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Nanopalladium-Catalyzed Oxidative Heck Reaction of Fluorinated Olefins: H_2O_2 as a Green Oxidant

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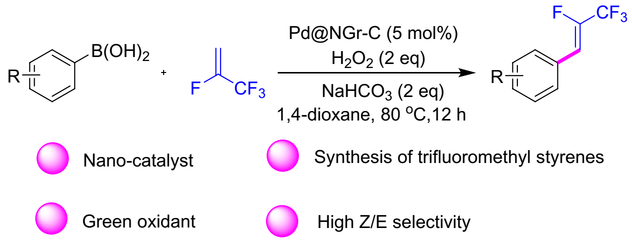
Abstract

Pd-based nanocatalysts were prepared through immobilization of $Pd(OAc)_2$/phenanthroline on nanocarbon materials and subsequent pyrolysis. The catalysts were characterized by X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS) and electron microscopy (TEM). Pd-based nanocatalysts can efficiently catalyze the oxidative Heck reaction of tetrafluoropropylene by using H_2O_2 as a green oxidant and generate (Z)-β-fluoro-β-(trifluoromethyl)styrenes in excellent yield. The yield and *Z/E* selectivity of the titled reaction remained higher than 90% after four reaction cycles.

Graphic Abstract



Keywords Oxidative heck · Nanosized pd · Fluorinated olefin · Green oxidant · Trifluoromethylstyrenes

1 Introduction

The development of heterogeneous catalysts for organic transformation is of interest for organic and material sciences [1–6]. In general, such catalysts present advantages over classical homogeneous systems due to their easy recovery and the possibility of recycling [7–12]. This is of particular importance when the catalyst is based on scarce and expensive noble metals. On the other hand, heterogeneous catalysts often display lower reactivity and selectivity than their homogeneous counterparts. Fluorine-containing aryl compounds have important applications in medicinal chemistry [13–15]. Therefore, many research groups are committed to developing new chemical reactions for the synthesis of such compounds. Among the various catalytic transformations applied for the synthesis of these compounds, palladium-catalyzed cross-coupling reactions are of exceptional importance. We have a long-standing interest in this area, especially in palladium-catalyzed cross-coupling of aryl halides and related substrates [16–18].

In the past, palladium has been mainly supported on "classic" inorganic oxides as well as carbon, silicon dioxide, and aluminum trioxide. Recently, the incorporation of dopants into the matrix of the parent support has become a highly active and interesting area in organic chemistry. More specifically, palladium-supported N-doped carbon materials (Pd/PdO@NGr-C) have generated major interest, and some interesting research has been performed by using this catalyst [19, 20]. We thought that such doping could improve the binding properties of the support and therefore minimize the leaching of palladium atoms (small clusters).

The Heck reaction is one of the most commonly employed transformations for the formation of carbon–carbon bonds.

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Because of the mild reaction conditions, the availability of reagents, and the broad functional group tolerance of this transformation, it has found extensive use in synthetic organic chemistry [21–23]. However, only a few oxidative Heck reactions can tolerate a wider range of fluorinated substrates because these cross-coupling reactions usually result in low yields or completely inhibit the catalyst [24–28]. For those reasons, a heterogeneous palladium catalyst in which the metal is immobilized on a solid support to allow highly effective catalysis of the oxidative Heck reaction is urgently needed.

Based on our previous palladium-catalyzed fluorinated olefin cross-coupling reaction [29, 30], herein, we report on the use of Pd/PdO@NGr-C as a heterogeneous catalyst in an oxidative Heck reaction using a wide range of arylboronic acids and 2,3,3,3-tetrafluoroprop-1-ene. (Z)-β-Fluoro-β-(trifluoromethyl)styrenes can be synthesized in high yield by using H_2O_2 (30% water solution) as a green oxidant.

2 Results

The preparation of Pd/PdO@NGr-C involves three steps, as shown in Scheme 1. First, palladium acetate (as the palladium precursor) and 1,10-phenanthroline were mixed in ethanol with stirring at 60 °C for 1 h. Second, the resulting mixture was adsorbed on carbon and dried at 60 °C overnight. Finally, the samples were subjected to pyrolysis under vacuum at 800 °C for 2 h under a N_2 atmosphere. The amount of palladium determined by elemental analysis was 4.6% wt%, while the nitrogen and carbon contents were 2.1 wt% and 86.2 wt%, respectively. The initial loading of palladium was 5.1%. This shows that this synthesis process does not have much metal loss.

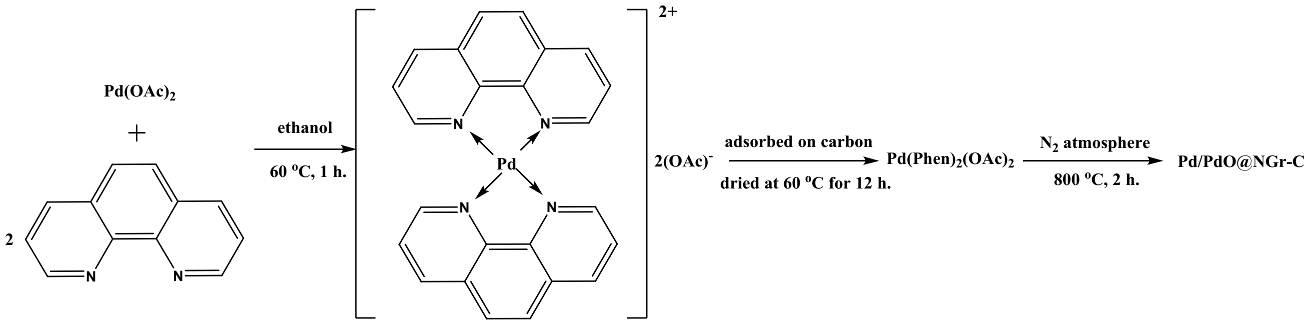
To investigate the structure of the catalyst in more detail, several characterization methods were used. The nature of the palladium and nitrogen species on the surface of the catalyst was analyzed by X-ray photoelectron spectroscopy (Fig. 1a). The Pd3d XPS data (Fig. 1b) reveal the presence of two Pd species. The first one has a binding energy of approximately 341.1 eV and is assigned as Pd(0) (41%). The second Pd species has a binding energy of approximately 343.8 eV and is assigned as Pd(II) in the form of palladium oxide (59%). Three distinct peaks are observed in the N1s spectra with electron-binding energies of 398.3 eV. 399.6 eV and 400.7 eV (Fig. 1c). Finally, the peak with the lowest binding energy can be attributed to pyridine-type nitrogen (sp2 hybridized, 41.1%).

2.1 XPS Spectra

The electron-binding energy of 399.6 eV is characteristic of a pyrrole-type nitrogen (sp3 hybridized, 24.5%). The peak at 400.7 eV is typical of quaternary N (sp2 hybridized, 24.3%). In addition to those three nitrogen types, N oxide of pyridinic N (small peak at 402.8 eV, 9.9%) was also observed, with the oxygen atoms probably arising from the acetate counterions. Additionally, the C1s spectra showed 3 peaks (Fig. 1d): the sharp peak at 284.1 eV corresponds to the sp2 carbon with C = C, while the smaller peaks at 285.4 eV and 286.8 eV are assigned to C-N and C = N, respectively. The peak observed at 289.8 eV is ascribed to the π-π* transition typical for aromatic rings.

2.2 XRD Pattern Analyses

As shown in Fig. 2, the X-ray diffraction (XRD) studies confirmed the presence of palladium dispersed into the carbon powder. By comparing the XRD patterns of the new material with the XRD patterns of Pd/C, it is possible to identify the characteristic broad peak of the amorphous carbon support (approximately 2θ = 24 °C), and the three peaks at 2θ = 40°, 48° and 68° are assigned to palladium(0). On the other hand, the peaks at 2θ = 42° and 54° demonstrate the existence of PdO. Rietveld refinement analysis further gives phase fractions of 88.9% Pd and 11.1% PdO, and an average particle size of 45 nm for PdO.



Scheme 1 Preparation of nanosized Pd

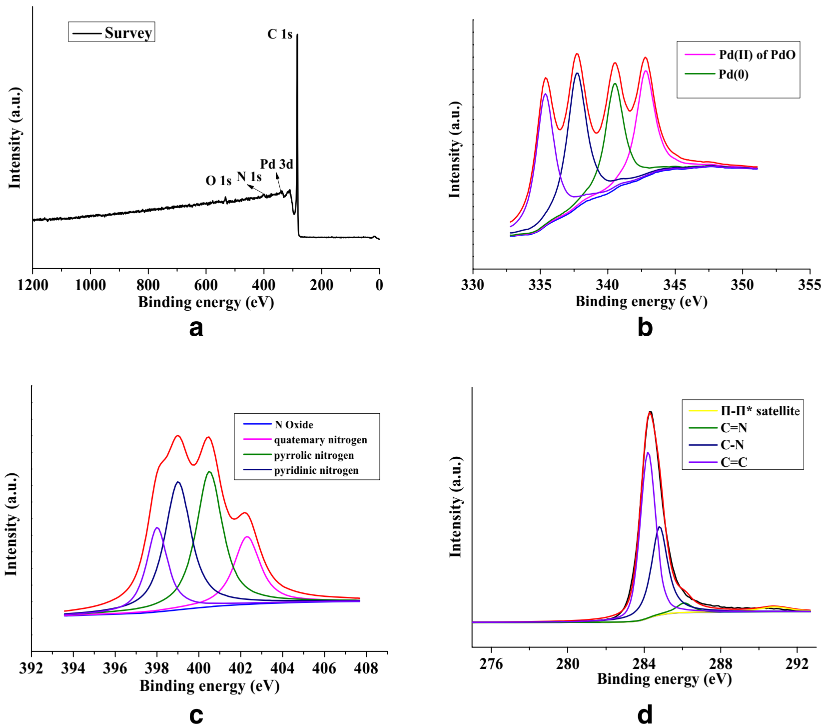


Fig. 1 **a** XPS spectra for palladium supported on N-doped carbon (Pd/PdO@NGr-C), **b** Pd3d XPS spectrum, **c** N 1 s XPS spectrum, **d** C1s XPS spectrum

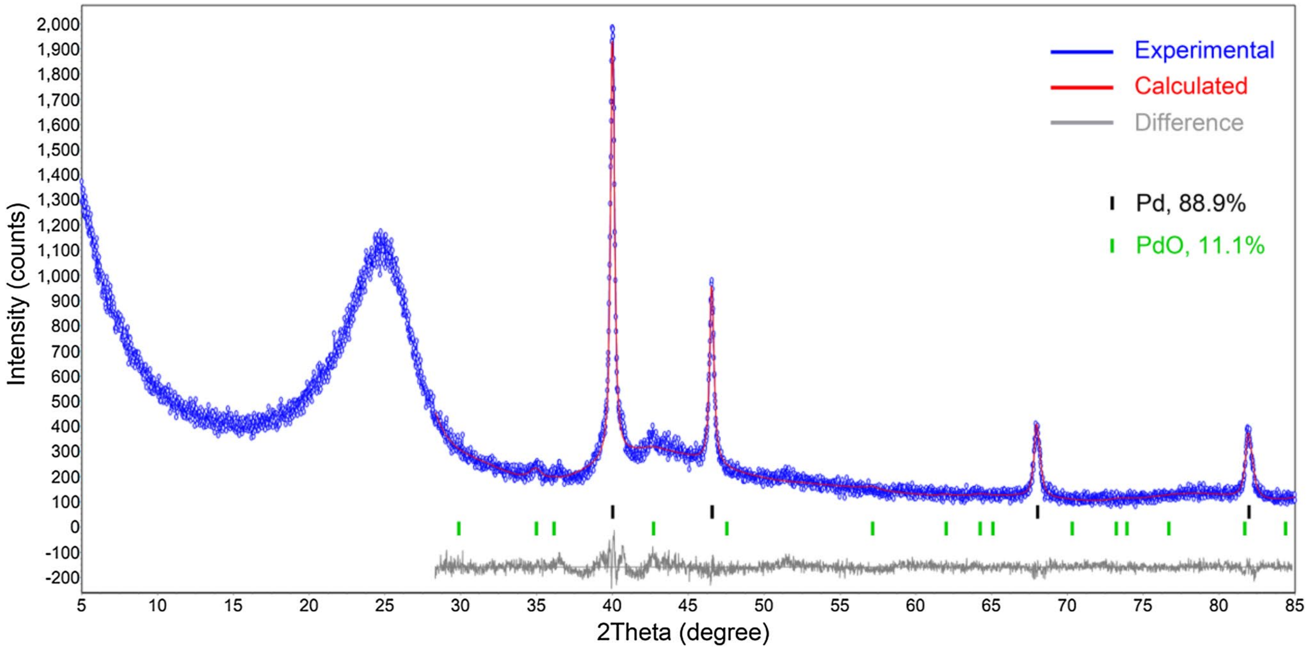


Fig. 2 Rietveld refinement of the powder XRD pattern of palladium supported on N-doped carbon

2.3 HRTEM Images

TEM analysis confirmed the presence of Pd nanoparticles with a very broad range of sizes (Fig. 3a). On some particles, several graphene layers formed as a result of carbonization of the nitrogen ligand. These layers cover or partially cover some of the Pd particles (Fig. 3b, c). Since the HRTEM images show the presence of Pd in an area without Pd particles, these finely distributed particles or clusters are likely PdO particles. However, due to the low quality of the HRTEM images, we are unable to distinguish Pd particles from the PdO particles directly.

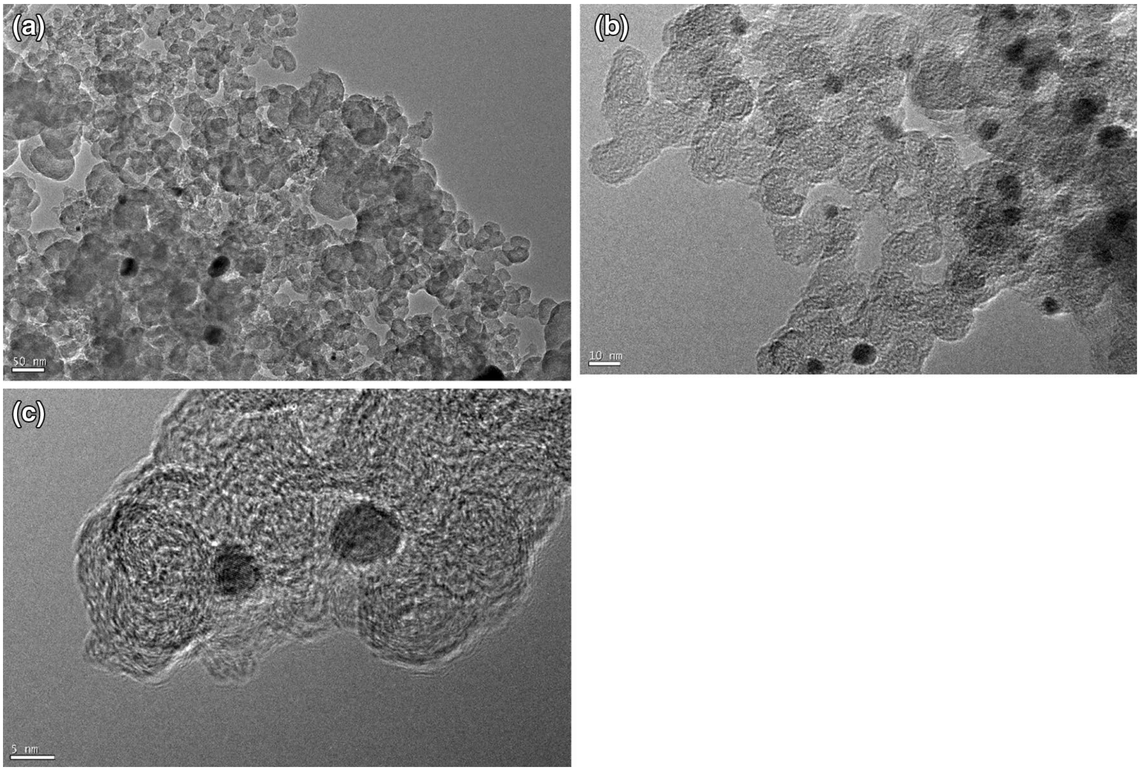


Fig. 3 HRTEM images of palladium supported on N-doped carbon (Pd@NGr-C) showing a broad range of different particle sizes

We initially chose 4-methoxyphenylboronic acid **1a** as a substrate for the screening of this coupling transformation. A solution of 4-methoxyphenylboronic acid **1a** (1.0 mmol) and 2,3,3,3-tetrafluoroprop-1-ene **2** (2.0 mmol) in MeCN (2.0 mL) was stirred, and Pd/PdO@NGr-C (1 mol%) was used as a catalyst, $NaHCO_3$ was used as a base and H_2O_2 (30% water solution) was used as an oxidant. Only (*Z*)-β-fluoro-β-(trifluoromethyl)styrene **3a** was formed in a low yield of 43%, albeit with a high *Z*/*E* ratio (Table 1, entry 1). Next, the influence of catalyst loading was examined. It could be seen that 5 mol% was the best loading for the reaction (Table 1, entries 2–4). Third, the oxidant was changed to O_2 (1 bar), and the product formed in a yield of 45% (Table 1, entry 5). Moreover, when the solvent was varied across a series including water and DMSO, a better yield was obtained when 1,4-dioxane served as the solvent (Table 1, entries 6–10). Moreover, the influence of the base was examined, and it was observed that $NaHCO_3$ was the best base for the reaction (Table 1, entries 11–13). Finally, when the temperature was raised to 80–100 °C, a good yield of **3a** (95%) was obtained (Table 1, entries 14–15). It is gratifying that the common palladium carbon as a catalyst also has catalytic activity for this reaction, but the yield is relatively low (Table 1, entry 16).

In summary, the best reaction conditions for this coupling process were as follows: Pd/PdO@NGr-C (5 mol%), 2,3,3,3-tetrafluoroprop-1-ene **2** (2.0 equiv), $NaHCO_3$ (2.0 equiv), H_2O_2 (2.0 eq), and 1,4-dioxane (2.0 mL) at 100 °C for 12 h.

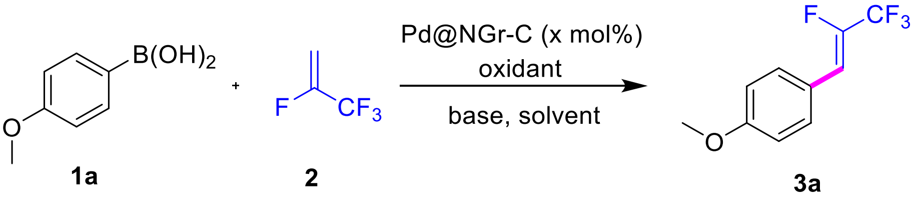
3 Discussion

3.1 Substrate Scope

To explore the scope of the coupling reaction, various arylboronic acids were examined for coupling with 2,3,3,3-tetrafluoroprop-1-ene **2** by using Pd/PdO@NGr-C as a heterogeneous catalyst and H_2O_2 as a green oxidant. The results are summarized in Table 2. Para-substituted phenylboronic acids reacted smoothly with 2,3,3,3-tetrafluoroprop-1-ene **2** to afford the desired products in excellent yields (Table 2, 3a-3 g). Next, substrates having *m*- or *o*-substituents also reacted with acceptable yields (Table 2, 3 h-3j). Disubstituted arylboronic acids were also tested, and good yields were obtained (Table 2, 3 k-3 m). Furthermore, a carbazole-derived boronic acid could also be converted into the corresponding product in moderate yield (Table 2, 3n).

It is well known that this kind of catalyst can be recycled by centrifugation and then reused for an additional process. After five runs without an obvious decrease in either the yield or the conversion, the yield remained at

Table 1 Optimization reaction conditions



Entry	Catalyst (mol%)	Solvent	Oxidant	Base	Yield[a] (%)	Z/E
1	1	MeCN	H_2O_2	$NaHCO_3$	43	> 99:1
2	2	MeCN	H_2O_2	$NaHCO_3$	56	> 99:1
3	5	MeCN	H_2O_2	$NaHCO_3$	62	> 99:1
4	10	MeCN	H_2O_2	$NaHCO_3$	58	> 99:1
5	5	MeCN	O_2 (1 bar)	$NaHCO_3$	45	> 99:1
6	5	H_2O	H_2O_2	$NaHCO_3$	34	> 99:1
7	5	1,4-dioxane	H_2O_2	$NaHCO_3$	79	> 99:1
8	5	MePh	H_2O_2	$NaHCO_3$	55	> 99:1
9	5	DMF	H_2O_2	$NaHCO_3$	42	> 99:1
10	5	DMSO	H_2O_2	$NaHCO_3$	37	> 99:1
11	5	1,4-dioxane	H_2O_2	Na_2CO_3	71	> 99:1
12	5	1,4-dioxane	H_2O_2	$KHCO_3$	75	> 99:1
13	5	1,4-dioxane	H_2O_2	K_2CO_3	77	> 99:1
14	**5**	**1,4-dioxane**	$\mathbf{H_2O_2}$	$\mathbf{NaHCO_3}$	**95**[b]	**> 99:1**
15	5	1,4-dioxane	H_2O_2	$NaHCO_3$	87[c]	> 99:1
16	Pd/C	1,4-dioxane	H_2O_2	$NaHCO_3$	29	> 99:1

The optimal reaction condition is given in bold

Reaction conditions: arylboronic acid **1a** (1.0 mmol), 2,3,3,3-tetrafluoroprop-1-ene **2** (2.0 mmol), catalyst (5 mol%), base (2.0 mmol), oxidant (2.0 mmol), solvent (2.0 mL), 60 °C, 12 h.

[a] Isolated yield

[b] 80 °C

[c] 100 °C

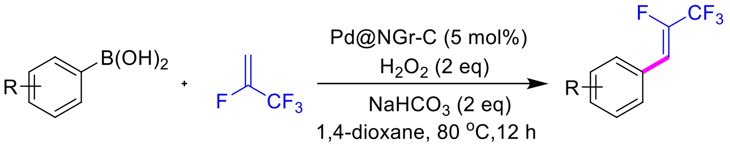
approximately 92%, which indicated the good stability of the Pd/PdO@NGr-C catalyst (Fig. 4).

We seriously conducted a recycling experiment on the recovered catalyst. The content of palladium metal in the solution after one cycle was tested. It can be seen that there is only 1PPM. There is almost no loss. After five trials, the yield decreased by about 10%, which may be the operation loss of some catalysts in the catalyst recovery experiment. After all, the amount of catalyst is relatively small. In addition, we have collected the reaction solution for ICP-MS measurement at the end of the first catalytic cycle. The concentration of palladium ions in the post-reaction liquid is very low (1 ppm in 2 mL solution), which shows that this catalytic cycle process is heterogeneous catalysis, not a homogeneous catalyst.

4 Materials and Methods

Unless otherwise mentioned, the solvents and reagents were purchased from commercial sources (Macklin, Heowns, Meryer Co. Ltd) and used as received. ^1H, ^{13}C and ^{19}F NMR spectra were recorded on 400 and 500 MHz spectrometers. ^1H NMR chemical shifts were determined relative to internal $(CH_3)_4Si$ (TMS) at δ 0.0 or to the signal of the residual protonated solvent: $CDCl_3$ δ 7.26. ^{13}C NMR

Table 2 Oxidative Heck reaction between 2,3,3,3-tetrafluoroprop-1-ene and arylboronic acids in the presence of Pd/PdO@NGr-C



1 **2** **3**

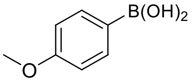
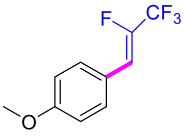
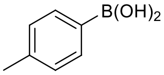
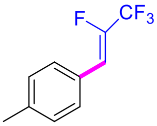
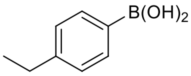
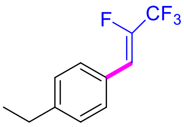
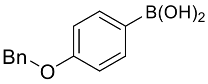
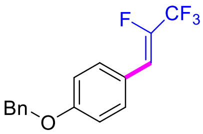
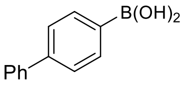
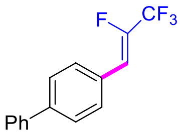
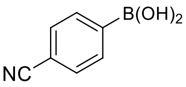
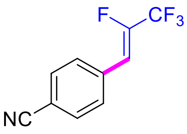
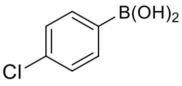
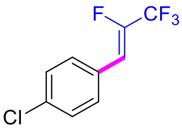
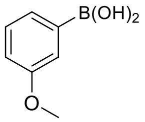
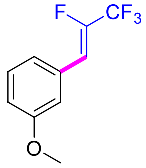
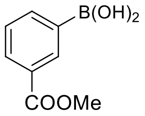
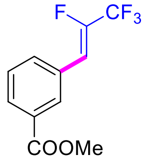
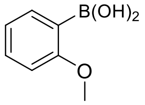
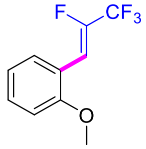
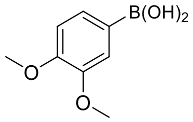
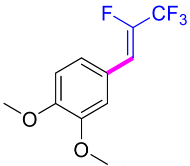
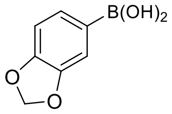
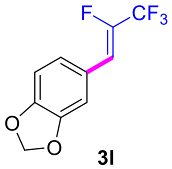
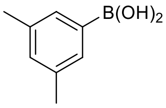
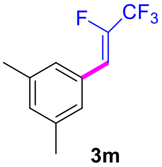
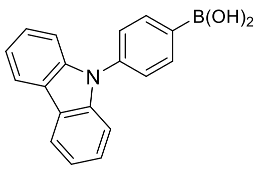
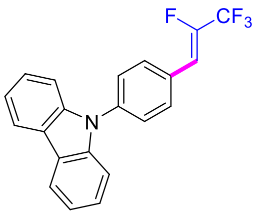
Entry	Boronic acid	Product	Yield [a] (%)	Z/E value
1	 **1a**	 **3a**	95	99:1
2	 **1b**	 **3b**	86	97:3
3	 **1c**	 **3c**	78	97:3
4	 **1d**	 **3d**	86	97:3
5	 **1e**	 **3e**	88	97:3
6	 **1f**	 **3f**	77	96:4
7	 **1g**	 **3g**	72	94:6

Table 2 (continued)

8	 **1h**	 **3h**	81	99:1
9	 **1i**	 **3i**	79	96:4
10	 **1j**	 **3j**	81	93:7
11	 **1k**	 **3k**	91	96:4
12	 **1l**	 **3l**	87	96:4
13	 **1m**	 **3m**	83	96:4
14	 **1n**	 **3n**	80	96:4

Reaction conditions: **1** (1.0 mmol), **2** (2.0 mmol), Pd/PdO@NGr-C (5 mol%), $NaHCO_3$ (2.0 mmol), H_2O_2 (30%, 2.0 mmol), 1,4-dioxane (2.0 mL), 80 °C, 12 h.

[a] Isolated yield

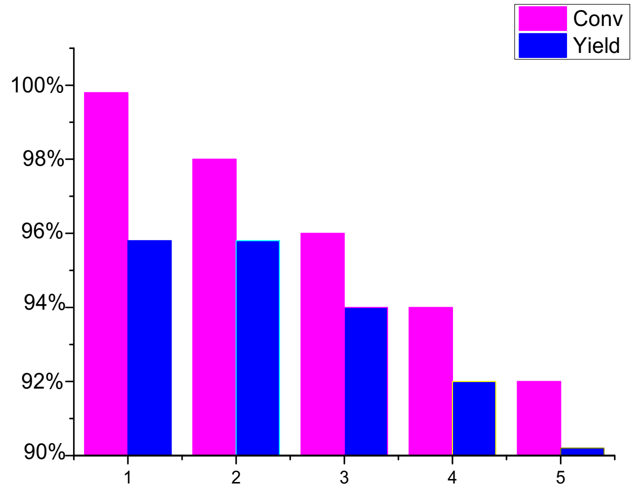


Fig. 4 Recycling and reuse of Pd/PdO@NGr-C in Heck oxidation

chemical shifts were determined relative to internal TMS at δ 0.0. For the isolated compounds, ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ at δ 0.0. ^{19}F NMR chemical shifts were determined relative to *p*-fluoroacetophenone at δ -107.5. Data for ^1H, ^{13}C and ^{19}F NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, br = broad). Mass spectra were obtained on a mass spectrometer. High-resolution mass data were recorded on a high-resolution mass spectrometer in ESI mode.

The reactions were carried out in glassware sealed with Teflon screw caps using the vacuum line technique. The reactions were stirred using Teflon-coated magnetic stir bars. The room temperature in the laboratory was 25 ± 2 °C. Elevated temperatures were maintained using thermostat-controlled silicone oil baths.

4.1 General Method

The reaction was carried out in an autoclave containing a 10 mL Teflon reaction tube. Catalysts (0.05 mmol), arylboronic acids (1.0 mmol), $NaHCO_3$ (2.0 mmol), H_2O_2 (30%, 2.0 mmol) and 1,4-dioxane (2.0 mL) were added to the tube. The autoclave was cooled to − 60 °C by liquid nitrogen, and then 2,3,3,3-tetrafluoropropylene (HFO-1234yf) was added to a set weight. Finally, the autoclave was warmed in an oil bath at 80 °C for 12 h. After the reaction, the autoclave was cooled to room temperature and vented to discharge the excess 2,3,3,3-tetrafluoropropylene (HFO-1234yf) carefully. Water (20 mL) was added, and *p*-fluoroacetophenone (80 mg) was added with a syringe. Then, the product was extracted with DCM (3*15 mL). The organic layers were washed with brine and dried over Na_2SO_4, and the organic solvent was evaporated by a rotatory evaporator under atmospheric pressure. The crude products were determined by ^{19}F NMR using *p*-fluoroacetophenone as an internal standard.

5 Conclusions

In summary, we developed a new strategy for the facile synthesis of (Z)-β-fluoro-β-(trifluoromethyl)styrene derivatives via a Pd/PdO@NGr-C-catalyzed oxidative Heck reaction with 2,3,3,3-tetrafluoroprop-1-ene as a fluorinated olefin. More importantly, H_2O_2 is used as a green oxidant during this process. The wide scope and remarkable tolerance, particularly to a large number of important arylboronic acids, make this strategy remarkably practical for the efficient synthesis of functional styrenes.

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References

1. Tang DTD, Collins KD, Glorius F (2013) Completely regioselective direct C-H functionalization of benzo[b]thiophenes using a simple heterogeneous catalyst. J Am Chem Soc 135:7450–7453
2. Bratt E, Verho O, Johansson MJ, Bäckvall J-E (2014) A general suzuki cross-coupling reaction of heteroaromatics catalyzed by nanopalladium on amino-functionalized siliceous mesocellular foam. J Org Chem 79:3946–3954
3. He L, Natte K, Rabeah J, Taeschler C, Neumann H, Brückner A, Beller M (2015) Heterogeneous platinum-catalyzed C-H perfluoroalkylation of arenes and heteroarenes. Angew Chem Int Ed 54:4320–4324
4. Zhu F, Li Y, Wang Z, Wu X-F (2016) Highly efficient synthesis of flavones via Pd/C-catalyzed cyclocarbonylation of 2-iodophenol with terminal acetylenes. Catal Sci Technol 6:2905–2909
5. Natte K, Neumann H, Wu X-F (2015) Pd/C as an efficient heterogeneous catalyst for carbonylative four-component synthesis of 4(3H)-quinazolinones. Catal Sci Technol 5:4474–4480
6. Li C-L, Qi X, Wu X-F (2015) Pd/C-catalyzed reductive homocoupling of iodobenzene with 5-(hydromethyl)furfural as the reductant: a case study. J Mol Catal A Chem 406:94–96
7. Fan X, Zhang G, Zhang F (2015) Multiple roles of graphene in heterogeneous. Chem Soc Rev 44:3023–3035
8. Schlögl R (2015) Heterogeneous catalysis. Angew Chem Int Ed 54:3465–3520
9. Lucarelli C, Vaccari A (2011) Examples of heterogeneous catalytic processes for fine chemistry. Green Chem 13:1941–1949
10. Yin L, Liebscher J (2007) Carbon−carbon coupling reactions catalyzed by heterogeneous palladium catalysts. Chem Rev 107:133–173

11. Climent MJ, Corma A, Iborra S (2011) Heterogeneous catalysts for the one-pot synthesis of chemicals and fine chemicals. Chem Rev 111:1072–1133
12. Molnàr A (2011) Efficient, selective, and recyclable palladium catalysts in carbon−carbon coupling reactions. Chem Rev 111:2251–2320
13. Wang J, Sánchez-Roselló M, Aceña JL, Pozo C, Sorochinsky AE, Fustero S, Soloshonok VA (2014) Fluorine in pharmaceutical industry: fluorine-containing drugs introduced to the market in the last decade (2001–2011). Chem Rev 114:2432–2506
14. Zhou Y, Wang J, Gu Z, Wang S, Zhu W, Aceña JL, Soloshonok VA, Izawa K, Liu H (2016) Next generation of fluorine-containing pharmaceuticals, compounds currently in phase II–III clinical trials of major pharmaceutical companies: new structural trends and therapeutic areas. Chem Rev 116:422–518
15. Hagmann W (2008) The many role for fluorine in medicinal chemistry. J Med Chem 51:4359–4369
16. Li Y, Xue D, Wang C, Liu Z-T, Xiao J (2012) Carboxylic acid anhydrides via Pd-catalyzed carbonylation of aryl halides at atmospheric CO pressure. Chem Commun 48:1320–1322
17. Li Y, Xue D, Lu W, Fan X, Wang C, Liu Z-T, Xiao J (2013) 3-Acylindoles via palladium-catalyzed regioselective arylation of electron-rich olefins with indoles. RSC Adv 3:11463–11466
18. Lu W, Li Y, Wang C, Xue D, Chen J-G, Xiao J (2014) Pd-catalyzed carbonylation for the construction of tertiary and quaternary carbon centers with sp3 carbon partners. Org Biomol Chem 12:5243–5249
19. Ziccarelli I, Neumann H, Kreyenschulte C, Gabriele B, Beller M (2016) Pd-supported on N-doped carbon: Improved heterogeneous catalyst for base-free alkoxycarbonylation of aryl iodides. Chem Commun 52:12729–12732
20. Zhang C, Leng L, Jiang P, Li J, Du S (2017) Immobilizing palladium nanoparticles on nitrogen-doped carbon for promotion of formic acid dehydrogenation and alkene hydrogenation. ChemistrySelect 2:5469–5474
21. Zhou A, Guo R-M, Zhou J, Dou Y, Chen Y, Li J-R (2018) Pd@ZIF-67 derived recyclable Pd-based catalysts with hierarchical pores for high-performance heck reaction. ACS Sustain Chem Eng 6:2103–2111
22. Djakovitch L, Koehler K (2001) Heck reaction catalyzed by Pd-modified zeolites. J Am Chem Soc 123:5990–5999
23. Albéniz AC, Espinet P, Martin-Ruiz B, Milstein D (2005) Catalytic system for the heck reaction of fluorinated haloaryls. Organometallics 24(15):3679–3684
24. Delcamp JH, Brucks AP, White MC (2008) A general and highly selective chelate-controlled intermolecular oxidative heck reaction. J Am Chem Soc 130:11270–11271
25. Dai Q, Zhao B, Yang Y, Shi Y (2019) Pd-catalyzed oxidative heck reaction of grignard reagents with diaziridinone as oxidant. Org Lett 13:5157–5161
26. Zhou Y-B, Wang Y-Q, Ning L-C, Ding Z-C, Wang W-L, Ding C-K, Li R-H, Chen J-J, Lu X, Ding Y-J, Zhan Z-P (2017) Conjugated microporous polymer as heterogeneous ligand for highly selective oxidative heck reaction. J Am Chem Soc 139:3966–3969
27. Werner EW, Sigman MS (2010) A highly selective and general palladium catalyst for the oxidative heck reaction of electronically nonbiased olefins. J Am Chem Soc 132(40):13981–13983
28. Nordqvist A, Björkelid C, Andaloussi M, Janson AM, Mowbray SL, Karlén A, Larhed M (2011) Synthesis of functionalized cinnamaldehyde derivatives by an oxidative heck reaction and their use as starting materials for preparation of mycobacterium tuberculosis 1-deoxy-d-xylulose-5-phosphate reductoisomerase inhibitors. J Org Chem 76:8986–8998
29. Li Y, Tu D-H, Gu Y-J, Wang B, Wang Y-Y, Liu Z-T, Liu Z-W, Lu J (2015) Oxidative heck reaction of fluorinated olefins with arylboronic acids by palladium catalysis. Eur J Org Chem 2015:4340–4343
30. Li Y, Zhao B, Dai K, Tu D-H, Wang B, Wang Y-Y, Liu Z-T, Liu Z-W, Lu J (2016) Palladium-catalyzed Suzuki-Miyaura reaction of fluorinated vinyl chloride: a new approach for synthesis α and α, β-trifluoromethylstyrenes. Tetrahedron 72:5684–5690