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Ligand-free Pd Catalyzed Cross-coupling Reactions in Aqueous Hydrotropic Medium

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Abstract

A simple, efficient and ligand-free protocol for the Suzuki-Miyaura reaction and base-free Heck-Matsuda reactions under mild reaction conditions has been developed over palladium supported on activated carbon (Pd/C) in aqueous hydrotropic solution. The catalyst Pd/C was fully characterized by TG-DTA, SEM, EDS, XRD, XPS, BET and ICP-AES analysis. This green methodology represents a cost-effective and operationally convenient method for synthesis of a variety of biaryls, prochiral ketones, and acrylates under conditions that are tolerant for a broad range of functional groups with good to excellent yields. The developed Pd/C-aqueous hydrotrope combined catalytic system is well suitable for 3R approach (reducible, robust, and recyclable) for different cross-coupling reactions without appreciable loss of its activity.

Keywords: Palladium, Cross-couplings, Pd/C, Hydrotropes, Aqueous, Prochiral Ketones, Acrylates.

Introduction

Biphenyls and acrylates constitute a class of key structural motifs present in numerous biologically important compounds, e. g. Biphenylindanone A, Nifedipine, Losartan HIV-1 Protease and Taxol as they are present as subunits in many marketed drugs.[1] They also constitute the basis for a number of natural molecules with different biological activities.[2] These compounds are also useful for the construction of structurally important compounds, such as triphenylamino-1,8-naphthalimides, poly(9,9-dihexyl)-fluorene and Benzothiadiazole– cyclopentadithiophene (BTZ-CDT),[3] which are widely used in solar cells and electroluminescent materials.[4] There has been considerable interest in designing and synthesizing compounds containing such motifs by using transition metal catalysts.[5] The number of palladium catalyzed C-C cross-coupling reactions were explored including Suzuki-Miyaura,[6] Stille,[7] Negishi,[8] Hiyama,[9] Songashira,[10] Mizoroki-Heck[11] and Heck-

Matsuda.[12] Out of these, Suzuki-Miyaura and Heck-Matsuda cross-coupling reactions are reliable and powerful methods to form C-C bond for the synthesis of biaryls,[13] prochiral ketones,[14] and acrylates.[15]

Recently, ligandless approach for the carbon-carbon bond forming cross-coupling reaction has attracted an increasing attention[16] as it renders the process more cost effective and also avoids the contamination of ligands and metal in the final product.[17] Such a ligandless catalysis is achieved by Pd(0) species in the form of Pd nanoparticles.[18] Although the ligandless Pd catalyzed reactions are frequently performed with reasonably faster rates in water, but many a times complete conversion of the substrate is not possible, due to the active Pd(0) species undergo quick agglomeration under these conditions.[19] This drawback of ligandless coupling may be overcome by dispersing catalytic material in in an aqueous hydrotropic medium as it possesses surfactant like properties.[20] In addition, hydrotropism[21] which is similar to miceller catalysis[22] has a great advantage of increasing the potential of water as a solvent for organic synthesis. This enables the replacement of toxic, expensive, flammable and volatile organic solvents by easily available water which is highly desirable, from economic as well as environmental points of view. Hydrotropism gives a very simple protocol for solubilizing several types of organic functionalities at room temperature in absence of co-solvent and without modification in commercial catalyst design. Recently, we reported the use of hydrotropes for synthesis of many heterocyclic compounds,[23] demonstrating that hydrotrope can serve as an excellent reaction medium.

Supported Pd catalysts were developed for C-C coupling reactions primarily with the objective of easy separation of precious Pd metal from reaction mixture.[24] For this purpose, activated carbon with high specific surface area and large pore size playshas been extensively used.[25-26] Activated carbon supported Pd catalysts have been widely applied for the oxidation of organic compounds,[27] chemical syntheses,[28] hydrogen storage,[28] electrocatalysis[29] and selective hydrogenation.[30] In addition Pd/C has also emerged as one of the promising heterogeneous catalyst for C-C bond forming reactions.[31]

Herein we report the realization of utility of Pd/C-aqueous hydrotrope mediated ligand-free Suzuki-Miyaura and base-free Heck-Matsuda cross coupling reactions at ambient temperature.

Results and Discussion

Characterization

Activated carbon supported Pd catalyst used for various Suzuki-Miyaura and Heck-Matsuda cross coupling reactions was thoroughly characterized by different techniques like

TG-DTA, SEM, EDS, XRD, XPS and BET. TG-DTA analysis (Fig. 1) shows that the catalyst was stable up to 550 °C. The loss in weight at temperatures below 200 °C was caused by the evaporation of physically adsorbed water molecules in the catalyst. The significant decrease in the weight up to 76.45 % observed in the range of 500-568 °C was mainly due to the decomposition of organics to form CO_2.[32] The stable weight fraction obtained after complete combustion showed that the 9.23 wt % loading of Pd on the carbon.

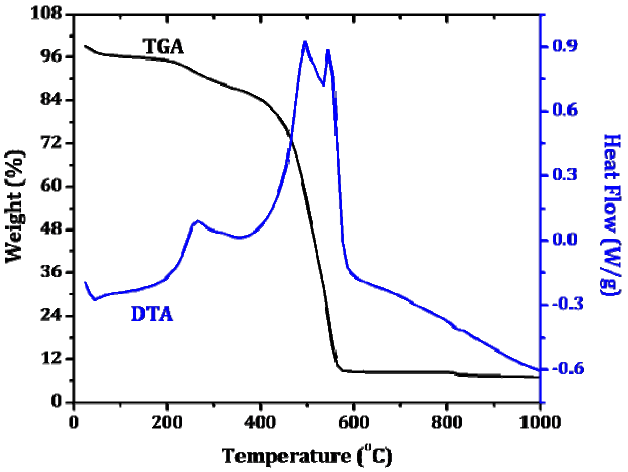


Fig. 1 TG-DTA spectra of Pd/C catalyst

Powder X-ray diffraction (XRD) analysis of fresh and recycled Pd/C catalysts is shown in Fig. 2. The XRD diffraction pattern of the recycled Pd/C was also identical with a fresh Pd/C catalyst. The reflection of peaks at 2θ= 40.11, 46.66, 68.12, 82.09 and 86.61°, corresponded to the (111), (200), (220), (311) and (222) planes of cubic lattice structure of Pd metallic phase (JCPDS 46-1043). The reflection peak observed at 2θ=26.62° (JCPDS 25-0284) was assigned to the (002) plane of the carbon. A broad peak at 2θ = 35° was likely to be due to the oxide phase, $PdO{\cdot}H_2O$ (JCPDS 09-0254). XRD pattern of recycled Pd/C did not show any additional peaks indicating that the Pd metal retained onto the surface of the carbon.[32a, 33]

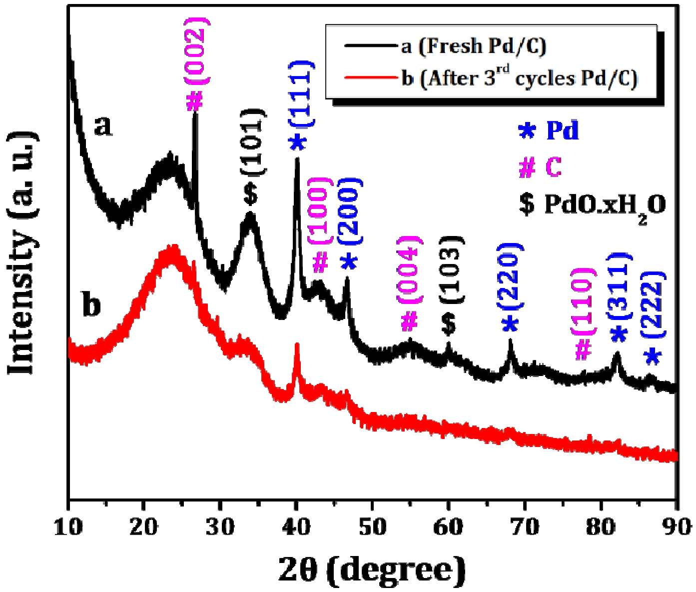


Fig. 2 XRD of Pd/C catalyst (a) fresh and (b) used (after 3rd cycle) samples

SEM micrograph (Fig. 3a) of Pd/C clearly revealed the distinct morphology as small white discrete particulates of Pd dispersed on the carbon material. The EDS spectrum (Fig. 3b) of the Pd/C taken at random points on the surface indicated composition as C, O and Pd in the weight % ratio of 83.79, 7.92 and 8.28, respectively.

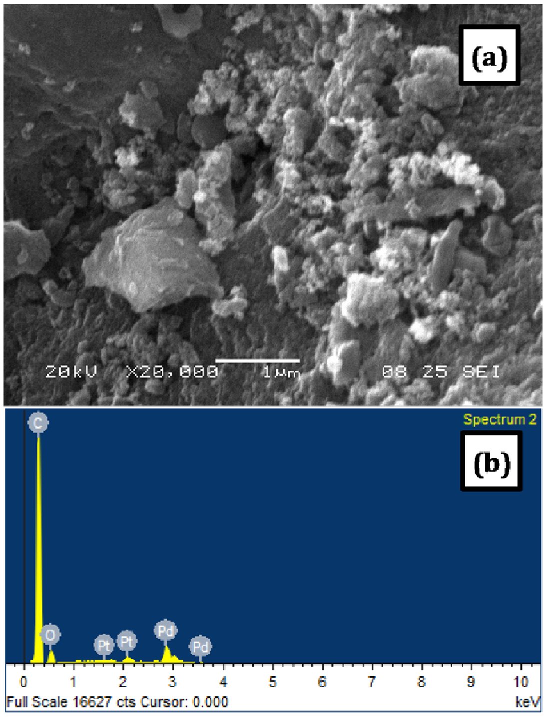


Fig. 3 SEM and EDS parameters of Pd/C catalyst

XPS analysis of the fresh Pd/C catalyst (Fig. 4a) and recovered Pd/C catalyst after third recycle (Fig. 4b) provided useful information about the chemical state of the Pd. Lower binding energy doublet was assigned to metallic Pd whereas higher binding energy one could be related to PdO.[34] The peaks due to Pd(0) were much stronger than those of Pd(II) in both the samples, suggesting that majority of the catalyst existed in a metallic Pd state and also that the Pd/C catalyst was highly stable for subsequent recycle runs.

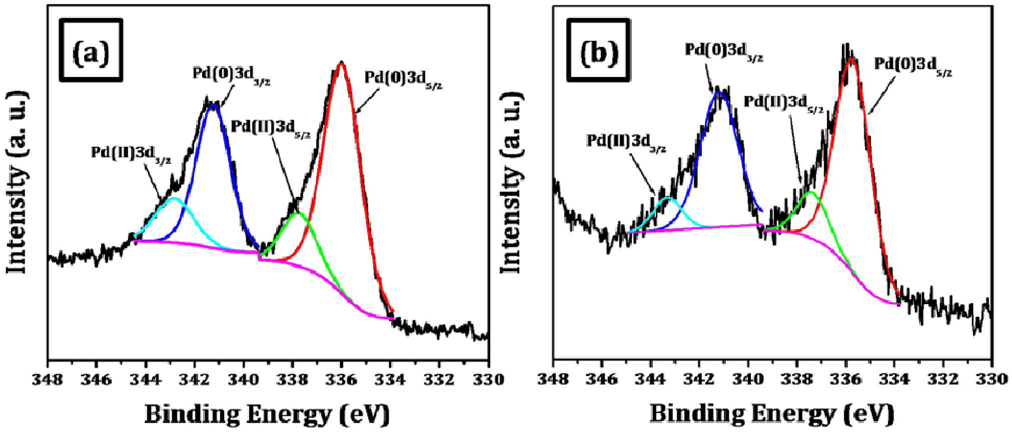
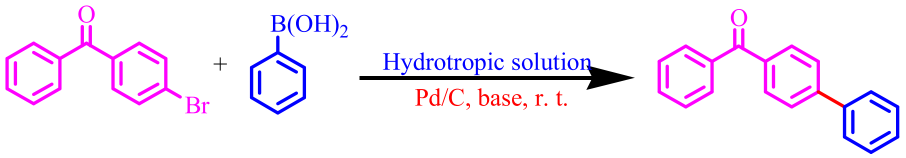


Fig. 4 XPS analysis of (a) fresh Pd/C catalyst, (b) used (after 3rd cycle) Pd/C catalyst

BET surface area measurement of the fresh and reused Pd/C catalyst showed that there was slight decrease in surface area from 1247.72 m^2g^{-1} to 1152.32 m^2g^{-1} which was in accordance to the corresponding decrease in pore diameter of the reused catalyst (13.78 nm), as compared to that of the fresh sample (17.96 nm).

Suzuki-Miyaura cross-coupling reaction of aryl halides, arenediazonium salts, and acyl chlorides with boronic acids

Suzuki-Miyaura coupling of 4-bromobenzophenone with phenylboronic acid was studied over Pd/C in presence of K_2CO_3 as a base at room temperature (Scheme 1).



Scheme 1 Suzuki-Miyaura cross-coupling reaction under ligand-free condition

The preliminary studies on screening and effect of concentration of hydrotropes showed that the nature of hydrotrope and its concentration had a significant effect on the yield and time of reaction. As shown in Fig. 5, a control experiment in water without any hydrotrope gave only 20 % yield in 12h. While the reaction performed in presence of a hydrotrope, 60 % sodium xylene sulphonate (NaXS) solution instead of only water, the yield was remarkably improved to 93 % in just 2h. Among the several hydrotropes screened in this work, sodium xylene sulphonate (NaXS) exhibited the highest yield of 93 %.

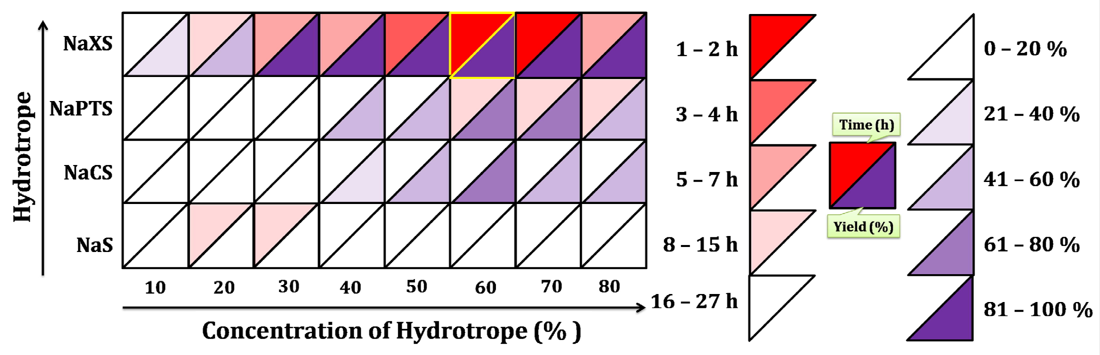


Fig. 5 Screening and optimization of various hydrotropes and its concentrations for Suzuki–Miyaura cross-coupling reaction.

In order to understand the role of a hydroptrope, another control experiment was carried out using a surfactant because hydrotrope, similar to the surfactant also contains amphiphilic head and hydrophilic tail. However, Pd/C catalyst in presence of a surfactant (SDS), gave only 10 % yield in 12h. The hydrophobic tail of a hydrotrope is smaller which forms aggregates instead of micelles in case of a surfactant [21-22] hence hydrotrope is believed to stabilize the active palladium species in water. In the presence of a hydrotrope, the substrate forms an emulsion in water and the powdered catalytic material is well dispersed in this emulsion, increasing the activity of catalyst. All the further studies were then carried in presence of a hydrotrope, NaXS.

Effect of reaction time on the yield of the final product was studied by carrying out the model reaction in a time range of 15 to 150 minutes. Fig. 6 shows that the percentage yield of the final product linearly increased with increase in reaction time from 15 to 120 min and after that it remained constant at ~ 93 %.

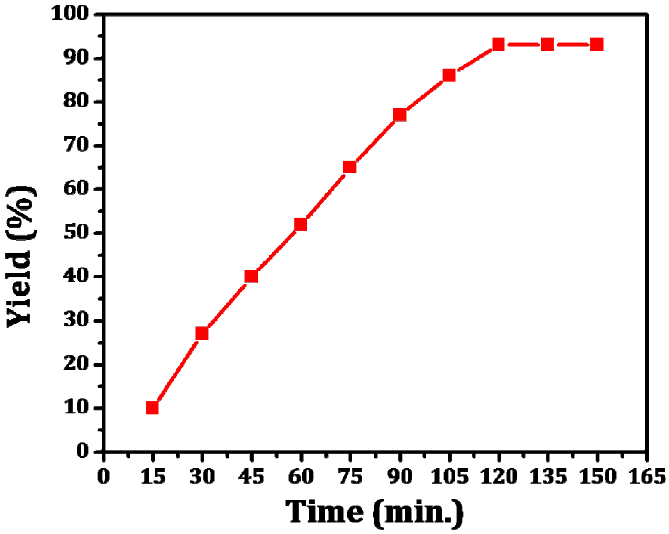


Fig. 6 Optimization of effect of reaction time on yield of desired product

Fig. 7 shows the results of screening of various organic and inorganic bases. The reaction did not proceed in the absence of a base and it was revealed that K_2CO_3 showed the best efficiency giving the maximum yield of 93 % in 2h.

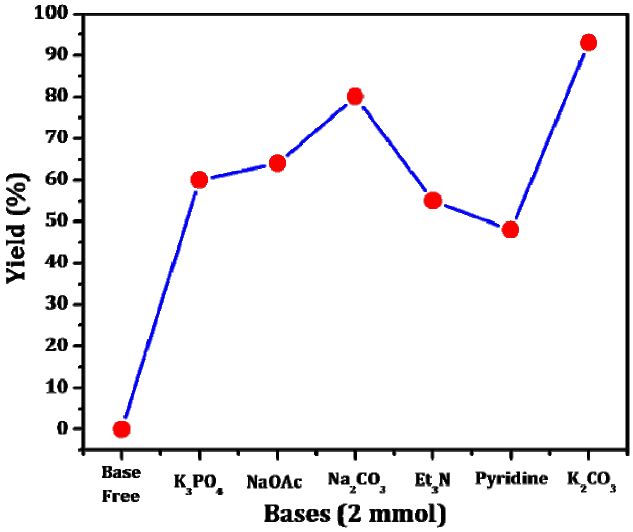


Fig. 7 Screening of bases for Suzuki–Miyaura cross-coupling reaction

The influence of catalyst concentration is very important as it not only affects the cost of process but also hinders the activity of catalyst due to Pd agglomeration beyond a certain concentration.[35] Optimization of catalyst loading showed that 2 mol % Pd was found to be the most effective with a maximum yield (93%) of the desired coupling product within 2h (Table

1, entry 6). The lower catalyst loading (0.25-1.5 mol %) furnishes lower conversion (50-85%).

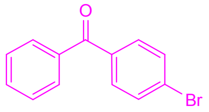
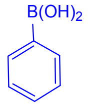
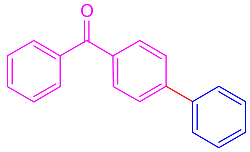
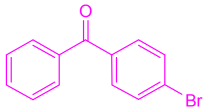
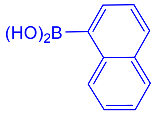
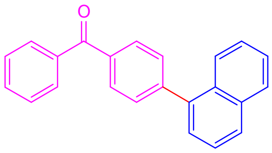
Table 1 Optimization of catalyst loading for Suzuki–Miyaura cross-coupling reaction[a].

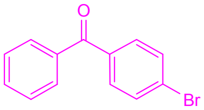
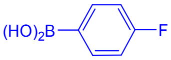
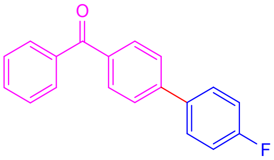
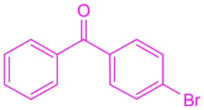
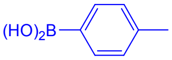
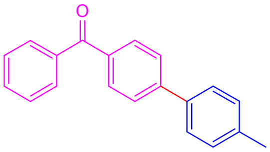
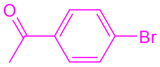
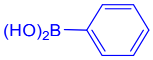
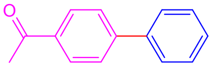
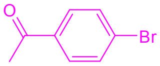
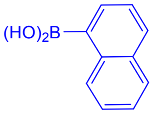
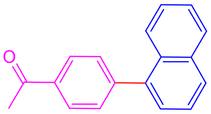
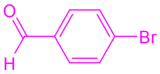
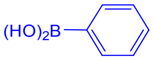
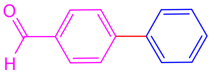
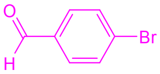
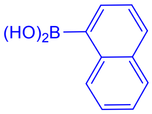
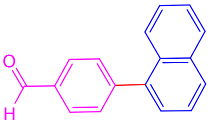
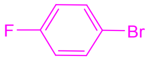
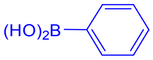
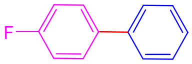
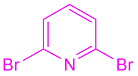
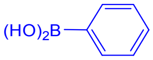
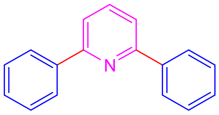
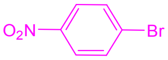
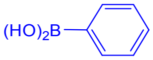
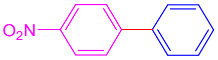
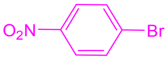
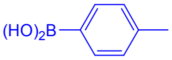
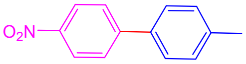
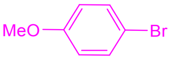
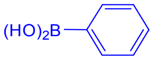
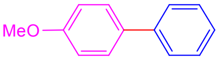
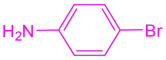
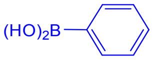
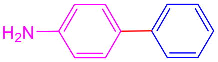
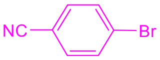
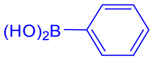
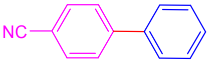
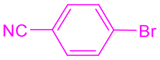
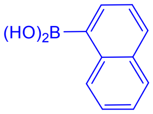
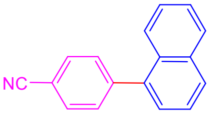
Entry	Pd/C (mol %)	Time (h)	Yield[b] (%)
1	0.25	12	50
2	0.50	10	55
3	0.75	8	65
4	1	4	70
5	1.5	3.5	85
6	2	2	93
7	3	2	93

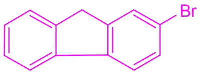
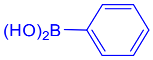
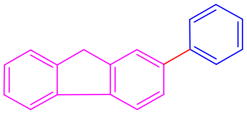
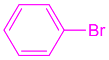
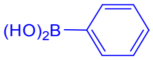
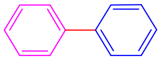
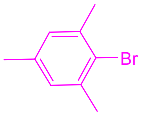
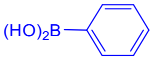
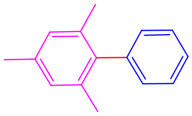
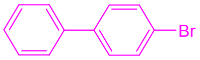
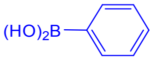
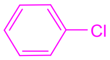
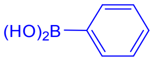
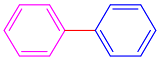
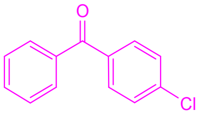
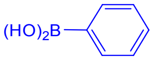
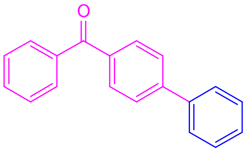
[a]Reaction conditions: 4-bromobenzophenone (1 mmol), phenylboronic acid (1 mmol), Pd/C (mol %), K_2CO_3 (2.0 mmol), 60 % NaXS solution (5.0 mL), at RT. [b]Isolated yields after column chromatography.

Having established the optimized reaction conditions, the scope and generality of the reaction was then explored by using a series of aryl halides and aryl boronic acids. As shown in Table 2, the substrates with different substituents on the benzene ring of aryl halides afforded the desired products in excellent yield. Even the sterically hindered trisubstituted mesitylene (Table 2, entry 19) was obtained (60 % 12h) by our catalyst-hydrotrope mediated Suzuki-Miyaura coupling reaction. However in case of 4-chlorobenzene and 4-chlorobenzophenone, yields obtained were in a range of 20-25% (Table 2, entries 21 and 22).

Table 2 The Suzuki-Miyaura Cross-coupling reaction of various aryl halides with boronic acids[a].

Sr. No.	Aryl Halides	Boronic Acids	Product	Time (h)	Yield[b] (%)
1				2	93
2				3.5	90

3				3	85
4				4	88
5				1.5	88
6				3.5	85
7				2	94
8				3	90
9				1.5	92
10				3.5	89
11				1.5	93
12				2	92
13				3.5	91
14				4	90
15				2	93
16				5.	86

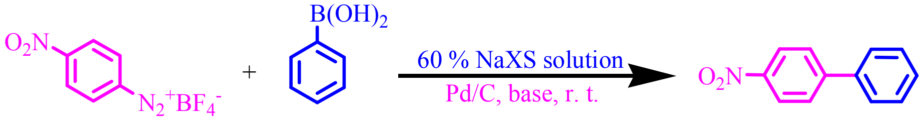
17				7	80
18				2	90
19				12	60
20				12	45
21				12	25
22				12	20

[a]Reaction conditions: aryl halides (1 mmol), arylboronic acids (1 mmol), Pd/C (2 mol %), K_2CO_3 (2.0 mmol), 60 % NaXS solution (5.0 mL), at RT. [b]Isolated yields after column chromatography.

Encouraged by the success of coupling aryl halides with boronic acids for making biphenyls, we then attempted to couple arenediazonium salts with aryl boronic acids. Though, considerable efforts have been exerted on the coupling of aryl halides under Suzuki−Miyaura coupling reactions conditions,[36] two major drawbacks associated with aryl halides are their insolubility in water and competing homocoupling reaction.[37] This can be overcome by using diazonium salts due to their high solubility in water. These can be easily and efficiently prepared from organoamine compounds by diazotization in water.[38]

The optimized reaction conditions were the same for the cross coupling of 4-nitroarendiazonium tertafluoroborate salt with phenylboronic acid as those used for aryl halide substrates (Table 3, entry 1). Here also inorganic base K_2CO_3 was more effective than organic bases (Table 3, entries 3 and 4) and the reaction did not proceed in the absence of a base (Table 3, entry 5). The reaction in aqueous medium at room gave a poor yield of the 4-nitrobiphenyl (Table 3, entry 6[c]).

Table 3 Screening of nature of bases for the Suzuki–Miyaura reaction[a]

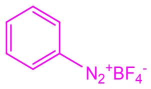
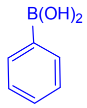
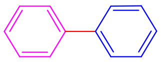
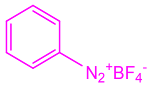
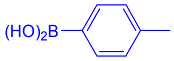
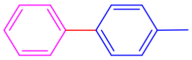
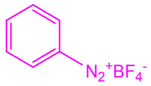
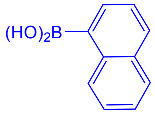
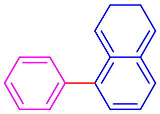


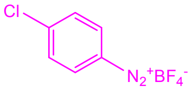
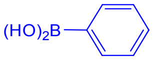
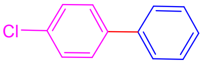
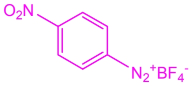
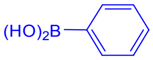
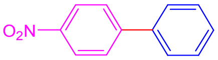
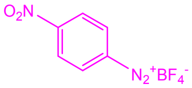
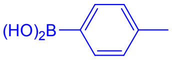
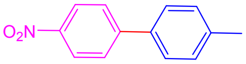
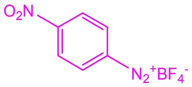
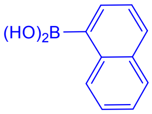
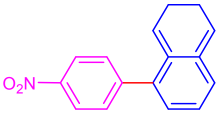
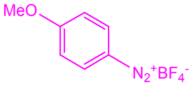
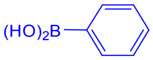
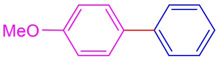
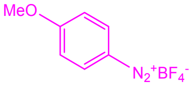
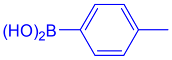
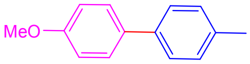
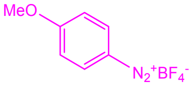
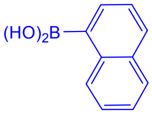
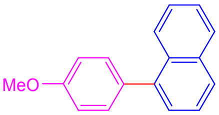
Entry	Base	Time (h)	Yield[b] (%)
1	K_2CO_3	1	90
2	NaOAc	1.5	85
3	Et_3N	2	86
4	Pyridine	1.5	80
5	free	12	15
6[c]	K_2CO_3	12	20

[a]Reaction conditions: 4-nitro-diazonium salt (1 mmol), arylboronic acid (1 mmol), Pd/C (2 mol %), base (2.0 mmol), 60 % NaXS solution (5 mL) at RT. [b]Isolated yields after column chromatography. [c]Reaction carried out in water.

To explore the scope and generality of the catalytic system, a variety of arenediazonium salts and aryl boronic acids were reacted under the optimized protocol and the results are shown in Table 4. Both activated and deactivated arenediazonium salts showed a maximum conversion in a range of 85-94 %. More importantly, it is interesting to that the chemoselectivity could be achieved in these coupling reactions using halogen-based arenediazonium salt with the olefin (Table 4, entry 4).

Table 4 Results on Suzuki-Miyaura Cross-coupling of various arenediazonium salts with boronic acids[a]

Sr. No.	Aryl Halides	Boronic Acids	Product	Time (h)	Yield[b] (%)
1				1	88
2				1.5	85
3				1.5	94

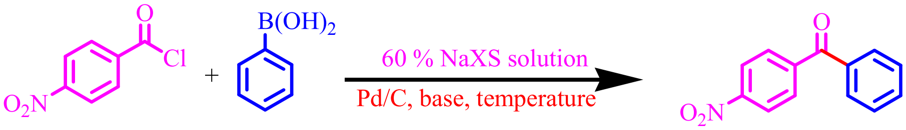
4				2.5	86
5				1	90
6				3.5	87
7				1.5	93
8				2.5	88
9				2	89
10				3	92

[a] Reaction conditions: arenediazonium salts (1 mmol), arylboronic acids (1 mmol), Pd/C (2 mol %), K_2CO_3 (2.0 mmol), 60% NaXS solution (5 mL) at RT. [b] Isolated yields after column chromatography.

Diarylketones exist as a common structural motif in natural products[39] as well biological and pharmaceutically important compounds.[40] The well-known method for synthesis of such compounds is the Friedel-Crafts acylation[41] having several inherent limitations. Recently, Pd catalyzed cross-coupling reactions of various electrophilic acid derivatives of carboxylic acids such as acid chlorides, acid esters, acid anhydrides and dimethyl dicarbonates with organoboranes have been reported.[42] These are also prepared by the cross-coupling reaction of aryl halides involving carbonylation with carbon monoxide in the presence of organometallic reagents.[43] Both these reactions have emerged as new catalytic tools for the synthesis of such important compounds. Herein, we report a much simpler synthesis of prochiral ketones under mild conditions without using CO, by Pd catalyzed ligand-free, Suzuki-Miyaura cross-coupling reactions of acid chlorides with organoboranes in water.

A model reaction of 4-nitrobenzoyl chloride (1 mmol) and phenylboronic acid (1 mmol) was studied under different reaction conditions and the results are shown in Table 5. Among the various bases screened, K_2CO_3 showed the excellent activity with 88 % yield at 60 °C (Table 5, entry 8). It was observed that with increasing temperature from 25 to 60 °C, the product yield significantly increased from 10 to 88% as well as the reaction time decreased significantly from 12 to 2 (Table 5, entries 5-8). When water used as the solvent the conversion was as low as 15% even after 12 h and at 60 °C (Table 5, entry 10).

Table 5 Optimization of reaction conditions for Suzuki-Miyaura cross-coupling of acid chlorides[a]

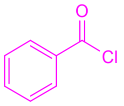
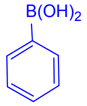
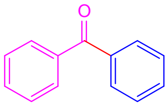


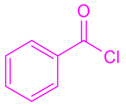
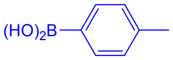
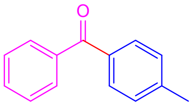
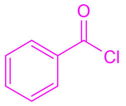
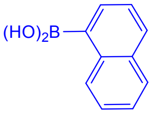
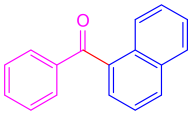
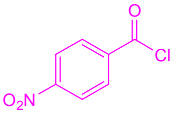
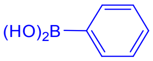
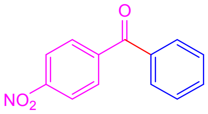
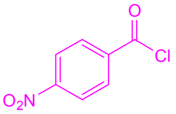
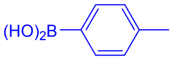
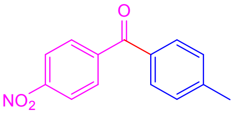
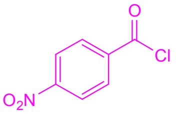
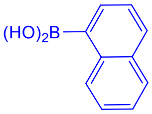
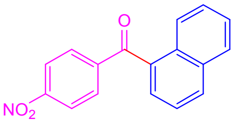
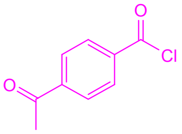
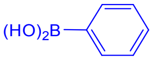
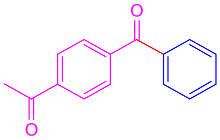
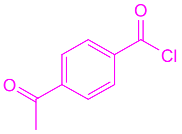
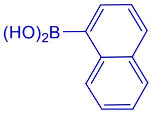
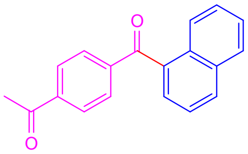
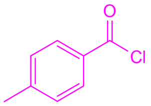
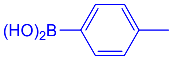
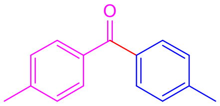
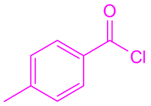
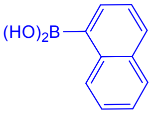
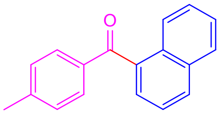
Entry	Base	Temperature (°C)	Time (h)	Yield[b] (%)
1	NaOAc	60	2.5	85
2	Et_3N	60	3.5	82
3	pyridine	60	3.5	78
4	base free	60	12	15
5	K_2CO_3	25	12	10
6	K_2CO_3	40	6	70
7	K_2CO_3	50	3.5	80
8	K_2CO_3	60	2	88
9	K_2CO_3	70	2	89
10[c]	K_2CO_3	60	12	15

[a]Reaction conditions: 4-nitrobenzoyl chloride (1 mmol), phenylboronic acid (1 mmol), Pd/C (2 mol %), base (2 mmol), 60 % NaXS solution (5 mL). [b]Isolated yields after column chromatography. [c]Reaction is carried out in water.

The generality and scope of this approach was proved by the successful coupling of various benzoyl chloride with aryl boronic acid substrates, using K_2CO_3 as a base at 60 °C and the results are summarized in Table 6. A wide range of prochiral ketones were obtained with excellent yields.

Table 6 The Suzuki-Miyaura Cross-coupling reaction of various acyl chlorides with boronic acids[a]

Sr. No.	Aryl Halides	Boronic Acids	Product	Time (h)	Yield[b] (%)
1				1.5	85

2				2	90
3				2.5	84
4				2	88
5				3	85
6				4	82
7				4	85
8				5	84
9				3.5	88
10				4.5	87

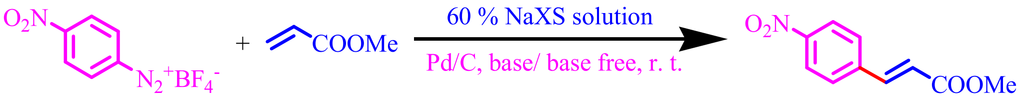
[a] Reaction conditions: acyl chlorides (1 mmol), arylboronic acids (1 mmol), Pd/C (2 mol %), K_2CO_3 (2 mmol), 60 % NaXS solution (5 mL) at 60 °C. [b] Isolated yields after column chromatography.

Ligand and base free Heck-Matsuda cross-coupling reaction of arenediazonium salts

We also extended the applicability of Pd/C combined with hydrotrope catalytic system for the Heck-Matsuda cross-coupling reaction involving arenediazonium tetrafluoroborate salts as excellent aryl electrophilic component.[38,44] The major advantage of the arenediazonium salt is that it undergoes easy oxidative addition during the mechanistic cycle to generate active cationic aryl-Pd (II) intermediate which increases the rate of the reaction.[45]

Initially, we screened various bases such as K_2CO_3, NaOAc, Et_3N and pyridine for the model reaction of 4-nitrodiazonium tetrafluoroborate with methyl acrylate in 60 % NaXS at room temperature. To our surprise, an excellent yield (93%) of the product was obtained under base-free condition in a comparatively very less reaction time of only 1 h (Table 7, entry 5). However, in water medium, (in absence of a hydrotrope) very low conversion of only 25% was observed (Table 7, entry 6).

Table 7 Effect of bases for Heck-Matsuda cross-coupling reaction[a]

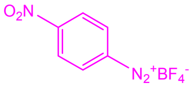
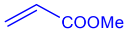
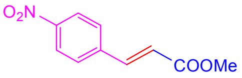
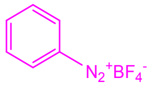
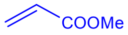
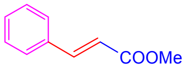
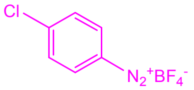
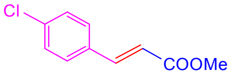
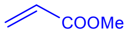
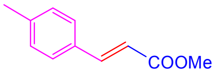
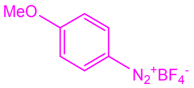
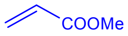
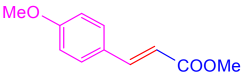
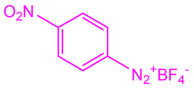
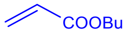
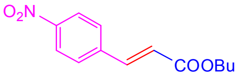
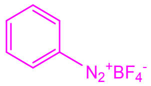
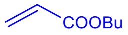
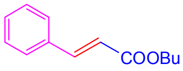
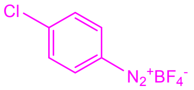
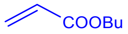
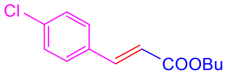
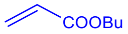
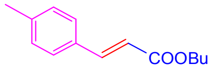
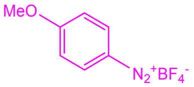
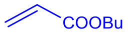
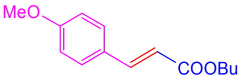
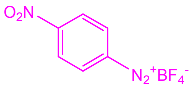
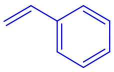
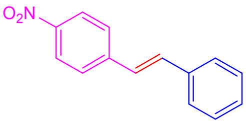
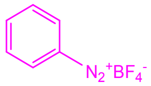
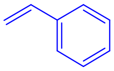
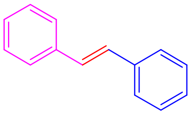


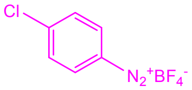
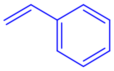
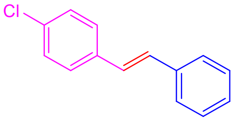
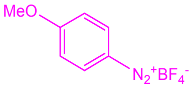
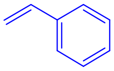
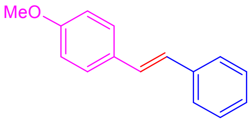
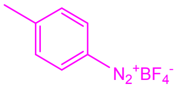
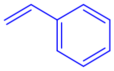
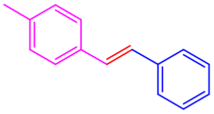
Entry	Base	Time (h)	Yield[b] (%)
1	K_2CO_3	5	65
2	NaOAc	6	68
3	Et_3N	4	40
4	Pyridine	8	60
5	base free	1	93
6[c]	base free	12	25

[a]Reaction conditions: 4-nitro-arenediazonium salt (1 mmol), methyl acrylate (1 mmol), Pd/C (2 mol %), base (2 mmol), 60 % NaXS solution (5 mL), at RT. [b]Isolated yields after column chromatography. [c]Reaction is carried out in water.

The synthesis of a variety of substituted acrylates could be successfully accomplished by reacting a range of olefins and arenediazonium salts. As can be seen from Table 8, various substrates with electron-rich or electron-poor functional groups could react smoothly with olefins to give the desired arylate products in good to excellent yields. It was found that the ratio of *E/Z* isomers was dramatically affected by the nature of substituent present on arenediazonium salt. *E*- and *Z*-isomers were confirmed by *J* coupling values of ^1H NMR spectra. The compounds containing electron withdrawing groups showed > 90 % *E*-isomers, but 4-chloroarenediazonium salt gave 100 % *E*-isomer formation (Table 8, entries 3, 8, and 13) while electron donating groups gave predominantly *Z*-isomers to the extent of 80-85%. Unfortunately, 4-methylarenediazonium salt gave 53:47 (*E/Z)* isomer ratio (Table 8, entry 4). Methyl acrylate reacted with different arenediazonium salts to give the corresponding product in 84-93 % yields. More bulky butyl acrylate showed a good activity to give 81-90 % yield with various diazonium salts. Different stilbene derivatives obtained were in comparatively lower yields of 58-80 % due to their steric hindrance (Table 8, entries 11-14).

Table 8 Results on Heck-Matsuda Cross-coupling of various arenediazonium salts with olefins[a]

Sr. No.	Aryl Halides	Boronic Acids	Product	Time (h)	Yield[b] (%) (E/Z ratio)
1				1	93 (92:08)
2				1	90 (100:00)
3				2	91 (100:00)
4				2.5	88 (53:47)
5				1	90 (100:00)
6				1.5	90 (95:05)
7				1	89 (100:00)
8				3	91 (100:00)
9				3	92 (55:45)
10				1.5	90 (82:18)
11				6	65 (81:19)
12				6	80 (91:09)

13				6	58 (96:04)
14				6	62 (94:06)
15				6	67 (65:35)

[a]Reaction conditions: arenediazonium salts (1 mmol), olefins (1 mmol), Pd/C (2 mol %), 60 % NaXS solution (5 mL), at RT. [b]Isolated yields after column chromatography.

Heterogeneity of Pd/C catalyst

It is obligatory to study the catalyst stability in terms of leaching of Pd from the solid support.[46] The leaching of Pd from the carbon was inveterate by carrying out an analysis of the desired product mixture of model reaction with The ICP–AES analysis of the reaction crude of Suzuki-Miyaura cross-coupling reaction, after separating the catalyst by filtration, showed that palladium metal was not leached out (< detection limit of 1ppm) as reported by Felpin *et al*[47]and Sajiki *et al.*[48] This result strongly supports that the Pd/C is characteristic heterogeneous in nature.

Possible mechanism

A generalized possible mechanism of C-C bond formation reactions in presence of an hydrotrope is shown in Fig. 8. The low solubility of organic reactants in water can often be overcome by using hydrotropes though amphiphilic in character, have hydrophobic chains and thus differ from classical surfactants; yet they display substantial ability to solubilize, non-polar compounds in water. In an aqueous medium, the water molecules hydrate the amphiphilic head groups of the hydrotrope decreasing the electrostatic interaction between these groups.[23] This makes the head groups to move apart creating the driving force for two hydrophobic chains to interact and facilitate aryl halide to bind with Pd/C in the oxidative addition step forming a Pd(II) intermediate complex. In the next step R-Pd-X undergoes transmetalation reaction with carbon nucleophile to form R-Pd$^{(II)}$-R' in presence of a base. The resultant complex undergoes reductive elimination to form coupling product with the regeneration of Pd (0) which participates in the next catalytic cycle.[6a]

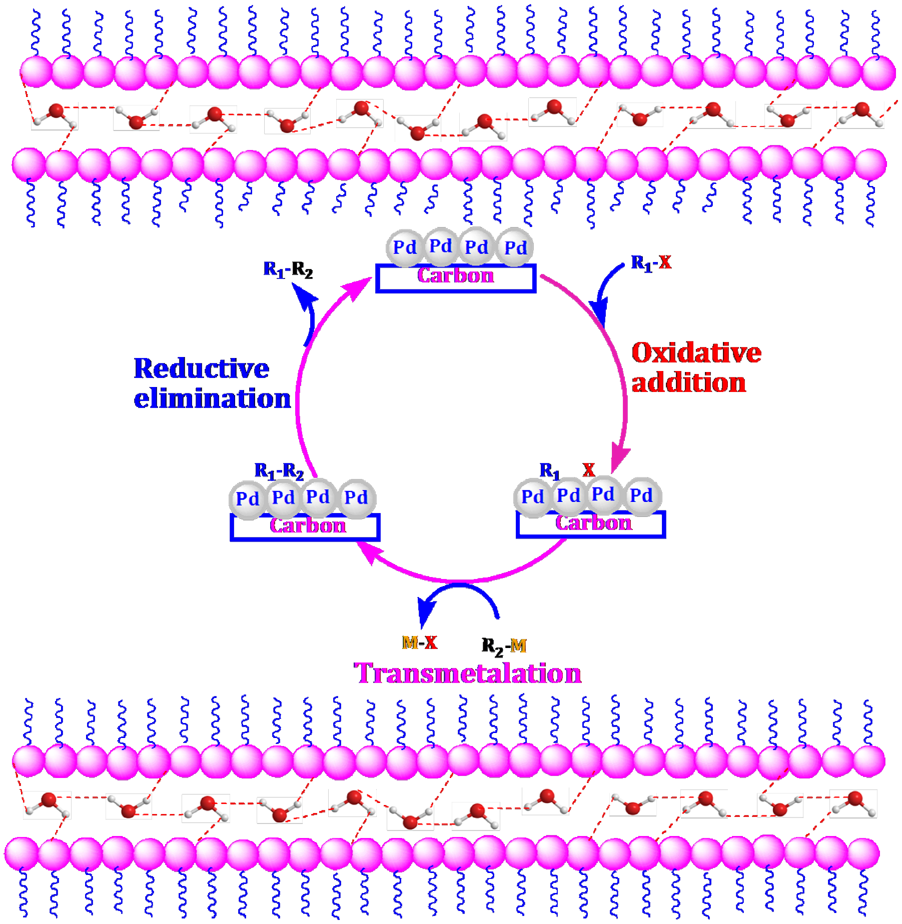


Fig. 8 Plausible mechanism of the C-C bond forming reactions in the presence of an Hydrotrope

Very importantly, the product precipitates on dilution with water from hydrotropic solution, which leads to the product formation in a crystalline form with an improved purity, and the mother liquor can be used to concentrate the hydrotrope for recycling.

Separation of catalyst

For any catalytic process, recovery and re-utilization of the catalyst is a very important aspect for sustainability for possible application on an industrial scale. The recyclability of Pd/C catalyst in the present work was investigated as follows. After the fresh catalytic cycle, the catalyst was recovered by simple filtration and was washed with water, DCM, and acetone and dried under vacuum. The recovered Pd/C catalyst was then used for next catalytic cycle (Fig. 9).

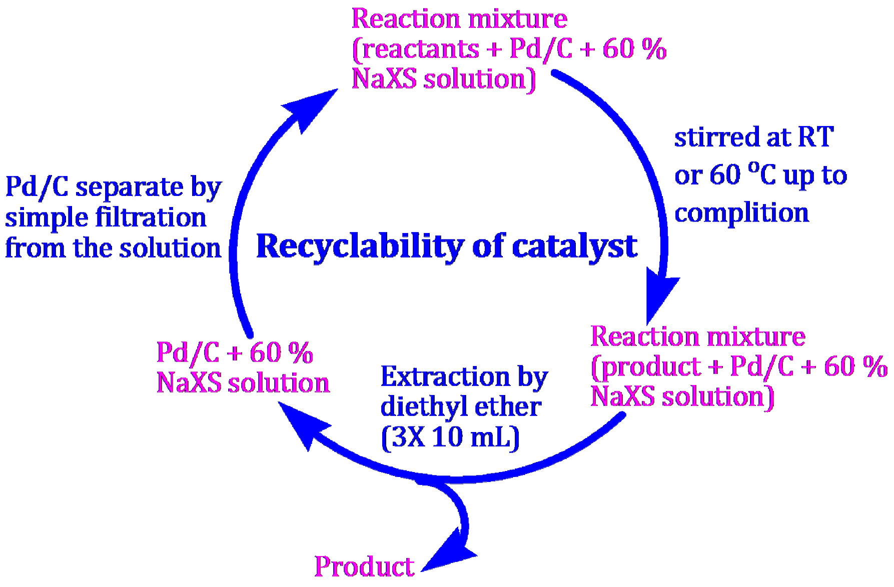


Fig. 9 Procedure for recyclability of Pd/C catalyst

The recycling results of Pd/C for model reactions of Suzuki-Miyaura and Heck-Matsuda cross-coupling were summarized in Fig. 10. The catalyst was recycled three times with no appreciable change in product yield at same reaction time of model reaction. These results revealed that the catalyst is stable and can be renewed for frequent use.

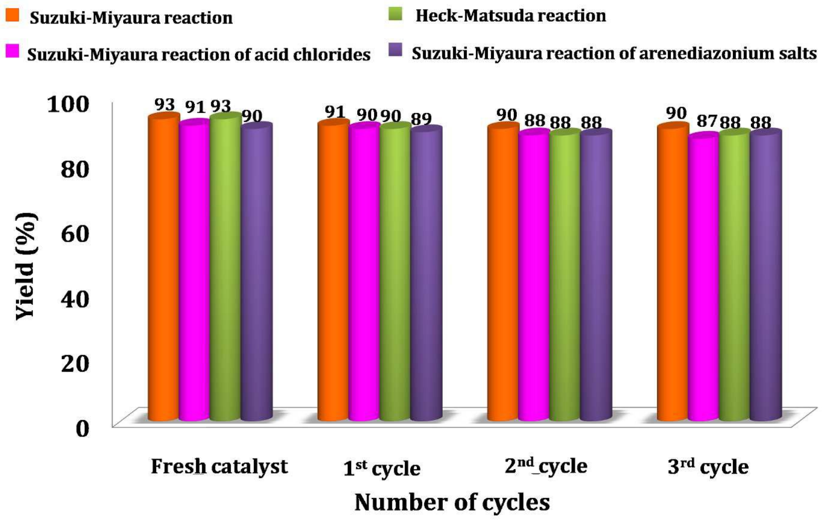


Fig. 10 Recyclability study of Pd/C

Conclusion

In this work, we developed a very simple route for the synthesis of diversely functionalized biphenyls, acrylates and prochiral ketones by ligand-free Suzuki-Miyaura and base-free Heck-Matsuda cross-coupling reactions using Pd/C catalyst combined with hydrotrope in an aqueous medium under atmospheric conditions. Initially, we used Suzuki-Miyaura cross-coupling reaction as model reaction for screening of various reaction conditions and then optimized reaction conditions are extended for the synthesis of biaryls (at room temperature), prochiral ketones (at 60 °C) and acrylates (at room temperature). This experimental method offers promising green development in terms of reaction time, wide scope of applicability, mild reaction conditions, good to excellent yields of desired product and operational simplicity. To best of our knowledge use hydrotrope as inexpensive, easily available, green reaction medium and Pd/C as reusable catalyst for C-C bond forming reaction. Further study is continued in our laboratory to investigate the mechanistic pathway of hydrotrope mediated C-C coupling reactions.

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Notes and references

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- **Supporting information**. ^{1}H and ^{13}C NMR spectra of our compounds.

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Ligand-free Pd Catalyzed Cross-coupling Reactions in Aqueous Hydrotropic Medium

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Graphical Abstract