmann-type coupling reaction.

the coupling of aryl bromide (entry 5) is smaller (46% for bromoanisole). In the simultaneous coupling of *p*-iodoanisole and trimethoxyiodobenzene (entry 3), there was no hetero coupling. However, in the simultaneous coupling of *p*-iodoanisole and iodobenzene (entry 6), hetero coupling to small extent (12% yield for 4-imethoxy-biphenyl) is observed. The results show a strong influence of the substitutent in the aryl halide on the Ullmann-type coupling reaction. In general, the catalyst showed high activity for the Ullmann-type coupling reaction. Apart from its high activity,

Table 2. Ullmann-type coupling of aryl halides over the Pd/ZrO_2 catalyst (prepared by the impregnation method)

Entry	Substrates	Reaction time (h)	Product	Yield (%)
1	*p*-Iodoanisole	5	4,4′-Dimethoxy-biphenyl	85
2	Iodobenzene	7	Biphenyl	88
3	*p*-Iodoanisole + 3,4,5-trimethoxyiodobenzene	5		64 (A) + 25 (B)
4	3,4,5-Trimethoxyiodobenzene	5		80
5	*P*-Bromoanisole	15		46
6	*p*-Iodoanisole + iodobenzene	7	4,4′-Dimethoxy-biphenyl A) + biphenyl (B) + 4-methoxy-biphenyl (C)	64 (A) + 21 (B) + 12(C)
7	*p*-Iodoanisole[a]	15	4,4′-Dimethoxy-biphenyl	<5
8	*p*-Iodoanisole[b]	8	4,4′-Dimethoxy-biphenyl	83
9	*p*-Iodoanisole[c]	20	4,4′-Dimethoxy-biphenyl	39
10	*p*-Iodoanisole[d]	20	4,4′-Dimethoxy-biphenyl	nil

[a] In the absence of catalyst.

[b] Fourth reuse of the catalyst.

[c] At 100 °C.

[d] At 0 or 50 °C.

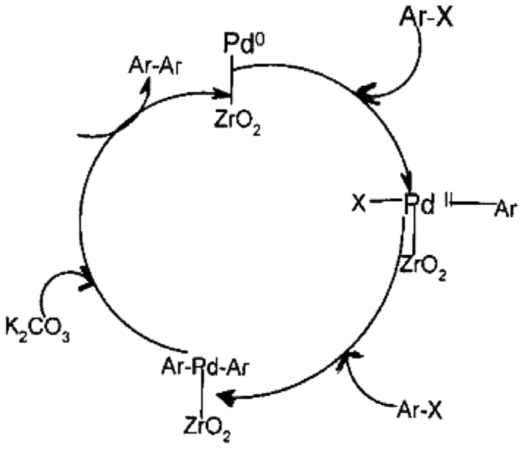
Table 3. Ullmann-type coupling of 4-iodoanisole to 4, 4′-dimethoxy biphenyl over Pd/ZrO_2 catalyst (prepared by the impregnation technique) in the presence of different bases or solvents

Base	Solvent	Reaction time (h)	Isolated product yield (%)
K_2CO_3	DMF	5	85
Na_2CO_3	DMF	20	20
NaOAC	DMF	20	25
Triethylamine	DMF	20	10
Pyridine	DMF	20	5
Zinc dust	DMF	20	30
K_2CO_3	NMP	10	19
K_2CO_3	Acetonitrile	12	14
K_2CO_3	Xylene	12	<5
K_2CO_3	Ethanol, 1,4-dioxane, toluene, or water	20	nil

the catalyst also showed excellent reusability in the coupling of 4-iodoanisole (Table 2). In the first, second, third and fourth reuse of the catalyst in the reaction, the product yields were 84, 84, 83, and 83%, respectively.

We have also studied the influence of reaction temperature (0–140 °C) on the coupling of 4-iodoanisole. Up to 50 °C, there was almost no reaction for 20 h, but at 100 °C (for 20 h) and 140 °C (for 5 h) the product yields were 39 and 85%, respectively (Table 2).

We have observed a strong influence of both the solvent and base on the Ullmann-type coupling reaction (Table 3) as follows. DMF was found to be the best solvent for the coupling of 4-iodoanisole. There was little or no reaction in the presence of ethanol, 1,4-dioxan, toluene, or water as solvents. However, for solvents, such as N-methyl pyrrolidone (NMP), xylene, and acetonitrile, the product yields were 19, 3, and 14%, respectively. Also, when K_2CO_3 was replaced by Na_2CO_3, NaOAC, trimethyl amine, pyridine, or zinc dust in the coupling of 4-iodoanisole, the product yield was much smaller. It was 20, 25, 10, 5, and 30%, respectively, even



Scheme 2. Plausible mechanism of Ullmann-type coupling of aryl halide over Pd/ZrO_2 catalyst in the presence of K_2CO_3.

though the reaction time was longer (20 h). This revealed that among the bases, K_2CO_3 is the most suitable base for the reaction.

It has long been known that the Ullmann reaction of substituted aryl halides results in the formation of biaryl bonds only at the carbon atom from which the reactive halogen has been displaced. The possible mechanism of Ullmann coupling of aryl halide over the Pd/ZrO_2 catalysts is shown in Scheme 2.

The coupling reaction seems to involve two steps: first an oxidative addition of catalyst to the aryl halide leads to the formation of an activated complex, which reacts preferentially with the second halide to form a diarylated palladium moiety. In the second step, a reductive elimination gives the biaryl product and the Pd(0) species to complete the catalytic cycle.

EXPERIMENTAL

The Pd/ZrO_2 catalyst (Pd loading = 2.5 wt%) was prepared by depositing $PdCl_2$ from its aqueous acidic (HCl) solution on zirconia support (prepared from zirconium nitrate by its hydrolysis with ammonium hydroxide, followed by washing and drying the zirconium hydroxide and then calcining it at 500 °C for 3 h) by the incipient wetness impregnation technique. After impregnation, the wet catalyst mass was dried at 100 °C for 4 h and then calcined in static air in muffle furnace at 500 °C for 3 h. The resulting catalyst mass was further treated with an ammoniacal solution of hydrazine on a water bath for transforming the Pd(0) (from the catalyst) to metallic Pd. The catalysts were also prepared by the coprecipitation (using ammonium hydroxide as precipitating agent), DP (using NaOH as precipitating agent), and HDP (using homogenously formed NH_4OH as precipitating agent) methods, followed by the pretreatment similar to that used for the catalyst prepared by the impregnation technique. The latter methods are described elsewhere.[7]

The presence of the metallic Pd phase in the reduced catalysts was confirmed by x-ray diffraction. The particle size of Pd in the catalysts was determined by their transmission electron microscopic (TEM) examination.

In a typical experiment, the reaction was carried out under the following reaction conditions: reaction mixture = 2.5 mmol aryl halide (with or without 2.5 mmol of second aryl halide) + 5 ml DMF (as a solvent) + 3.62 mmol potassium carbonate (as a base) +catalyst (10 wt% of aryl halide), temperature = 140 °C and reaction time = 6–20 h. The reaction was monitored by thin-layer chromatography (TLC). After completion of reaction, the catalyst was separated by filtration. Then the filtrate was quenched with water, followed by extraction with ethyl acetate to give the crude product, which was subsequently purified by column chromatography on silica gel with petroleum ether / ethyl acetate as an eluent. The catalyst was further washed with acetone, dried, and reused. The reaction products were isolated by column chromatography and were confirmed by NMR.

4,4′-Dimethoxy-biphenyl: ^1H NMR ($CDCl_3 + CCl_4$. 50 MHz): δ 7.47 (d, 4H, $J = 8$ Hz), 6.95 (d, 4H, $J = 8$ Hz), 3.85 (s, 6H); ^{13}C NMR ($CDCl_3 + CCl_4$, 50 MHz): δ 158.7 (2C), 133.5 (2C), 127.7 (4C), 114.2 (4C), 55.2 (2C); IR (chloroform): 3019, 2957, 1608, 1500, 1215, 1182, 1041, 824 cm^{-1}; GC mass: m/z 214.

In conclusion, the zirconia-supported Pd (prepared by the impregnation method) is a highly active and environmentally friendly (easily separable, reusable, and also nontoxic) catalyst for the Ullmann-type coupling of aryl iodides or bromides with high product yields in the presence of DMF (as a solvent) and K_2CO_3 (as a base). The catalytic performance of Pd/ZrO_2 in the reaction is strongly influence by the method of catalyst preparation and also by the base and/or solvent used in the reaction.

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