Organic LETTERS

Letter

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Supported Palladium Nanoparticle-Catalyzed Carboxylation of Aryl Halides, Alkenylsilanes, and Organoboronic Acids Employing Oxalic Acid as the C_1 Source

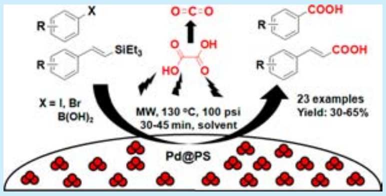
Arun K. Shil,[†,‡,§] Sandeep Kumar,[†,‡,§] C. Bal Reddy,[†,‡] Sumit Dadhwal,[†] Vandna Thakur,[†,‡] and Pralay Das*,[†,‡]

[†]Natural Product Chemistry and Process Development, CSIR-Institute of Himalayan Bioresource Technology, Palampur 176061, HP, India

[‡]Academy of Scientific & Innovative Research, New Delhi 110025, India

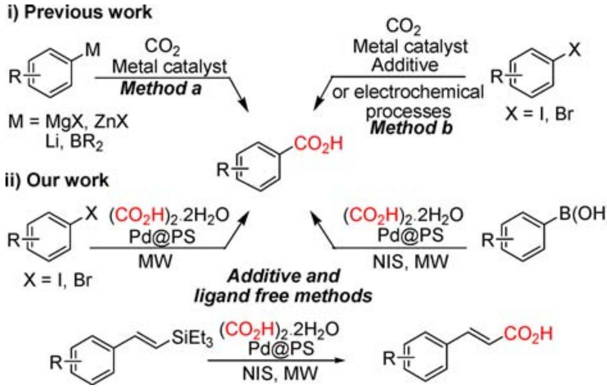
Supporting Information

ABSTRACT: Polystyrene-supported palladium(0) (Pd@PS) nanoparticles as a heterogeneous catalyst have been developed for caboxylation of aryl halides, alkenylsilanes, and organoboronic acids to produce the corresponding carboxylic acids with minor quantities of corresponding aldehydes using bench-stable and inexpensive oxalic acid as the C_1 source under focused microwave irradiation. The close vicinity of oxalic acid to Pd@PS maintained through ionic bonding helped to produce CO_2 over the catalytic surface that concurrently participated in the carboxylation reaction.



Carboxylation of aryl halides by homogeneous transition metal catalysts employing CO_2 and CO has gained a lot of interest for the direct synthesis of carboxylic acids and their derivatives.[1] Although the thermodynamic and kinetic stability of the CO_2 molecule imposes major challenges, such as harsh reaction conditions, use of specific metal catalysts and energized substrates has been suggested for selective carboxylation. The use of highly active CO gas as the C_1 source is restricted due to its toxicity.[2] Classical[3] and stoichiometric protocols using organometallic reagents[4] for the synthesis of carboxylic acid are limited because of inherent drawbacks such as poor selectivity, low substrate scope, the use of pyrophoric reagents, and side reactions. Recently, several reports have described carboxylation processes using transition metal catalysts in a high-pressure CO_2 atmosphere for substrates of varied structure using homogeneous catalysts (Scheme 1, method a).[5] Seminal work on Pd-catalyzed electrochemical carboxylation of aryl halides employing CO_2 has been reported. These processes lack generality because of limited substrate scope and inefficient synthetic methods.[6a,b] In addition,

Scheme 1. Metal-Catalyzed Carboxylation Reactions



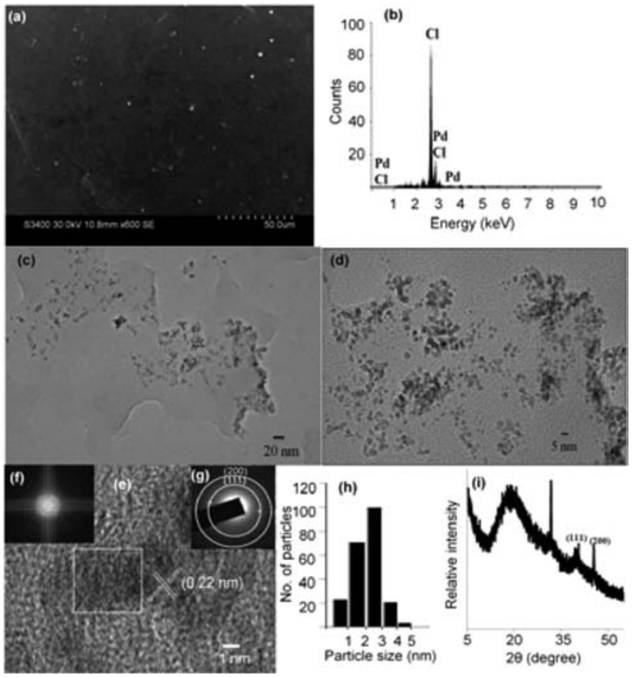


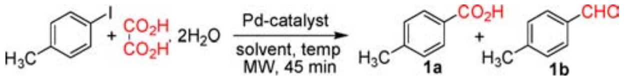
Figure 1. (a) SEM, (b) EDS, (c) TEM, (d) HRTEM, (e) HRTEM image showing lattice fringe spacing, (f) FFT of selected region from (e), (g) SAED diffraction pattern, (h) particle size distribution histogram as calculated from (d), and (i) XRD diffraction pattern of the Pd@PS catalyst.

Received: September 18, 2015
Published: October 19, 2015

ACS Publications

DOI: 10.1021/acs.orglett.5b02701
Org. Lett. 2015, 17, 5352−5355

Table 1. Reaction Conditions for Carboxylation of 4-Iodotoluene



entry	catalyst (mol % of Pd)	solvent	base/additive (1 equiv)	temp (°C)	yield[a] of **1a** (%)	yield[a] of **1b** (%)
1	Pd@PS (2)	DMF	Et_3N	130	20	nd
2	Pd@PS (2)	DMF	DABCO	130	40	nd
3	Pd@PS (2)	PEG-400	K_2CO_3	130	53	17
4	Pd@PS (2)	PEG-400	LiCl	130	62	18
5	Pd@PS (2)	1,4-dioxane		130	60	15
6	Pd@PS (2)	toluene		130	35	15
7	Pd@PS (2)	CH_3CN		130	60	17
8	**Pd@PS (2)**	**PEG-400**		**130**	**65**	**20**
9	Pd@PS (2)	DMF		130	40	nd
10	Pd@PS (2)	PEG-400		110	5	nd
11	Pd@PS (2)	PEG-400		140	65	18
12[b]	Pd@PS (2)	PEG-400		130	65	20
13	Pd@PS (1)	PEG-400		130	58	19
14[c]	Pd@PS (2)	PEG-400		130	25	12
15[d]	Pd@PS (2)	PEG-400		130	6	nd
16[e]	Pd@PS (2)	PEG-400		130	nd	nd
17	Pd@PS (3)	PEG-400		130	65	20
18	Pd/C (2)	PEG-400		130	20	nd
19	Pd/C (2)	1,4-dioxane		130	42	4
20	Pd/C (4)	1,4-dioxane		130	44	5
21	Pd/C (2)	1,4-dioxane	CTAB	130	44	4
22[d]	Pd/C (2)	1,4-dioxane	CTAB	130	nd	nd
23[f]	Pd/C (2)	1,4-dioxane	CTAB	130	nd	nd
24	$Pd(PPh_3)_4$ (2)	1,4-dioxane	CTAB	130	35	5
25	$Pd(OAc)_2$ (2)	1,4-dioxane		130	20	15
26	$Pd(PPh_3)_4$ (2)	PEG-400		130	25	nd
27	$Pd(OAc)_2$ (2)	PEG-400		130	15	nd

[a] All are isolated yields; nd = no data. [b] 2 equiv of triethylsilane was used as reducing agent. [c] 3 equiv of oxalic acid dihydrate was used. [d] Conventional heating with closed vessel (12 h). [e] Conventional heating under CO_2 balloon (12 h). [f] Conventional heating with open vessel (12 h). CTAB = *N*-cetyl-*N*,*N*,*N*, trimethylammonium bromide.

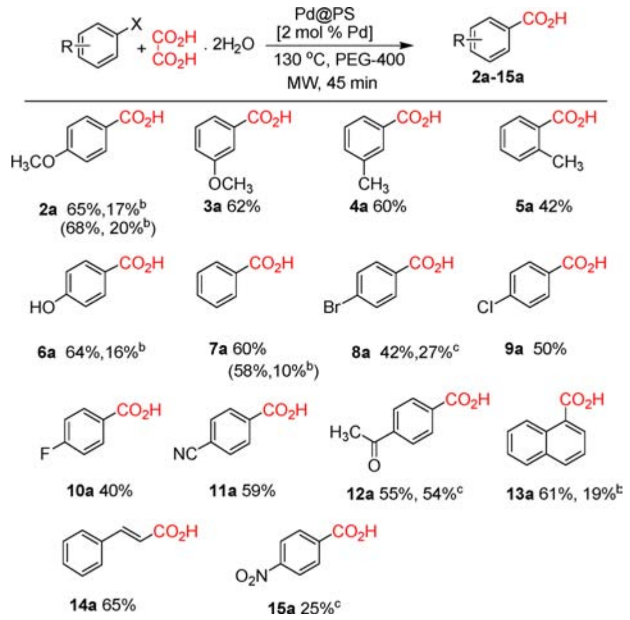
the Pd-catalyzed non-electrochemical carboxylation of aryl zinc halides and aryl bromides under high-pressure CO_2 has recently been reported (Scheme 1, method b).[6c,d] Though the nontoxic characteristics, renewability, and potentiality of CO_2 are quite attractive for use in carboxylation processes, the handling of a gas remains a continuing problem and requires the use of sophisticated instrumentation. Furthermore, the use of costly ligands, pyrophoric additives, and air-sensitive substrates severely limits existing methodologies. The only heterogeneous catalyst reported for the synthesis of carboxylic acids from aryl halides is a Pd–NHC complex tagged onto Co/C nanomagnets using CO as the C_1 source.[7] To solve the problem of gas handling in the carbonylation reactions, the production of CO gas from different precursors, such as silacarboxylic acids,[8a] *N*-formylsaccharine,[8b,c] and paraformaldehyde,[8d] has recently been reported. Therefore, the development of a mild, operationally simple alternative protocol for the carboxylation process with greater substrate scope would be desirable. In a continuation of an investigation dealing with the application of heterogeneous transition metal nanoparticles (NPs) in different organic transformations,[9,10] a microwave-assisted Pd@PS (formerly known as SS-Pd) NP-catalyzed direct carboxylation of aryl or alkenyl halides, arylboronic acids, and 2-arylalkenylsilanes using oxalic acid as the C_1 source has been developed. The in situ decomposition of oxalic acid to generate CO_2 and its activation on the Pd@PS surface represent the essence of a new catalytic carboxylation process.

The Pd@PS catalyst was prepared by a reduction deposition approach using Amberlite IRA 900 Cl^- form resin as PS (solid support) and $Pd(OAc)_2$ as metal salt precursor (Supporting Information, SI).[9] The Pd@PS catalyst thus obtained was washed and dried under reduced pressure. The morphology and structure of the Pd@PS catalyst were studied using scanning electron microscopy (SEM), transmission electron microscopy (TEM), and X-ray diffraction (XRD) studies. The SEM and SEM-EDS (energy-dispersive spectra) study of Pd@PS for the analysis of particles at the solid surface revealed the dispersion of palladium NPs in the matrix. An insight into catalyst by TEM was done for particle distribution and crystal structure determination (Figure 1). The embedded NPs of different shapes were observed with the largest average number of NPs having a size between 1 and 3 nm as calculated from the TEM image (Figure 1h). The high-resolution TEM (HRTEM) of Pd@PS performed for crystal structure analysis showed an interplanar distance of 0.22 nm corresponding to the (111) plane of face-centered cubic Pd (Figure 1e). The diffused rings and spots were observed in a selected area electron diffraction (SAED) pattern of the Pd@PS corresponding to (111) and (200) planes (Figure 1g), which is also supported by a powder XRD pattern of the same (Figure 1i). The diffractions due to other planes were not observed in SAED and powder XRD analysis due to favored growth of nanocrystals in the (111) and (200) directions.

To establish the best methodology for the carboxylation, detailed screening of catalyst loading and different solvents and bases was carried out (details in SI). The effect of CTAB as an additive in the Pd/C catalyst (Table 1, entries 18−23) and $Pd(OAc)_2$ and $Pd(PPh_3)_4$ (Table 1, entries 24−27) under different conditions gave a low yield of product. The highest yield (65%) of **1a** was obtained under the following reaction conditions: Pd@PS (2 mol %), $(CO_2H)_2{\cdot}2H_2O$ (6 equiv) in PEG-400 (1.5 mL), 130 °C (100 W, 100 psi) under microwave irradiation for 45 min, with 20% of 4-tolylaldehyde **1b** (Table 1, entry 8). The combined role of microwave irradiation, Pd@PS, and oxalic acid is crucial for the conversion of aryl halide into the corresponding carboxylic acid, with the polystyrene support playing an anchoring role for the fruitful reaction (SI).

Optimized reaction conditions were applied for the carboxylation of a number of aryl halides containing various substituents (Scheme 2). Carboxylation of aryl iodides containing electron-donating and electron-neutral (−H) substituents under standard reaction conditions gave moderate to good yields of the corresponding carboxylic acids **2a**−**7a**. The chemoselective carboxylation reaction was observed for halo-substituted aryl iodides to produce **8a**−**10a** haloaryl carboxylic acids in moderate yields. Acid-sensitive electron-withdrawing functional groups were well-tolerated under the standard reaction conditions, giving **11a** and **12a** in good yields. Similarly, carboxylation of 1-styryl iodide generated cinnamic acid **14a** in moderately high yield. Under the optimized conditions, aryl bromides were much less reactive than the corresponding aryl iodides. Interestingly, minor modification of reaction conditions by addition of LiCl (1 equiv), widely used in the coupling reactions involving aryl halides, provided the best result by suppressing the debromination reaction in a mixed solvent (PEG-400/1,4-dioxane (1:1)) system, giving 25−54% of the corresponding carboxylic acids.[11]

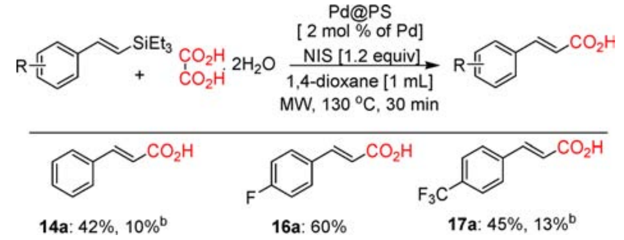
Scheme 2. Carboxylation of Aryl Halides Using Oxalic Acid as a the C_1 Source[a]



[a] Reaction conditions: aryl iodide (0.917 mmol), oxalic acid dihydrate (5.50 equiv), Pd@PS (2 mol % of Pd), PEG-400 (1.5 mL), MW (100 W, 130 °C, 100 psi), and 45 min; all are isolated yields. Yield in parentheses corresponds to gram-scale reaction using Pd@PS (1 mol %) in PEG-400/1,4-dioxane (1:1). [b] Isolated yields of the corresponding aryl aldehydes. [c] Reactions of aryl bromide by adding LiCl (1 equiv) in PEG-400/1,4-dioxane (1:1).

Further, the industrially demanding scale-up of the microwave-assisted synthesis of aryl carboxylic acids (**2a** and **7a**) in moderately good yields is possible using comparatively low catalyst loading. In both cases, the corresponding arylaldehydes are obtained in 20 and 10% yields, respectively. For the first time, alkenylsilanes have been subjected to the carboxylation reaction to produce cinnamic acids following a tandem approach. Interestingly, variously substituted 2-arylalkenylsilanes, when treated with Pd@PS, oxalic acid, NIS, and 1,4-dioxane under microwave irradiation, gave the corresponding cinnamic acids in moderate to good yields (Scheme 3).

Scheme 3. Pd@PS-Catalyzed Desilylative Carboxylation of 2-Arylalkenylsilanes[a]

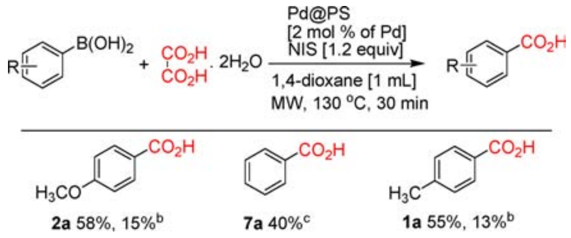


[a] Isolated yields. [b] GCMS yield of styrene.

No carboxylation product was observed in the absence of NIS, supporting that the reaction proceeds through a desilylative iodination carboxylation pathway.[12]

The same methodology was used for the conversion of aryl boronic acids to the respective carboxylic acids in appreciable yields, accompanied by the formation of minor quantities of arylaldehydes (Scheme 4). The reaction also follows the iodination carboxylation pathway, and aryl halides are formed by reaction of boronic acid with NIS after 5 min under standard conditions.[13]

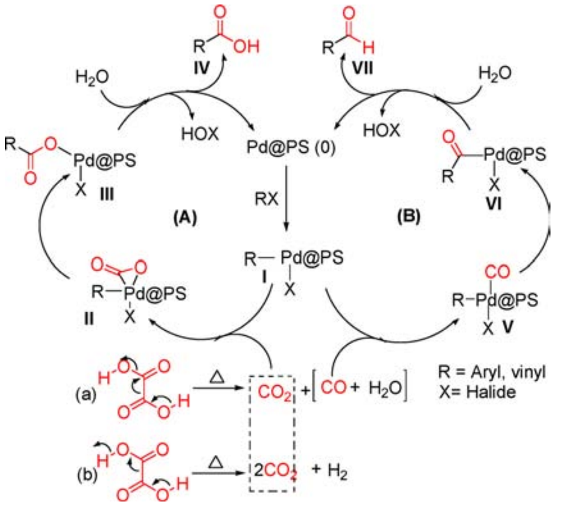
Scheme 4. Pd@PS-Catalyzed Deborylative Carboxylation of Arylboronic Acids[a]



[a] Isolated yields. [b] Isolated yield of corresponding aldehydes. [c] Traces of benzaldehyde detected.

Oxalic acid is a thermolabile dicarboxylic acid which likely undergoes decomposition via two pathways (Scheme 5, A and B) to produce a comparatively high concentration of CO_2 in the reaction vessel.[14] The relatively high concentration of carbon dioxide produced may enhance the formation of carboxylic acid. Moreover, the generation of CO_2 gas from oxalic acid under the catalytic conditions in the absence of substrate under a conventional heating condition is also detected by a $Ca(OH)_2$ test (SI). Thermodynamically stable CO_2 participates in a Pd-catalyzed cycle for carboxylation. This represents an excellent example of a simultaneous three-phase interaction (gaseous CO_2, solvated substrate, and solid Pd@PS catalyst) for product formation. Presumably, this process is mechanistically similar to that reported earlier for metal-catalyzed carboxylation

Scheme 5. Possible Mechanistic Pathways



(Scheme 5, cycle A)[6d] as well as carbonylation (Scheme 5, cycle B).[8c] The possibility of obtaining the carboxylic acids by a hydroxycarbonylation pathway is ruled out by using Et_3SiH as the hydride source (Table 1, entry 12). As per previous reports for the carbonylation of aryl halides, the intermediate (VI) is formed and, under reduction conditions, is converted to the corresponding aldehyde.[8b] The major product obtained should be the aldehyde after the addition of Et_3SiH if the reaction follows the hydroxycarbonylation pathway.

In addition, the Pd@PS catalyst was found to be reactive for up to five cycles without significant loss of catalytic activity. The leaching of <1 ppm of Pd metal was detected by ICP-AES analysis of the reaction mixture. Low product yield (**1a**; 25%) in a Hg poisoning experiment reflects the true heterogeneity of the catalyst system (SI).

In conclusion, Pd@PS NP, well-characterized by SEM, EDS, TEM, SAED, and XRD, was found to be an efficient heterogeneous catalyst for the carboxylation of aryl/alkenyl halides, alkenylsilanes, and aryl boronic acids under microwave irradiation. The minor quantities of corresponding aldehydes were also obtained by a parallel carbonylation reaction with aryl halides and aryl boronic acids. The benefits of this process are the ability to exploit oxalic acid as a sustainable CO_2 source and the transfer carboxylation strategy. The operational simplicity, gram-scale synthesis, chemoselective profile, and mild reaction conditions present a powerful alternative to common catalytic carboxylation protocols employing in situ CO_2 gas.

Caution must be taken while handling as CO gas is in situ generated from oxalic acid. Mercury (Hg) should be handled carefully and recovered safely after reaction.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02701.

> Preparation of the Pd@PS catalyst, recyclability experiment, Hg poisoning experiment, detection of CO_2 gas, typical experimental procedures, ^{1}H and ^{13}C NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: pdas@ihbt.res.in. Fax: +91-1894-230433.

Author Contributions

[§] A.K.S. and S.K. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the Director CSIR-IHBT for providing necessary facilities during the course of the work. We thank Dr. G. Saini and AIRF, JNU-New Delhi, India, for the TEM; Biotechnology Division, CSIR-IHBT, for SEM and EDS analysis; and SAIF, PU-Chandigarh, for XRD analysis. We thank CSIR, New Delhi, for financial support as part of XII Five Year Plan programme under the title ORIGIN (CSC-0108). A.K.S., S.K., C.B.R., S.D., and V.T. thank CSIR and UGC, New Delhi, for awarding fellowships.

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