



Suzuki cross-coupling reactions of aryl halides with arylboronic acids catalysed by Pd(II)-NaY zeolite

Hatice Bulut,^a Levent Artok^{a,*} and Selahattin Yilmaz^b

^aDepartment of Chemistry, Faculty of Science, Izmir Institute of Technology, Urla 35437 Izmir, Turkey

^bDepartment of Chemical Engineering, Faculty of Engineering, Izmir Institute of Technology, Urla 35437 Izmir, Turkey

Received 26 September 2002; revised 26 October 2002; accepted 8 November 2002

Abstract—Pd(II)-exchanged NaY zeolite showed high activity in the Suzuki cross-coupling reactions of aryl bromides and iodides without added ligands. The DMF:water ratio, and the type and amount of base were found to be critical for the efficiency of the reaction. The catalyst is reusable after regeneration. © 2002 Elsevier Science Ltd. All rights reserved.

The Pd-catalysed Suzuki cross-coupling reaction of aryl halides or triflates with arylboronic acids has proved to be a most versatile reaction in the synthesis of both symmetrical and unsymmetrical biaryl compounds and has found widespread application in many areas of organic synthesis.¹ This reaction can be performed under moderate conditions, in aqueous medium, and is compatible with a wide variety of functional groups.

Many Pd complex types have been investigated in homogeneous systems both with and without added ligands. However, although the industrial use of heterogeneous catalysts is more desirable owing to the ease of catalyst separation and recycling, there are only very few reports of heterogeneous and reusable catalysts for the Suzuki reaction.

Zhang and Allen investigated the activity of a resin-bound palladium catalyst for the Suzuki reaction.² This catalyst appeared very active toward aryl iodides and aryl bromides activated by electron withdrawing groups. Nevertheless, the coupling was slow when inactivated aryl bromides were used and the catalyst activity deteriorated after 2–3 cycles. Kosslick et al. found that a palladium–phosphine complex loaded MCM-41 zeolite actively catalyses the cross-coupling of 4-iodoanisole with phenylboronic acid.³ It was shown that Pd/C, without added ligand, catalyses the cross-coupling of activated chloroarenes and arylboronic acids in excellent yield and inactivated ones in good yield.⁴ However, no information regarding the reusability of the catalyst was given in their report. Sakurai et al. found that Pd/C

catalyses the Suzuki reaction of halophenols in aqueous media.⁵ In the latter study, the Pd leaching propensity of the Pd/C catalyst was not reported. In a recent study, it was shown that Pd leaches into the reaction solution to a much higher extent from C or SiO₂ supports as compared to the zeolite support types, during Heck reactions.⁶

Recently, Djakovitch and Köhler found that Pd(II)-NaY zeolite activates aryl halides toward Heck,⁷ α -arylation of malonate⁸ and amination⁹ reactions. In this paper we

Table 1. Pd(II)-NaY catalysed Suzuki cross-coupling reaction of 4-bromoanisole and phenylboronic acid^a

Entry	Base (Mol equiv.)	DMF/H ₂ O	Yield (%) ^b
1	Na ₂ CO ₃ (4)	1/1	93 (92)
2	Na ₂ CO ₃ (4)	2/1	65
3	Na ₂ CO ₃ (4)	2/1	77
4	Na ₂ CO ₃ (3)	1/1	81
5	Na ₂ CO ₃ (5)	1/1	77
6 ^c	Na ₂ CO ₃ (4)	1/1	>99
7	K ₂ CO ₃ (4)	1/1	>99
8	Li ₂ CO ₃ (4)	1/1	63
9	Cs ₂ CO ₃ (4)	1/1	68
10	NaOAc (4)	1/1	3
11	N(C ₂ H ₅) ₃ (4)	1/1	3
12	NaOH (4)	1/1	7

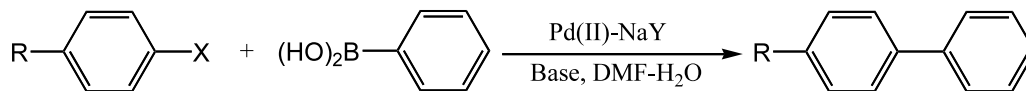
^a Reaction conditions: 1.0 mmol of 4-bromoanisole, 1.2 mmol of phenylboronic acid, 0.025 mmol Pd, 10 ml of a DMF–H₂O mixture, 1 h at room temperature.

^b GC yield based on 4-bromoanisole. The isolated yields are in parenthesis.

^c At 50°C.

* Corresponding author. Tel.: +90-232-498 7529; fax: +90-232-498 7509; e-mail: artok@likya.iyte.edu.tr

report that Pd(II)-exchanged NaY zeolite which was prepared by calcination of Pd(NH₃)₄²⁺ loaded NaY zeolite¹⁰ under an O₂ atmosphere, is also very active as a reusable catalyst for the Suzuki reaction of aryl halides.¹¹



Variation of reaction conditions on the Suzuki reaction was examined for the cross-coupling of 4-bromoanisole with phenylboronic acid and the results are given in Table 1.¹² Only with a chloroarene agent was homo-coupling side reactions observed under any conditions employed in this study.

In the presence of Na₂CO₃ as a base (entries 1–6), the optimum base/aryl halide and DMF/water ratios were determined to be 4 and 1, respectively, when the reactions were performed at room temperature for 1 h (entry 1). The conversion was quantitative when the reaction was carried out at 50°C and the optimum amount of Na₂CO₃ and DMF/water ratio were used (entry 6).

The effect of base type on the reaction efficiency was also screened (entries 1, 7–12). The coupling product formation was quantitative in the presence of K₂CO₃ at room temperature, while only moderate with Li₂CO₃ or Cs₂CO₃. The catalyst showed very poor activity in the presence of N(C₂H₅)₃, NaOH or NaOAc as bases (< 8%).

The reaction of 4-bromoanisole was also conducted at 0.5 and 1.5 h reaction times in the presence of Na₂CO₃ under the conditions of entry 1. In both cases the yield was identical to that obtained at 1 h. This could be associated with the deactivation of the palladium catalyst, as the formation of coupled product ceased in the first 0.5 h of the reaction and aryl bromide conversion was incomplete. Ultimately, it was realised that this catalyst could not be reused without activation, as the catalyst recovered (entry 1) revealed no activity to the coupling reaction under the same reaction conditions. This result contrasts with the previous reports wherein Pd(II)-NaY was shown to preserve its activity after use

in a Heck reaction.⁷ Nevertheless we determined that the used catalyst recovers its activity when it is re-calcined under O₂ by using the same method applied for the preparation of the fresh catalyst. It is evident that the first regeneration process increased the catalyst

activity as the yield was quantitative at the second use of the catalyst (Table 2). However, there was a little decrease in activity at the third, affording a 90% yield, and the yield was reduced to 62% at the fourth use of the catalyst at room temperature. But, the catalyst showed again high activity at the fourth use when the reaction was carried out at 50°C, in this case product formation being quantitative.

The exact nature of the palladium species in the fresh, the used and the regenerated catalyst is not yet known and will be identified through characterisation of these catalyst samples.

The catalyst was also tested on a variety of aryl halide types (Table 3). 4-Bromonitrobenzene afforded only a moderate yield of the corresponding coupled product (54% by GC, entry 13) though it is an activated aryl bromide, while phenyl bromide (entry 14) and other activated aryl bromides (entries 15 and 16) afforded excellent product formation under the established conditions. 4-Iodoanisole was converted to the corresponding coupled product quantitatively (entry 17). A moderate yield was obtained with an activated chloroarene, 4-chlorobenzotrifluoride (52% by GC) when the reaction was performed at 100°C. Nevertheless the conversion of the activated chloroarene was complete and the fate of the remaining starting material is unknown as no dehalogenated or any other side products could be determined by GC analysis.¹³

After the catalyst was filtered and washed with dichloromethane, we observed a Pd concentration less than 1.4 ppm (<0.5% loss based on the initial Pd) in the reaction mixtures. In order to check whether the dissolved amount of Pd can catalyse the Suzuki reaction, we performed the reactions of 4-bromoanisole with

Table 2. Reaction of 4-bromoanisole with phenylboronic acid using recovered and regenerated Pd(II)-NaY as catalyst^a

Catalyst cycle	Yield (%) ^b
First	93
Second	>99
Third	90
Fourth	62
Fourth ^c	>99

^a Reaction conditions are the same as those of entry 1 in Table 1.

^b GC yield based on 4-bromoanisole.

^c At 50°C.

Table 3. Pd(II)-NaY catalysed Suzuki cross-coupling reaction of aryl halides and arylboronic acids^a

Entry	Aryl halide	Arylboronic acid	Yield (%) ^b
13	4-NO ₂ C ₆ H ₄ Br	C ₆ H ₅ B(OH) ₂	54 (44)
14	C ₆ H ₅ Br	4-MeC ₆ H ₄ B(OH) ₂	(94)
15	4-CNC ₆ H ₄ Br	C ₆ H ₅ B(OH) ₂	90 (64, 78 ^c)
16	4-MeCOC ₆ H ₄ Br	C ₆ H ₅ B(OH) ₂	>99 (88)
17	4-MeOC ₆ H ₄ I	C ₆ H ₅ B(OH) ₂	>99
18	4-CF ₃ C ₆ H ₄ Cl	C ₆ H ₅ B(OH) ₂	52 ^d

^a Reaction conditions are the same as those of entry 1 in Table 1.

^b GC yield based on aryl halide. The isolated yields are in parenthesis.

^c Isolated by re-crystallisation from hexane.

^d At 100°C.

phenylboronic acid in the presence of $(\text{CH}_3\text{CO}_2)_2\text{Pd}$ as a homogenous catalyst, with the amount of 0.025 mmol and with the concentration of 1.4 ppm, at 0.5 h reaction time under the conditions of entry 1. While the coupling product formation was quantitative in the former, in the lower concentration of Pd its formation was only 3%. These may indicate that the leaching of Pd cannot explain the overall activity of the catalysts.

Some ligand additives, particularly phosphines, are used in many Pd catalysed reactions. Benzothiazolium salts were also found to activate palladium as a ligand.¹⁴ However, in our case, the addition of $\text{PPh}(\text{CH}_3)_2$ or 3-methylbenzothiazolium iodide which possess suitable molecular sizes to be able to penetrate through the zeolite apertures ($\sim 7 \text{ \AA}$), in an amount that is twofold molar equivalent with respect to the Pd amount, brought the coupling reaction to a halt.

In summary, we have found that aryl bromides and aryl iodides, in general, can be coupled with arylboronic acids in excellent yield using Pd(II)-exchanged NaY zeolite. The catalyst can be recycled and reused subsequent to regeneration.

Acknowledgements

This work was financially supported by the Research Funding Office of IZTECH with project No. FEN 2000 01. Authors would like to thank Dr. A. Eroğlu, Mr. S. Yilmaz and Ms. A. Erdem for AAS analysis.

References

1. (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2475; (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *57*, 147.
2. Zhang, T. Y.; Allen, M. J. *Tetrahedron Lett.* **1999**, *40*, 5813.
3. Kosslick, H.; Mönnich, I.; Paetzold, E.; Fuhrmann, H.; Fricke, R.; Müller, D.; Oehme, G. *Microporous and Mesoporous Mater.* **2001**, *44–45*, 537.
4. LeBlond, C. R.; Andrews, A. T.; Sun, Y.; Sowa, R. S., Jr. *Org. Lett.* **2001**, *13*, 1555.
5. Sakurai, H.; Tsukuda, T.; Hirao, T. *J. Org. Chem.* **2002**, *67*, 2721.
6. Dams, M.; Drijkoningen, L.; Pauwels, B.; Tandeloo, G. V.; Vos, D. E. D.; Jacobs, P. A. *J. Catal.* **2002**, *209*, 225.
7. (a) Djakovitch, L.; Heise, H.; Köhler, K. *J. Organomet. Chem.* **1999**, *584*, 16; (b) Djakovitch, L.; Köhler, K. *J. Mol. Catal. A: Chem.* **1999**, *142*, 275; (c) Djakovitch, L.; Köhler, K. *J. Am. Chem. Soc.* **2001**, *123*, 5990.
8. Djakovitch, L. M.; Köhler, K. *J. Organomet. Chem.* **2000**, *606*, 101.
9. Djakovitch, L.; Wagner, M.; Köhler, K. *J. Organomet. Chem.* **1999**, *592*, 225.
10. $\text{Pd}(\text{NH}_3)_4^{2+}$ -NaY has been shown to be an active catalyst precursor for Heck reactions (Refs. 6 and 7). However it showed no activity in the Suzuki reaction of 4-bromoanisole under the reaction conditions used for entry 1.
11. **Catalyst preparation:** NaY zeolite was prepared from NH_4Y (Zeolyst International, Si/Al: 2.5, 70\$/pound) by ion exchange method: NH_4Y zeolite (25 g) was suspended in 250 ml water containing 10 wt% of NaNO_3 . After stirring and refluxing the suspension for 24 h, the solid phase was isolated by filtration. This procedure was repeated twice and the Na^+ exchanged zeolite was finally washed with a large amount of water and calcined at 400°C for 10 h. $\text{Pd}(\text{NH}_3)_4^{2+}$ was introduced into the NaY zeolite by ion exchange with 0.1 M NH_4OH solution of $\text{Pd}(\text{NH}_3)_4\text{Cl}_2$, corresponding approximately to 1 wt% of Pd on the zeolite, by following the procedure given in References 6–8. Pd(II)-NaY was obtained by calcination of $\text{Pd}(\text{NH}_3)_4^{2+}$ -NaY in a vertical quartz tube under a flow of oxygen (200 ml/min), using a heating rate of $1^\circ\text{C}/\text{min}$ from room temperature to 500°C and maintaining the maximum temperature for 2 h. In order to analyse the palladium content of the zeolite, Pd(II)-NaY was dissolved in a mixture of concentrated HBF_4 , HNO_3 , and HCl (3:3:2) in a Teflon reactor by heating at 180°C and subjecting it to 600–650 Watt microwave power. The AAS gave 1.0 ± 0.1 wt% of Pd.
12. **Typical reaction procedure:** In a 50 ml flask equipped with a magnetic stirring bar was charged aryl halide (1 mmol), Na_2CO_3 (4 mmol), arylboronic acid (1.2 mmol) and Pd(II)-NaY (0.025 mmol Pd) in succession. The flask was attached to an argon line and subsequently the reaction was started by the addition of a 10 ml DMF/water mixture (1/1). The mixture was vigorously stirred for 1 h at room temperature. The catalyst was filtered off and washed with dichloromethane and 0.6 mmol of tetradecane was added to the solution as an internal standard. The organic phase was separated from the aqueous phase and dried over Na_2SO_4 . Products were analysed by GC and GC/MS and isolated by column chromatography on silica gel using hexane and hexane–ethyl acetate mixture (9:1 v/v) as eluents, successively.
13. Biaryl product (≈ 0.05 mmol) was determined in the reaction product formed by homo-coupling of phenylboronic acid.
14. (a) Calò, V.; Sole, R. D.; Nacci, A.; Schingaro, E.; Scordari, F. *Eur. J. Org. Chem.* **2000**, 869; (b) Calò, V.; Nacci, A.; Monopoli, A.; Lopez, L.; di Cosmo, L. *Tetrahedron* **2001**, *57*, 6071.