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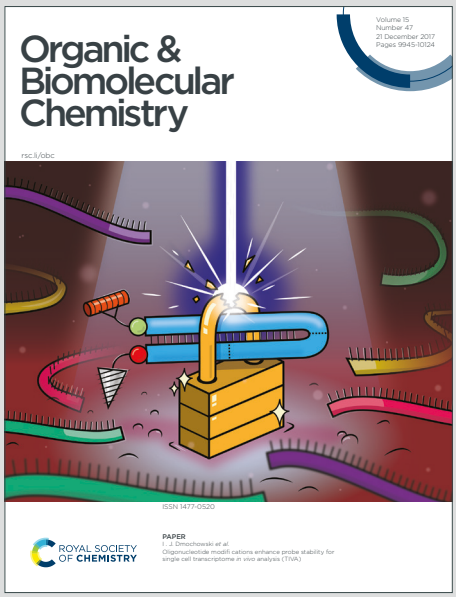

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ARTICLE

Supported palladium catalyzed aminocarbonylation of aryl iodides employing bench-stable CO and NH_3 surrogates

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A simple, efficient and phosphine free protocol for carbonylative synthesis of primary aromatic amides under polystyrene supported palladium (Pd@PS) nanoparticles (NPs) catalyzed conditions has been demonstrated. Herein, instead of using two toxic and difficult to handle gases simultaneously, we have employed solid, economic, bench stable oxalic acid as CO source and ammonium carbamate as NH_3 source in a single pot reaction. For the first time, we have applied two non-gaseous surrogates simultaneously under heterogeneous catalyst (Pd@PS) conditions for synthesis of primary amides using easy to handle Double-Vial (DV) system. The developed strategy displayed wide range of functional group tolerance of aryl iodides and delivered good yields of primary aromatic amides. The Pd@PS catalyst was found to be easy to separate and can be recycled up to four consecutive run with small loss in catalytic activity. We have successfully extended the scope of the methodology for the synthesis of isoindole-1,3-diones from 1,2-dihalobenzene, 2-halobenzoates and 2-halobenzoic acid following double and single carbonylative cyclization approaches.

Introduction

Over the years, amide functionality has gained a key importance in pharmaceutical industry due to its wide occurrence in plethora of biologically active potent molecules.[1] Owing to their diverse importance, various protocols have been developed till now for synthesis of amide moieties.[2] In this context, carbonylation chemistry offers a straightforward technique for accessing amides using amines as nucleophiles in presence of carbon monoxide (CO) as an indispensable C1 source. Although, carbonylation chemistry is very well explored for synthesis of secondary and tertiary amides,[3] however, in case of primary amides this methodology is still a formidable challenge. The poor nucleophilicity and difficulty in handling of ammonia gas could possibly explain the could possibly explain the challenges associated with synthesis of primary amides through carbonylation reaction. Furthermore, development of recyclable catalytic system and environmental benign protocol is highly desirable for the synthesis of primary amides to overcome the deficiencies associated with homogeneous catalytic system such as non-recyclable catalyst, difficulty in product separation, air/moisture sensitive phosphine ligands etc. The direct utilization of two gases explicitly, CO and NH_3 further add to complexity to the reaction protocol. Hence, utilization of bench stable and sustainable CO and NH_3 sources could eradicate the problem associated with direct use of two gases in a single vessel.

Moreover, phthalimides or isoindoline-1,3-dione derivatives are important class of pharmaceutically active molecules.[4] Although, there are various reports of N-substituted phthalimides synthesis via double carbonylation under heterogeneous conditions.[5] However, to the best of our knowledge, unsubstituted phthalimides synthesis using ammonia or ammonia surrogate through similar protocol is still underexplored.

After the initial work been carried out by Beller and co-workers,[6] chemists have employed several ammonia sources in palladium catalyzed carbonylations such as HMDS,[7] formamides,[8] N-tert butyl amine[9] titanium nitrogen complex,[10] NH_4Cl,[1a] ammonium carbamate[11] and aq. NH_3,[12] to get rid of ammonia gas. But, use of flammable HMDS, high reaction temperature, multistep reaction procedure, non-recyclable catalytic system, use of bulky and air/ moisture sensitive phosphine ligands and high pressure of CO gas were the major limiting factor of aforementioned protocols for general laboratory practices. In this regard, Bhanage and co-workers has contributed significantly to this field.[13] To circumvent the issues of recyclability of costly catalyst, they developed Pd/C catalyzed protocol for synthesis of primary amides using ammonium carbamate as ammonia source.[14] However, limitations of this protocol such as low substrate scope, high catalyst loading and high CO pressure, encouraged us to work in this direction for its further sustainable development. Moreover, to avoid the use of toxic CO gas, the work of Skrydstrup and co-workers is worth mentioning where they synthesized primary amides in presence of homogeneous palladium/ligand catalyst and 9-fluorenylcarbonyl chloride as ex situ CO source.[15] However, implementation

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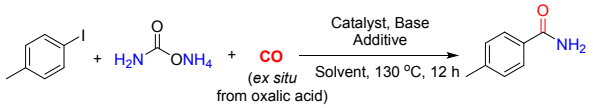
of sophisticated apparatus, expensive phosphine ligands, and requirement of additives for decomposition of CO source were the major challenges associated with this methodology. Alternatively, expensive metal carbonyls in combination with ammonia sources have also been employed for palladium catalyzed aminocarbonylation such as $Mo(CO)_6$ and hydroxylamine,[16] and $Co_2(CO)_8$ in combination with NH_4Cl for the synthesis of primary amides.[17] Recently, Liu *et al.* demonstrated ligand bite angle dependent $PdCl_2(CH_3CN)_2$/Xanthphos catalyzed synthesis of primary amides where NH_4HCO_3 played dual role of base and ammonia source.[18] Furthermore, NH_4HCO_3 as ammonia source and formic acid as CO source have been utilized by Wu and co-workers for synthesis of primary aromatic amides under homogeneous and non-recyclable $Pd(OAc)_2/PPh_3$ catalyzed conditions.[19]

In continuation of previous advancements of our group in the field of polystyrene supported transition metal NPs as catalyst and its application in carbonylation reactions using oxalic acid as C1 source.[20] Herein, we have developed a phosphine free, Pd@PS catalyzed aminocarbonylation of aryl halides utilizing bench stable and sustainable ammonium carbamate as ammonia source and oxalic acid as CO surrogate. We prepared Pd@PS nano-catalyst according to our previously established protocol through reduction deposition technique. First time, we have applied this combination for vast primary amides synthesis using an easy to handle double-vial (DV) single screw cap system. The same strategy was also successfully extended to rarely followed isoindoline-1,3-diones or phthalimides synthesis.

Results and discussion

Under this development, we have employed a double-vial (DV) system to carry out the aminocarbonylation of aryl iodides which contains an inner vial and an outer vial sealed with PTFE faced cap. We began our study with 4-iodotoluene (1equiv.), ammonium carbamate as ammonia source (4 equiv.) and K_2CO_3 (2 equiv.) in DMF (inner vial) and oxalic acid in DMF (outer vial) as ex situ CO source. Unfortunately, we have not succeeded for the synthesis of aminocarbonylated product **3a**. Instead, we got 4-methyl benzoic acid as major product under applied reaction conditions (Table 1, entry 1). However, the use of organic base i.e., NEt_3 (2 equiv.) didn't procure the desired product **3a** (Table 1, entry 2). To our dismay, with increasing the catalyst loading we have not noticed the desired product formation (Table 1, entry 3). Furthermore, we have also checked the reactions conditions using DABCO (2 equiv.) as base and KI (1 equiv.) as additive. But, these reaction conditions found to be unable to give the desired product (Table 1, entry 4). This may be attributed to the poor nucleophilicity of ammonia that restrict its nucleophilic addition during the course of the reaction cycle. Hence, additives are required that can form active palladium acyl intermediates to promote aminocarbonylation of ammonia under heterogeneous reaction conditions.[21] Keeping this point in view, we used DMAP (1 equiv.) as an additive to get desired product **3a**. Fortunately, addition of DMAP resulted in the 32% yield of 4-methylbenzamide (**3a**) (Table 1, entry 5). This observation led us to investigate the more additives that could help in aminocarbonylation of aryl halides. According to literature survey, it was found that DMAP and imidazole are known to be powerful Lewis bases and acylating agents as well.[21,17] Delightfully, we got 45% yield of **3a** on utilizing 0.50 equiv. of imidazole (Table 1, entry 6) under our reaction conditions. On increasing the catalyst loading from 2 to 3 mol% Pd in Pd@PS, the aminocarbonylated product **3a** was formed in 57% yield (Table 1, entry 7). Furthermore, on increasing the equivalency of imidazole to 0.75 equiv., resulted in 72% yield, while more increment in imidazole quantity led to unidentified side products, thus lowering in yield of the product (Table 1, entries 8 and 9). No reaction was observed in absence of Pd@PS which clearly reflected the role of the catalyst (Table 1, entry 10). On altering the equivalency of base from 2 to 2.5, the yield of 4-methylbenzamide (**3a**) increased to 75%, while no product was detected in absence of base (Table 1, entry 11-12).

Table 1. Optimization of reaction conditions



1a **2** **3a**

S.No.	Catalyst (mol%)	Base (equiv.)	Additive (equiv.)	Solvent	Yield (%)[a]
1	Pd@PS (2)	K_2CO_3 (2)	-	DMF	nd
2	Pd@PS (2)	NEt_3 (2)	-	DMF	nd
3	Pd@PS (3)	NEt_3 (2)	-	DMF	nd
4	Pd@PS (2)	DABCO (2)	KI (1)	DMF	nd
5	Pd@PS (2)	NEt_3 (2)	DMAP (1)	DMF	32
6	Pd@PS (2)	NEt_3 (2)	Imidazole (0.50)	DMF	45
7	Pd@PS (3)	NEt_3 (2)	Imidazole (0.50)	DMF	57
8	Pd@PS (3)	NEt_3 (2)	Imidazole (0.75)	DMF	72
9	Pd@PS (3)	NEt_3 (2)	Imidazole (1)	DMF	65
10	-	NEt_3 (2)	Imidazole (0.75)	DMF	nr
11	**Pd@PS (3)**	**NEt_3 (2.5)**	**Imidazole (0.75)**	**DMF**	**75**
12	Pd@PS (3)	-	Imidazole (1)	DMF	nd
13	Pd@PS (3)	K_2CO_3 (2.5)	Imidazole (0.75)	DMF	nd
14	Pd@PS (3)	Cs_2CO_3 (2.5)	Imidazole (0.75)	DMF	Traces
15	Pd@PS (3)	K^{t}OBu (2.5)	Imidazole (0.75)	DMF	26
16	Pd@PS (3)	DBU (2.5)	Imidazole (0.75)	DMF	nd
17	Pd@PS (3)	DiPEA	Imidazole (0.75)	DMF	45
18	Pd@PS (3)	NEt_3 (2.5)	Imidazole (0.75)	DMA	62
19	Pd@PS (3)	NEt_3 (2.5)	Imidazole (0.75)	NMP	30
20	Pd@PS (3)	NEt_3 (2.5)	Imidazole (0.75)	Xylene	Traces
21	Pd@PS (3)	NEt_3 (2.5)	Imidazole (0.75)	Anisole	Traces
22	Pd@PS (3)	NEt_3 (2.5)	Imidazole (0.75)	PEG-400	nd
23[b]	Pd@PS (3)	NEt_3 (2.5)	Imidazole (0.75)	DMF	29
24[c]	Pd/C (3)	NEt_3 (2.5)	Imidazole (0.75)	DMF	45
25[d]	$Pd(OAc)_2$ (3)	NEt_3 (2.5)	Imidazole (0.75)	DMF	54

Reaction conditions: aryl iodides (1equiv.), ammonium carbamate (4 equiv.), Pd@PS (0.03 equiv.) Imidazole (0.75 equiv.), NEt_3 (2.5 equiv.), DMF (2 mL) in inner vial; CO surrogate in solvent (0.2 mL) in outer vial stirred at 130 °C for 12 h. (a) isolated yield, (b) reaction temperature 120 °C, (c) 5 wt% of Pd/C (d) PPh_3 (6 mol%)

Encouraged by these results, we also scrutinized different organic and inorganic bases such as K_2CO_3, Cs_2CO_3, KO^{t}Bu, DBU and DIPEA to get good yield of the desired product **3a** (Table 1, entries 13-17). Among these, NEt_3 base was found to be the most suitable base for aminocarbonylation of aryl iodides and

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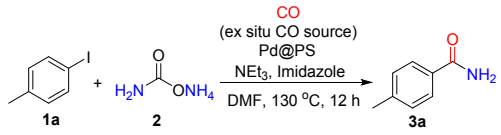
ammonium carbamate. In addition, we have also tested different polar and non-polar solvents, and DMF was found to be best (Table 1, entries 18-22). Furthermore, we have also checked the reaction at 120 °C and lower yield of aminocarbonylated product i.e., 29% was obtained (Table 1, entry 23). This could be due to partial decomposition of oxalic acid at this temperature. Intriguingly, we also screened other catalysts under optimized reaction conditions. But, none of the catalyst was found to be as effective as Pd@PS nanocatalyst (Table 1, entries 24-25). Hence, aryl iodide (1 equiv.), ammonium carbamate (4 equiv.), Pd@PS (0.03 equiv. Pd), NEt_3 (2.5 equiv.) in DMF (2 mL) (inner vial) and oxalic acid (6 equiv.) in 0.3 mL DMF (outer vial) was the best optimized reaction conditions for aminocarbonylation of aryl iodides.

Furthermore, we have also checked different CO sources, equivalency of CO surrogate, solvents, and compatibility of various other CO surrogates under optimized reaction conditions, results summarized in Table 2. When we decreased the equivalency of CO surrogate to 4 equiv. the desired product **3a** was found in 40% yield (Table 2, entry 1). It was found that 6 equiv. of oxalic acid in DMF was suitable for aminocarbonylation of aryl iodides (Table 2, entry 2). Further, we

Table 2. Screening of ammonia sources



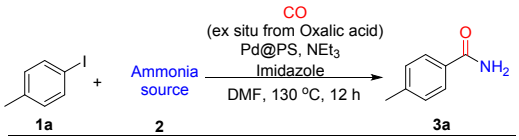
S.No.	CO surrogate (equiv.)	External solvent	Yield %[a]
1	$(COOH)_2$ (4)	DMF	40
2	$(COOH)_2$ (6)	DMF	75
3	$(COOH)_2$ (6)	DMA	55
4	$(COOH)_2$ (6)	NMP	30
5	$(COOH)_2$ (6)	Toluene	Traces
6	-	DMF	nd
7	N-formyl saccharin (6)	DMF	74
8	Formic acid (6)	DMF	Traces
9	Paraformaldehyde (6)	DMF	Traces

Reaction conditions: aryl iodides (1equiv.), ammonium carbamate (4 equiv.), Pd@PS (0.03 equiv.) Imidazole (0.75 equiv.), NEt_3 (2.5 equiv.), DMF (2 mL) in inner vial; CO surrogate in solvent (0.2 mL) in outer vial stirred at 130 °C for 12 h. (a) Isolated yield

have investigated combination of various solvents with oxalic acid such as DMA, NMP and toluene (Table 2, entries 3-5). In similar lines with our previous reports, oxalic acid in DMF was found to be suitable combination for aminocarbonylation. We havn't observed amniocarbonylated product in absence of oxalic (Table 2, entry 6). The other CO surrogates were also tested under given reaction conditions such as N-formyl saccharin, formic acid and paraformaldehyde (Table 2, entries 7-9). To our surprise, 6 equiv. of N-formyl saccharin in DMF was found to be equally compatible for aminocarbonylation under developed reaction conditions and gave **3a** in 74% yield. However, being economic, easy availability and low waste generation, we opted for oxalic acid as CO source for this transformation.

After the screening of CO sources, thereafter, we shifted our focus towards screening of ammonia surrogates such as NH_4HCO_3, $(NH_4)_2CO_3$, NH_4Cl, NH_4OAc, $HCOONH_4$ and aq. NH_3 for the standard reaction under optimized reaction conditions as shown in Table 3. We found that NH_4HCO_3 and $(NH_4)_2CO_3$ gave the product **3a** in 50 and 40% yield respectively, while aminocarbonylated product was not detected in case of NH_4Cl and $HCOONH_4$ (Table 3, entries 1-4). In case of ammonium acetate as ammonia surrogate the final product **3a** obtained in 20% yield (Table 3, entry 5). Furthermore, on utilizing aqueous

Table 3. Optimization of NH_3 sources



S.No.	Ammonia surrogate (equiv.)	Yield(%)[a]
1	NH_4HCO_3 (4)	50
2	$(NH_4)_2CO_3$ (4)	40
3	NH_4Cl (4)	Traces
4	$HCOONH_4$ (4)	Traces
5	CH_3COONH_4 (4)	20
6	Aq. NH_3	30
7	NH_2COONH_4 (3)	53
8	NH_2COONH_4 (4)	75

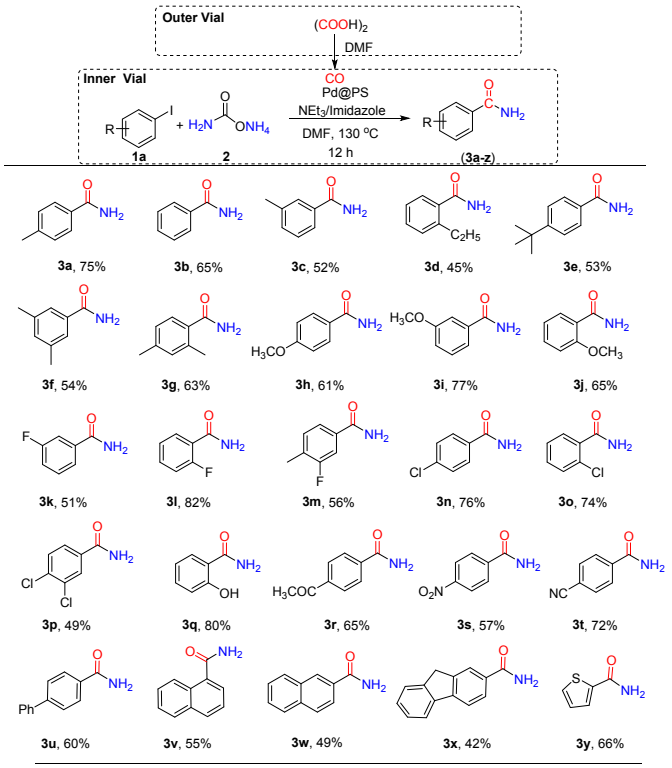
Reaction conditions: aryl iodides (1equiv.), ammonium sources (4 equiv.), Pd@PS (0.03 equiv.) Imidazole (0.75 equiv.), NEt_3 (2.5 equiv.), DMF (2 mL) in inner vial; CO surrogate in solvent (0.3 mL) in outer vial stirred at 130 °C for 12 h. (a) Isolated yield

ammonia as ammonia source we got 30% of product **3a**, in addition to 4-methylbenzoic acid and 4,4'-dimethyl-1,1'-biphenyl as side products (Table 3, entry 6). Among all these, ammonium carbamate was found to be best for aminocarbonylation of aryl iodides. Next, we also studied the loading of ammonia surrogate and 4 eq. of ammonium carbamate found to be optimum to deliver 75% yield of the product.

With the suitable reaction conditions in hand, we endeavoured to explore the transformation of different aryl iodides to corresponding primary amides. We have scrutinized wide array of aryl iodides for aminocarbonylation, results summarized in Table 4. During the course of the reaction, it was found that electronic and steric effect of differently substituted aryl iodides influenced the reaction dramatically. Firstly, the carbonylation of iodobenzene afforded the benzamide (**3b**) in 65% yield. Aryl iodides bearing electron donating groups such as 3-me, 2-ethyl, 4-tert butyl, 1,5-dimethyl and 1,4-dimethyl substituents resulted in moderate to good yields of the corresponding amides (Table 4, **3c-g**). In contrast, methoxy group at para-, meta- and ortho- positions successfully delivered the aminocarbonylated products (**3h-j**) in 61-77% yields. Further, we have checked the halogen substituted aryl iodides for aminocarbonylation. In case of fluoro substituted aryl iodides, the reaction of 4-fluoroiodobenzene was found to be sluggish to deliver the desired product, whereas, 3- and 2-fluoro

substituted iodobenzene delivered the desired products (**3k** and

Table 4. Substrate scope for synthesis of primary amides

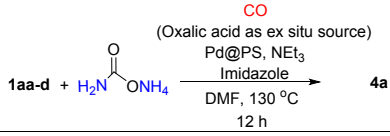


[a] Reaction conditions: aryl iodides (1equiv.), ammonium carbamate (4 equiv.), Pd@PS (0.03 equiv. of Pd), imidazole (0.75 equiv.), NEt_3 (2.5 equiv.), DMF (2 mL) in inner vial; Oxalic acid (6 equiv.) in DMF (0.2 mL) in outer vial stirred at 130 °C for 12 h

3l) in 51 and 82% yields respectively. Intriguingly, 3-fluoro-4-methyliodobenzene also obtained the substituted benzamide **3m** in moderate yield 56%. Encouraged by these results, 4-Cl, 2-Cl, 3,4- dichloro were also attempted and gave comparably good yields of the corresponding products (**3n-p**), while in case of 3-Cl aryl iodide, the aminocarbonylated product was formed in traces. Unfortunately, the reaction of 4-NH_2 and 4-OH substituted analogues were found to be unreactive under the optimized reaction conditions. Whereas, in case of 2-iodoaniline, we got N, N-diphenyl urea (ESI, **3a'**) as major product. To our surprise, we got 80% yield of product **3q** when 2-OH substituted aryl iodide was subjected for aminocarbonylation. To our delight, aminocarbonylations of the electron withdrawing groups i.e., 4-$COCH_3$, 4-NO_2, 4-CN and 4-Ph performed smoothly to obtain desired amides **3r-u** in good yields i.e., 57-72%. Prompted by above results, 1-iodonapthalene, 2-iodonapthalene and 2-iodofluorene were also attempted to get aminocarbonylated products **3v-x** in moderate yields. Moreover, we also subjected heterocyclic aryl iodides and obtained desired amide (**3y**) in 66% yield in case of 2-iodothiophene.

Further to explore the scope of aryl iodide, we have also subjected 1,2-diiodo-benzene (**1aa**) and 1-bromo-2-iodobenzene (**1ab**) for aminocaronylation under optimized reactions. Intriguingly, we got isoindoline-1,3-dione (**4a**) via tandem double carbonylation of o-dihalobenzenes and cyclization resulted in 90 and 60% yield respectively (Table 5,

Table 5. synthesis of isoindoline-1,3-dione



S.No.	Substrate	Product	Yield(%)
1	1aa	4a	90
2	1ab	4a	60
3	1ac	4a	82
4	1ad	4a	75

[a] Reaction conditions: aryl iodides (1 equiv.), ammonium carbamate (4 equiv.), Pd@PS (0.03 equiv. of Pd), imidazole (0.75 equiv.), NEt_3 (2.5 equiv.), DMF (2 mL) in inner vial; oxalic acid (6 equiv.) in DMF (0.2 mL) in outer vial stirred at 130 °C for 12 h.

entries 1 and 2). Furthermore, we have also attempted methyl-2-iodobenzoate (**1ac**) and 2-iodobenzoic acid (**1ad**) as substrates for aminocarbonylation and obtained **4a** in 82 and 75% yields (Table 5, entries 3 and 4) through carbonylative cyclization.

After completion of the reaction, the mixture was quenched with water and then the organic layer was extracted using ethyl acetate as extracting solvent. Further, the Pd@PS catalyst was filtered from the reaction mixture and washed with acetone, and then finally dried under reduced pressure. The resulting Pd@PS catalyst was reused for the next catalytic cycle. It was observed that the recycled Pd@PS catalyst displayed good catalytic activity and can be reused and recycled up to five runs with small amount of loss in catalytic activity. Further, after 4th cycle, Pd@PS catalyst was analysed through TEM at 200 nm and 500 nm (Figure 2a and d). The average particle size distribution of **Fig. 2a** showed between 6-12 nm (Figure 2b). The deposition of Palladium was also detected by SEM-EDX analysis (Figure 2c). In an another image in **Fig. 2d**, after 4th cycle, more aggregated Palladium particles were noticed at 500 nm. Although, according to our previously reported protocols, the maximum average particle size of freshly prepared catalyst was found to be in between 2-4 nm.[20a,d] Thus, increase in average size of particles due to aggregation might be the reason for decrease in the catalytic activity of the recycled Pd@PS catalyst, which is also in concordance with our earlier reports.[20a,d]

To investigate and support the role of imidazole as additive in

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the catalytic cycle, we have carried out a set of control experiments as shown in Scheme 1. As we have also mentioned

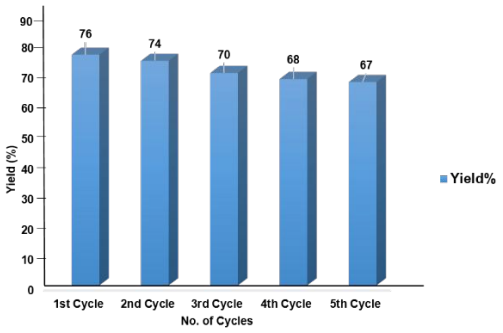


Figure 1. Recyclability Experiment.

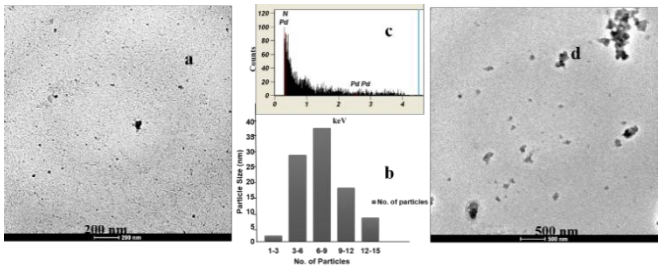
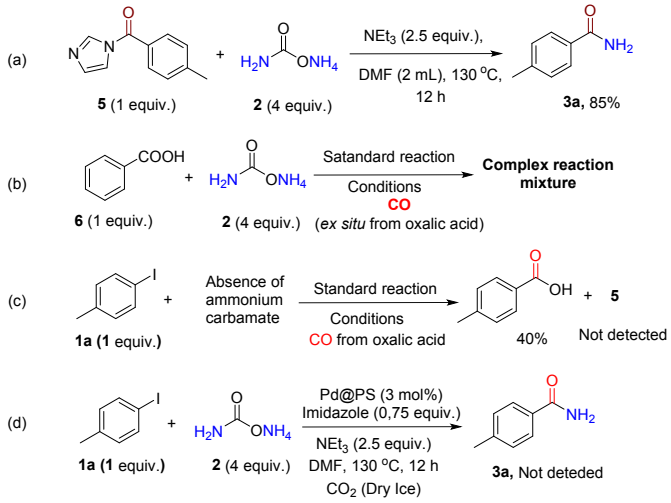


Figure 2. (a) TEM image recorded at 200 nm; (b) Particle size distribution calculated from TEM image of (a); (c) SEM-EDX spectra of recycled Pd@PS catalyst; (d) TEM image recorded at 500 nm.

in Table 1 that in the absence of imidazole, we ended up the reaction with 4-methylbenzoic acid as major product. This observation indicated the low nucleophilicity of ammonia and weak electrophilicity of palladium acyl intermediate (Figure 1., **IV**) towards ammonia to give the desired product **3a**. Inspired by literature reports,[21] and keeping observations of Table 1 in our mind, we think (1H-imidazol-1-yl) (*p*-tolyl)methanone (**5**) could be the intermediate for this transformation. In this context to decipher the role of imidazole, we have also carried out the reaction of (1H-imidazol-1-yl) (p-tolyl)methanone (**5**) under our experimental conditions and got 85% yield of aminocarbonylated product **3a** (Scheme 1, entry a). This observation led us to conclude that imidazole act as acylating agent and help in generating the electrophilic centre to be



Scheme 1: Control experiments

attacked by ammonia. After exhaustive literature survey, we have also found the intermediate **5** mediated conversion of aryl carboxylic acid into corresponding amide.[22] Hence, we have attempted the reaction of benzoic acid (**6**) under optimized reaction conditions (Scheme 1, entry b). But, we got complex reaction mixture which led us to conclusion that benzoic acid (**6**) didn't contribute to formation of product **3a**. Furthermore, we have also carried out reaction in absence of ammonium carbamate under optimized reaction, but we didn't get intermediate **5** during the course of the reaction (Scheme 1, entry c). This might be due to instability of acyl imidazole under present reaction conditions.[23] We have also checked the fate of carbon dioxide produced due to decomposition of oxalic acid and ammonium carbamate. For this, we have carried out the standard reaction in the presence of CO_2 (dry ice) and didn't obtained the product **3a** (Scheme 1, entry d). This observation clearly indicates that CO_2 formed due to decomposition of oxalic acid and ammonium carbamate does not contribute in formation of **3a**.

An insight into reaction mechanism was carried out, and plausible reaction pathway was proposed based upon the literature reports and control experiments, illustrated in Figure 3. The path of catalytic cycle from intermediate (**I**) to (**IV**) is well supported in literature.[20] Initially, Pd@PS catalyst (**I**) underwent oxidative addition into C-X bond of aryl halide to produce intermediate (**II**). Simultaneously, in outer vial, oxalic acid in DMF under heating conditions got decomposed into CO, CO_2 and H_2O.[24] This ex situ generated CO further participated in catalytic cycle to procure intermediate (**III**). The intermediate (**III**) through migratory insertion of aryl group gave intermediate (**IV**). The role of imidazole as acylating agent is well documented in literature[25] and also supported with the help of control experiments. Hence, with the aid of base, imidazole reacted with intermediate (**IV**) and converted into intermediate (1H-imidazol-1-yl)(p-tolyl)methanone (**4**) with subsequent regeneration of Pd@PS catalyst. During the course of the reaction, ammonia was generated via decomposition of ammonium carbamate under heating and basic conditions. This ammonia further reacted with intermediate (**4**) to produce product **3a** and imidazole.

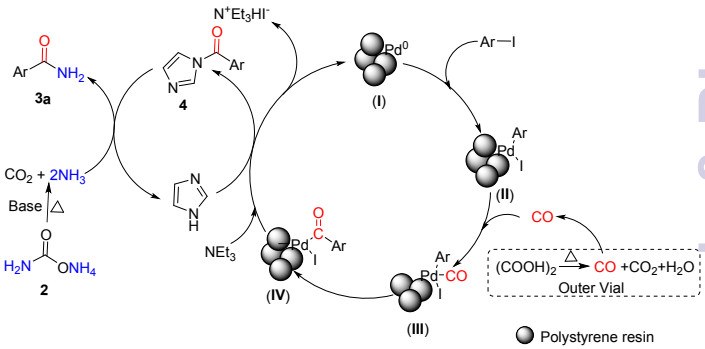


Figure 3: Plausible mechanism

Conclusions

A simple, phosphine ligand free heterogeneous Pd@PS NPs catalyzed methodology has been developed for aminocarbonylation of aryl iodides. The methodology involved the use of non-gaseous, solid, bench stable, sustainable and economic, CO and ammonia precursors. The decomposition of oxalic acid and ammonium carbamate has been efficiently utilized under Pd@PS conditions. Furthermore, the DV-set up used for aminocarbonylation is economic, easy to handle and decreases the complexity to carry out the reaction in presence of two gases simultaneously. The present protocol tolerated wide range of functional groups and delivered moderate to good yields of primary amides and isoindole-1,3-diones. Moreover, the prepared Pd@PS catalyst recovered by simple filtration and can be recycled up to four consecutive cycles with small loss in catalytic activity.

Experimental

In a double vial system (inner vial is of 2mL and another which is outer is of 5mL), 4-methyl iodobenzene (0.229 mmol, 50 mg), ammonium carbamate (0.917 mmol, 69.7mg), Pd@PS (0.0069 mmol, 70 mg), TEA (0.573 mmol, 79.7 µl), imidazole (0.172 mmol, 13 mg) and DMF (1.5 mL) were added in inner vial (2 mL) while the outer vial was charged with oxalic acid (1.37 mmol, 123.8 mg) and DMF (0.3 mL). After completion of the addition, the inner vial containing contents was placed carefully inside outer vial (5 mL) having oxalic acid. Further, the 5 mL reaction vessel tighten with the solid PTFE faced solid cap and Teflon tape. The system was further stirred in oil bath heated at 130 ^{o}C for the required time. The reaction progress was monitored by TLC and after the completion of the reaction, the inner vial was removed. The contents of the inner vial in a separatory funnel. Further, water was added in the reaction mixture and extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude mixture was further purified by silica gel column chromatography using hexane:ethyl acetate (60:40) as elutent, afforded **3a** as white solid (23 mg, 75%).

^{1}H (600MHz, DMSO-d*6*), (δ ppm) 2.34 (s, 3H), 2.34 (s, 3H), 7.245 (d, *J* = 7.98 Hz, 2H), 7.28 (brs, 1H), 7.775 (d, *J* = 8.1 Hz, 2H), 7.90 (brs, 1H). ^{13}C (150 MHz, DMSO-d*6*), δ (ppm) 21.40, 127.90, 129.19, 131.94, 141.51, 168.25. The expected ESI-MS, $[M+H]^+$ calculated for $C_8H_{10}NO^+$ 136.0757, observed 136.0755.

Conflicts of interest

There are no conflicts to declare.

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TOC Graphic

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An efficient and phosphine free synthesis of primary amides and phthalimides via aminocarbonylation and carbonylative cyclization has been demonstrated using bench stable CO and NH_3 surrogates under recyclable Pd@PS catalyzed conditions.