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Heterogeneous Suzuki and Stille coupling reactions using highly efficient palladium(0) immobilized MCM-41 catalyst

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ABSTRACT

An efficient palladium(0) immobilized MCM-41 catalytic system for C–C cross-coupling reaction has been developed. Ligand-free Pd(0)-MCM-41 catalyst can be successfully used in coupling reaction between various aryl halides including deactivated chlorobenzene with aryl borane and organotin to give biaryls in excellent yields with high turnover frequency (TOF) (the maximal TOFs are up to 6990 for the reaction of bromobenzene with phenylboronic acid). The catalyst can be recycled and reused without any loss of catalytic activity.

Compounds containing biaryl linkage are an important class of organic compounds and have found widespread applications in many areas of organic synthesis,[1] natural product synthesis such as tellimagrandins,[2,3] gossypol,[4] polymer science,[5] and in material science as precursors to rigid liquid crystals.[6] Several methods are available in the literature for the preparation of biaryls.[1,7–10] Amongst them Suzuki and Stille cross-coupling reactions are found to be most effective.[1,8] The relative thermal stability, insensitivity to air or moisture, and low toxicity[1] of boronic acid constitute a highly valuable practical advantage for both academic and industrial applications. Besides, the tin reagents that are used in the Stille coupling reactions can be easily synthesized and purified.[11]

For the Suzuki reactions soluble palladium complexes such as $Pd(PPh_3)_4$ and $Pd(PPh_3)_2Cl_2$ are usually used as catalysts along with the bases such as soluble amines. Although homogeneous palladium catalysts have proven to be efficient, it is difficult to recover them from products and it is still very uneconomic to use them for large-scale preparation. From the standpoint of environmentally benign organic synthesis, development of ligand-free[12] immobilized palladium catalysts is challenging and important.[13]

The mesoporous silica-based materials designated as M41S have attracted a lot of attention in catalysis study[14] since its invention by the scientists of Mobil Corporation.[15] MCM-41 is one of the members of this family having uniform hexagonal arrays of one-dimensional channels of mesopores with pore diameter in the range of 20–100 Å. Heterogenization of homogeneous catalysts by anchoring metal complex on the modified surface of MCM-41 via covalent bond shows impressive catalytic properties.[16] In the course of our continuing investigation in different organic reactions using ordered mesoporous silica materials as heterogeneous catalyst we have found that the hybrid organic–inorganic material demonstrates excellent catalytic efficacy. Herein, we describe an entirely heterogeneous ligand-free palladium-catalyzed carbon–carbon cross-coupling reaction system that is very effective with the less expensive bromobenzenes, and requires very small amounts of the solid palladium catalyst which is entirely recoverable and reusable.

The catalyst, Pd(0)-MCM-41 was prepared via simultaneous incorporation of $[Pd(NH_3)_4]^{2+}$ ions into the mesoporous material during the synthesis of MCM-41 and subsequently upon treatments with hydrazine hydrate, Pd^{2+} ions present in mesoporous silica matrix were reduced to Pd(0) almost instantaneously. Pd(0)-MCM-41 has been characterized thoroughly and reported in our recent publication.[17] The Pd content of the catalyst was quantified by PerkinElmer A-Analyst 200 atomic absorption spectrometer and found to be 0.008 (wt %) (7.52×10^{-5} mol %).

To illustrate the catalytic activity, Pd(0)-MCM-41 was first used as a heterogeneous catalyst for the synthesis of biphenyls via Suzuki cross-coupling reactions. In a typical experiment for Suzuki coupling reaction,[18] substituted and non-substituted aryl halides, phenylboronic acid, K_2CO_3, and solvent were placed in the flask, followed by the addition of the catalyst. The reactions are conveniently carried out in air at atmospheric pressure and at a temperature of 80 °C. In all our experiments dry and distilled solvents were used, while the distilled water was used for mixed solvent system. The organic products were isolated by extraction and then analyzed by the ^1H NMR spectroscopy. As for bases, potassium

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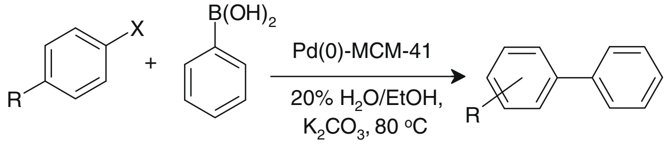
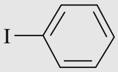
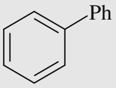
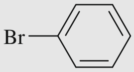
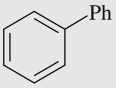
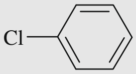
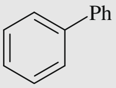
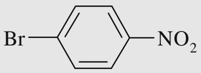
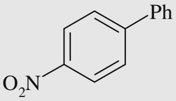
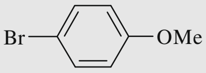
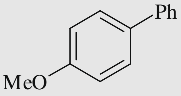
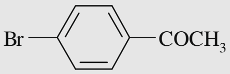
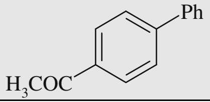
Table 1
Pd(0)-MCM-41 catalyzed Suzuki cross-coupling reaction of aryl halides and phenylboronic acid[a]



$R = H, NO_2, OCH_3, COCH_3$
$X = I, Br, Cl$

Entry	Aryl halide	Product	Time (h)	Conversion[b] (wt %)	Yield[c] (wt %)	TOF[d] (h^{-1})
1			20	100	93	3911
2			12	100	90	6990
3			24	24	24	803
4			12	97	97	6585
5			20	97	97	4139
6			24	65	64	2172

[a] Reaction conditions: 3 mmol of aryl halide, 3.6 mmol of phenylboronic acid, 3 mmol of K_2CO_3, and 0.05 g of Pd(0)-MCM-41 in 20% H_2O/EtOH at 80 °C.
[b] Conversion of reactant is determined by gas chromatography.
[c] Isolation yields were calculated from the mass of the product after separation by column chromatography. All the isolated products showed more than 99% of GC purity.
[d] TOF (turnover frequency) = moles converted/(mol of active site × time).

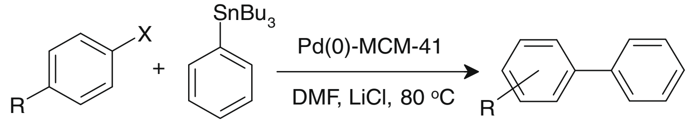
carbonate appeared to be a better choice. The use of sodium acetate or trialkylamine as base in coupling reaction between iodobenzene and phenylboronic acid resulted in low yield (10% for NaOAc and ~2% for Et_3N). Among non-substituted aryl halides, iodobenzene and bromobenzene (Table 1, entries 1 and 2) showed comparable yields which are higher than that of chlorobenzene. However, iodobenzene requires longer time for 100% conversion. Iodobenzene generally shows greater reactivity than bromobenzene in the cross-coupling reactions. Nevertheless, there are some exceptions where reverse catalytic activity is observed in palladium nanoparticle-based catalysts.[19,20] In a recent study it has been proposed that the I^- or I_2 generated from iodobenzene can act as inhibitor during the catalytic process.[20] Pd(0)-MCM-41 catalyst is capable of activating chlorobenzene (Table 1, entry 3) which normally remains unreactive in C–C coupling reactions, however, the yield is much lower in comparison to the recent report on Suzuki reaction using Pd nanoparticle catalyst in ionic liquid media.[21] The *para*-substituted substrates ($R_1 = -NO_2$, $-OCH_3$, and $-COCH_3$) not only exhibit enhanced activity but also afford 99% selectivity of the products in Suzuki reactions.

Catalytic efficacy of Pd(0)-MCM-41 has been tested also with Stille reaction. Substituted and non-substituted aryl halides are coupled with organotin, namely, tributylphenyltin in DMF in the presence of LiCl in air at 100 °C.[22] The desired products are obtained in good yields and TOFs of the reactions are remarkably high. Notably the reaction does not proceed without the use of LiCl. The exact role of LiCl as an additive in Stille reaction is not well understood. However, it has been proposed that the chloride ion undergoes exchange with coordinated iodide in the oxidative addition product prior to the transmetalation step in the catalytic cycle of Stille reaction.[23,24] The chloro complex of palladium thus formed facilitates the transmetalation via the formation of stable Bu_3SnCl.[25] The reaction does not occur in ethanol and acetonitrile media. Both bromobenzene and iodobenzene showed impressive conversion with comparable yields (Table 2, entries 1 and 2) in Stille reactions among the non-substituted aryl halides while chlorobenzene exhibited only about 30% conversion.

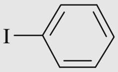
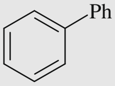
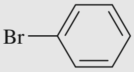
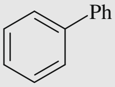
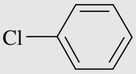
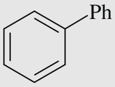
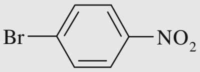
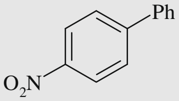
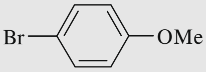
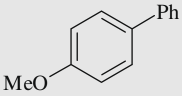
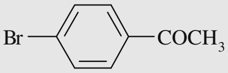
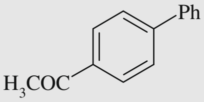
In search of an efficient heterogeneous catalyst for cross-coupling reactions several systems such as Pd/C, Pd onto KF/Al_2O_3 and other systems have been used.[26] Recently, Cai et al. have used MCM-41-supported sulfur palladium(0) complex and MCM-41-supported bidentate phosphine palladium(0) complex in Suzuki[26c] and Stille[27] coupling reactions, respectively. However, the catalytic turnover number (TON) for a single run is very low (less than 200) with their catalyst. This is the major drawback of a heterogeneous catalytic system in comparison to their homogeneous counterpart. Palladium–phosphine complex impregnated onto MCM-41 matrix is found to be active toward Suzuki cross-coupling reaction of 4-iodoanisole with phenylboronic acid.[28] In this case also low TONs and leaching of Pd complex are the major problems. Coelho et al.[29] reported ligand-free $Pd/CaCO_3$ for the Stille reaction and proposed a reaction mechanism revealing that the leaching occurred to give rise to a very active 'mononuclear Pd(0) species' that react faster with aryl halide resulting in a homogeneous catalytic cycle.

The most definitive test available to date to ascertain the true heterogeneity of the Pd-based catalyst in C–C coupling reactions

Table 2
Pd(0)-MCM-41 catalyzed Stille cross-coupling reaction of aryl halides and tributylphenyltin[a]

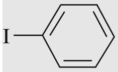
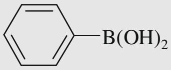
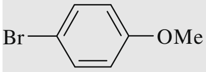
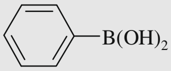
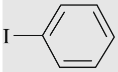
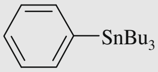
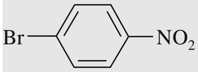
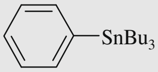


R = H, NO_2, OCH_3, $COCH_3$
X = I, Br, Cl

Entry	Aryl halide	Product	Time (h)	Conversion[b] (wt %)	Yield[c] (wt %)	TOF[d] (h^{-1})
1			20	80	72	522
2			18	76	70	715
3			24	32	32	315
4			24	100	99	549
5			24	43	42	255
6			24	100	98	557

[a] Reaction conditions: 1 mmol of aryl halide, 1 mmol of tributylphenyltin, 2.89 mmol of LiCl, and 0.05 g of Pd(0)-MCM-41 in 4 mL of DMF at 100 °C.
[b] Conversion of reactant is determined by gas chromatography.
[c] Isolation yields were calculated from the mass of the product formed from aryl halide after separation by column chromatography.
[d] TOF (turnover frequency) = moles converted/(mole of active site × time).

Table 3
Performance of the Pd(0)-MCM-41 catalyst in solid-phase poisoning test[31]

Aryl halide	Phenylboronic acid/tributylphenyltin	Coupling reaction	Temp (°C)	SH-SiO_2 added	Conversion[c] (Yield) (wt %)
		Suzuki[a]	80	No	100 (93)
				Yes	100 (95)
			80	No	97 (96)
				Yes	95 (94)
		Stille[b]	100	No	80 (72)
				Yes	78 (69)
			100	No	100 (99)
				Yes	100 (>99)

[a] Reactions were carried out in air using 3 mmol of aryl halide, 3.6 mmol of phenylboronic acid, 3 mmol of K_2CO_3, 0.12 mmol of SH-SiO_2, and 0.05 g of Pd(0)-MCM-41 in 20% H_2O/EtOH at 80 °C.
[b] Reactions were carried out in air using 1 mmol of aryl halide, 1 mmol of tributylphenyltin, 2.89 mmol of LiCl, 0.12 mmol of SH-SiO_2, and 0.05 g of Pd(0)-MCM-41 in 4 mL of DMF at 100 °C.
[c] Conversion of reactant is determined by gas chromatography.

Table 4
Recycling of Pd(0)-MCM-41 catalysts in the Suzuki and Stille cross-coupling reactions with iodobenzene

Entry	Run	Coupling reaction	Conversion[c] (wt %)	Yield (wt %)	TOF[c] (h^{-1})
1	1st	Suzuki[a]	100	93	3911
2	2nd		100	95	3911
3	3rd		95	90	3715
4	4th		98	93	3832
5	1st	Stille[b]	80	72	522
6	2nd		78	70	509
7	3rd		75	72	490
8	4th		72	68	470

[a] Reactions were carried out in air using 3 mmol of iodobenzene, 3.6 mmol of phenylboronic acid, 3 mmol of K_2CO_3, and 0.05 g of Pd(0)-MCM-41 in 20% H_2O/EtOH at 80 °C.

[b] Reactions were carried out in air using 1 mmol of iodobenzene, 1 mmol of tributylphenyltin, 2.89 mmol of LiCl, and 0.05 g of Pd(0)-MCM-41 in 4 mL of DMF at 100 °C.

[c] TOF (turnover frequency) = moles converted/(mole of active site × time).

is the solid-phase poisoning test suggested by Richardson and Jones.[30] Since, recovery and reuse of catalyst are important issues in the C–C cross-coupling reactions, we have performed solid-phase poisoning tests using commercially available (purchased from Sigma–Aldrich) 3-mercaptopropyl-functionalized silica (SH-SiO_2) as an effective palladium scavenger which selectively coordinates and deactivates the leached out palladium. Poisoning test was performed for both Suzuki and Stille coupling reactions.[31] Comparison of percentage of conversion in C–C coupling reactions (Table 3) clearly shows that the catalytic efficacy of Pd(0)-MCM-41 is not affected when SH-SiO_2 is added to the reaction mixture. This indicates that probably no leaching of Pd species is occurring in the Pd(0)-MCM-41 catalyzed C–C coupling reactions.

For the recycling study, both Suzuki and Stille coupling reactions were performed with iodobenzene maintaining the same reaction conditions.[18,22] After first cycle of reaction the catalyst was recovered by centrifugation and then washed thoroughly with DMF followed by copious amount of water to remove the base present in the used catalyst and finally by dichloromethane. The recovered catalyst was dried under vacuum at 110 °C overnight. The performance of the recycled catalyst in C–C coupling reactions up to four successive runs is summarized in Table 4. The catalytic efficacy of the recovered Pd(0)-MCM-41 remains almost the same for both coupling reactions in every run.

In conclusion, Pd(0) immobilized mesoporous ligand-free heterogeneous catalyst, Pd(0)-MCM-41, shows high activity toward Suzuki and Stille carbon–carbon coupling reactions. The catalyst has shown a notable activity toward a wide variety of substrates with a high turnover frequency. Additionally, the possibility of easy recycle makes the catalyst cheap and highly desirable to address the environmental concerns.

Acknowledgments

Financial support from the Department of Science and Technology (DST), Government of India, by a grant (SR/S1/IC-23/2003) (to SK) is gratefully acknowledged. Financial assistance from Ministry of Environment and Forest, Govt. of India is also acknowledged. S.J. (SRF) and S.H. thank CSIR for the research fellowship.

Supplementary data

All products are known compounds. The detailed experimental procedures, and ^1H NMR spectrum of the isolated products. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.05.098.

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18. *General procedure for Suzuki cross-coupling reaction*: The coupling reaction was carried out in a glass batch reactor. At first, aryl halide (3 mmol) and phenylboronic acid (0.73 g, 3.3 mmol) were dissolved in 4 mL ethanol. This reactant mixture was then added to the solution of K_2CO_3 (1.658 g, 3 mmol) in 1 mL of water under stirring condition. To this 0.05 g of Pd(0)-MCM-41 (Pd content 7.52×10^{-5} mol %) catalyst was added and the reaction mixture was refluxed at a temperature of 80 °C in an oil bath. To study the progress of the reaction the products were collected at different time intervals and identified and quantified by a Varian CP-3800 Gas Chromatograph using a CP-Sil 8 CB capillary column. For isolation of products at the end of the catalytic reaction, the catalyst was first separated out by filtration and then the filtrate was extracted with hexane (3 × 15 mL). The organic layers thus collected were combined and washed with water to remove excess K_2CO_3, with brine and dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using n-hexane/ethyl acetate mixture (9:1 v/v) to give the corresponding biphenyl. The product was analyzed by GC/MS, ^1H NMR, ^{13}C NMR reported in the Supplementary data.
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22. In a glass batch reactor, aryl halide (1 mmol), LiCl (0.12 g, 2.89 mmol), and 5 mL of DMF were added successively. To this 0.05 g of Pd(0)-MCM-41 catalyst was added and the mixture was heated to a temperature of 100 °C in an oil bath. Finally, tributylphenyltin (0.204 g, 1 mmol) was added and the reaction mixture was stirred vigorously. Progress of the reaction was monitored by GC at regular intervals and when the reaction was completed, the solid catalyst was filtered. The filtrate was treated similarly as given in Ref.[18].
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31. *Solid-phase poisoning test*: For Suzuki reaction, SH-SiO_2 (0.10 g, 0.12 mmol) and 0.05 g of Pd(0)-MCM-41 catalyst (Pd content 7.52×10^{-5} mol %) were taken in the solution containing aryl halides (3 mmol), phenylboronic acid (0.4 g, 3.3 mmol), and K_2CO_3 (0.14 g, 1 mmol) in 5 mL of 20% H_2O/EtOH. The mixture was stirred continuously maintaining the temperature of the oil bath at 80 °C. The progress of the reaction was monitored by the method described above. Poisoning test was also performed for Stille reaction using aryl halide (1 mmol), tributylphenyltin (0.204 g, 1 mmol), and LiCl (0.12 g, 2.89 mmol) in 5 mL of DMF at a temperature of 100 °C in the presence of SH-SiO_2 (0.10 g, 0.12 mmol) and 0.05 g of Pd(0)-MCM-41 catalyst.