ACS APPLIED NANO MATERIALS

www.acsanm.org

Article

Versatile Nanoporous Organic Polymer Catalyst for the Size-Selective Suzuki–Miyaura Coupling Reaction

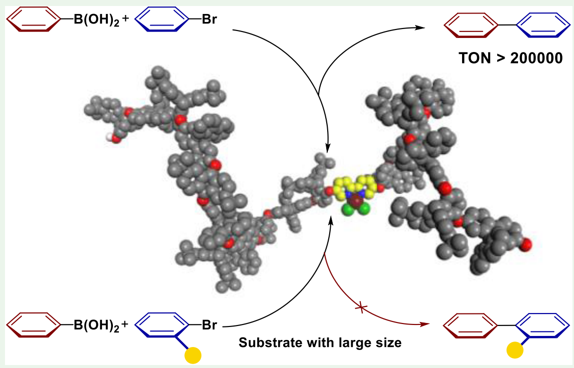
Sheng Guo,[‡] Yifan Wu,[‡] Shao-Xiong Lennon Luo, and Timothy M. Swager*

Cite This: *ACS Appl. Nano Mater.* 2022, 5, 18603–18611

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Heterogenous catalysts with confined nanoporous catalytic sites are shown to have high activity and size selectivity. A solution-processable nanoporous organic polymer (**1-BPy-Pd**) catalyst displays high catalytic performance (TON > 200K) in the heterogeneous Suzuki–Miyaura coupling (SMC) reaction and can be used for the preparation of the intermediates in the synthesis of pharmaceutical agents. In comparison to the homogeneous catalyst analogue (2,2′-BPy)$PdCl_2$, the heterogenous system offers size-dependent catalytic activity when bulkier substrates are used. Furthermore, the catalyst can be used to create catalytic impellers that simplify its use and recovery. We found that this system also works for applications in heterogenous Heck and nitroarenes reduction reactions. The metal-binding nanoporous polymer reported here represents a versatile platform for size-selective heterogeneous and recyclable catalysts.



KEYWORDS: *nanoporous organic polymer, heterogeneous catalyst, Suzuki–Miyaura coupling reaction, size-selective reaction, catalyst processing*

■ INTRODUCTION

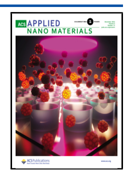
Sustainable catalysts are a base requirement for the development of green chemistry.[1−4] Heterogeneous catalysts with high catalytic activity, long-term stability, and easy recyclability are of increasing importance to organic chemistry.[5,6] Heterogeneous catalysts are often classified by their catalytic support, including silica, polymers, modified nanocarbons, metal–organic frameworks, and covalent–organic frameworks.[7] The polymer-supported catalysts can offer the advantages of convenient recycling, structural tunability, and high catalytic stability.[8,9] However, to date, there have been drawbacks of these polymer catalysts, such as low loading capacity and poor mechanical properties, which have limited their application in large-scale processes.[7,8,10]

Nanoporous organic polymers (NOP) have shown great efficiency as catalyst supports in heterogeneous catalysis due to their easy preparation and characterization, high surface area, tunable porosity and functionality, and good physical and chemical stability.[9,11−16] The catalytic metal centers confined in nanoporous cavities of NOPs generally give a high turnover number (TON), high-chemical regioselectivity, high recyclability, and low metal contamination in the products.[17−23] As a result of these advantages, NOP-supported Pd catalysts have been used as highly efficient heterogeneous catalysts for Suzuki–Miyaura coupling (SMC) reactions.[17−37] The SMC reaction has been widely applied in the synthesis of natural products, pharmaceuticals, polymers, agrochemicals, and advanced materials.[38,39] In addition to high catalytic performance, NOP-supported Pd catalysts enable size-selective SMC reactions.[24,25,40] The Yavuz group reported a size-selective SMC reaction using Pd(II)-containing COF catalysts.[24] Furthermore, the Xie group reported efficient size-selective SMC and hydrogenation reactions enabled by NOP-supported Pd nanoparticles.[25] The catalytic sites embedded within NOPs are confined within a nanospace, which restricts the size of the substrates.

Pd heterogeneous catalysts that are readily processed facilitate practical applications,[10,41−43] and solution processing is generally preferred for the immobilization of heterogeneous catalysts.[44] However, the polymer-supported catalysts should be intrinsically insoluble in the reaction solvents or made to be insoluble by cross-linking of films/particles. It is also important that the porosity is maintained after solvent treatments.

Here, we report an efficient two-step strategy for the preparation of a NOP-supported Pd catalyst that combines the properties of size selectivity and solution processability. This system has very low metal loading but exhibits extremely high

Received: October 6, 2022
Accepted: November 28, 2022
Published: December 5, 2022



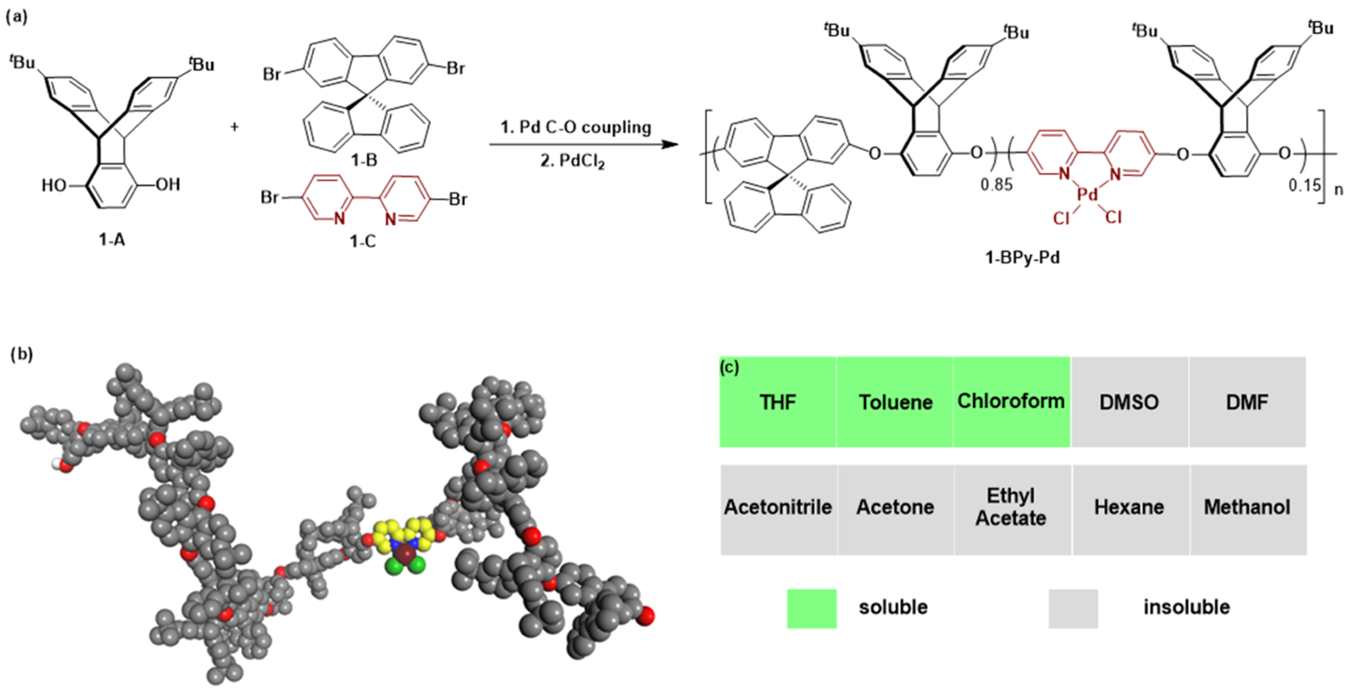


Figure 1. (a) Synthesis of **1-BPy-Pd**, **1-BPy**. (b) Schematic representation of **1-BPy-Pd** showing 9 repeating units, with a 3D model optimized via the COMPASS II forcefield. (c) Solubility of **1-BPy-Pd** in different organic solvents (the approximate solubility of **1-BPy-Pd** in different solvents is shown in Supporting Information Table S1).

catalytic activity in the SMC reaction and can be used for the preparation of the intermediates for the synthesis of pharmaceuticals. The size-selective heterogeneous SMC reaction reflects the space-confined Pd catalytic sites. In comparison with the previously reported MOF- and COF-supported Pd catalysts for the size-selective SMC reaction,[24,25,40] this polymer catalyst is solution-processable and can be coated on the impeller of an overhead stirrer rod to simplify reaction conditions and allow for the catalyst recovery. The NOP-supported Pd catalyst is also effective in other important chemical transformations, including the Heck reaction and nitroarene reduction.

■ EXPERIMENTAL SECTION

Materials and Physical Measurements. All reagents used in this paper were purchased from commercial sources (Sigma-Aldrich, Ambeed, TCI America, and Combi-Blocks) and used as received. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker Avance 500 MHz spectrometer. Thermogravimetric analysis (TGA) was carried out using a TGA 550 from TA Instruments under a nitrogen atmosphere. The molecular weight and molecular weight distribution of polymers were determined using GPC following the method reported in our previous study.[45] N_2 adsorption−desorption isotherms were measured on a Micromeritics ASAP 2020. The surface area of polymer samples was calculated with Brunauer−Emmett−Teller (BET) theory over the relative pressure range of 0.05−0.20 P/P_0. X-ray photoelectron spectroscopy (XPS) spectra were measured with a Thermo Scientific K-α+ X-ray photoelectron spectrometer equipped with a hemispherical energy analyzer and a monochromated X-ray source (Al K-α). All Fourier-transform infrared (FT-IR) spectra were measured with a Thermo Scientific Nicolet iS5 spectrometer equipped with an iD5 ATR accessory. Surface morphology and particle sizes were investigated using a Zeiss Sigma 300 VP field emission scanning electron microscope (SEM). Pd residue was measured with an Agilent 7900 inductively coupled plasma mass spectrometer (ICPMS).

Catalyst Preparation. Bipyridine-based poly(arylene ether) **1-Bpy** was synthesized following a procedure described in our previous study.[44] The Pd concentration of **1-BPy** was determined to be 102 ppm by weight using ICPMS.

1-BPy-Pd. Palladium chloride (48.0 mg, 0.27 mmol) was dissolved in hot acetonitrile (10 mL), and then **1-Bpy** (412 mg) was added. The mixture was kept refluxing for 48 h. The resulting solid was isolated by filtration. The crude product was transferred to a 50 mL flask. Hot acetonitrile (10 mL) was added, and the mixture was kept refluxing for 1 h. The purified polymer was obtained by filtering and washing with hot acetonitrile (3 × 20 mL), then dried at 100 °C under vacuum overnight to yield **1-Bpy-Pd** as a brown powder (410 mg). The Pd concentration of **1-BPy** was determined to be 21600 ppm by weight using ICPMS.

General Procedure for the Suzuki−Miyaura Coupling Reaction. To a screw-cap reaction tube (20 mm × 125 mm, Fisherbrand, part # 1495937A) was added aryl halide (1.0 mmol), phenylboronic acid (183.0 mg, 1.5 mmol, 1.5 equiv), K_2CO_3 (276 mg, 2.0 mmol, 2.0 equiv), **1-Bpy-Pd** (6.0 mg, 0.12 mol %), and 2.0 mL of the 1.0/1.0 EtOH-H_2O (v/v) mixture sequentially. The reaction tube was capped with a Teflon/silicone septum screw cap (National, part # B7995-18; Kimble Chase, part # 73804-15425) and then placed in an oil bath preheated to 80 °C. After the indicated reaction time, the reaction mixture was removed from the oil bath and allowed to cool to rt. To the reaction mixture was added hexane (10 mL) and water (5 mL). The polymer catalyst was recycled by filtration. The recycled catalyst was washed with MeOH and EtOAc and then dried at 100 °C under vacuum. The filtrate was transferred to a separatory funnel. The organic layer was removed and saved. The aqueous layer was then extracted with hexane (20 mL). The combined organic phase was washed with water once. The solvent was removed under vacuum. The residue was purified by flash column chromatography with hexane or hexane/EtOAc = 10:1 as the eluent. The structures of the products were confirmed by the ^{1}H and ^{13}C NMR spectral data.

Procedure for the Heck Reaction. An oven-dried Schlenk tube was charged with **1-Bpy-Pd** (6.0 mg, 0.24 mol %). The reaction tube was evacuated and backfilled with nitrogen from the Schlenk line (this process was repeated a total of five times), and then styrene (115 μL, 1.0 mmol, 2 equiv), iodobenzene (102 mg, 0.5 mmol, 1 equiv),

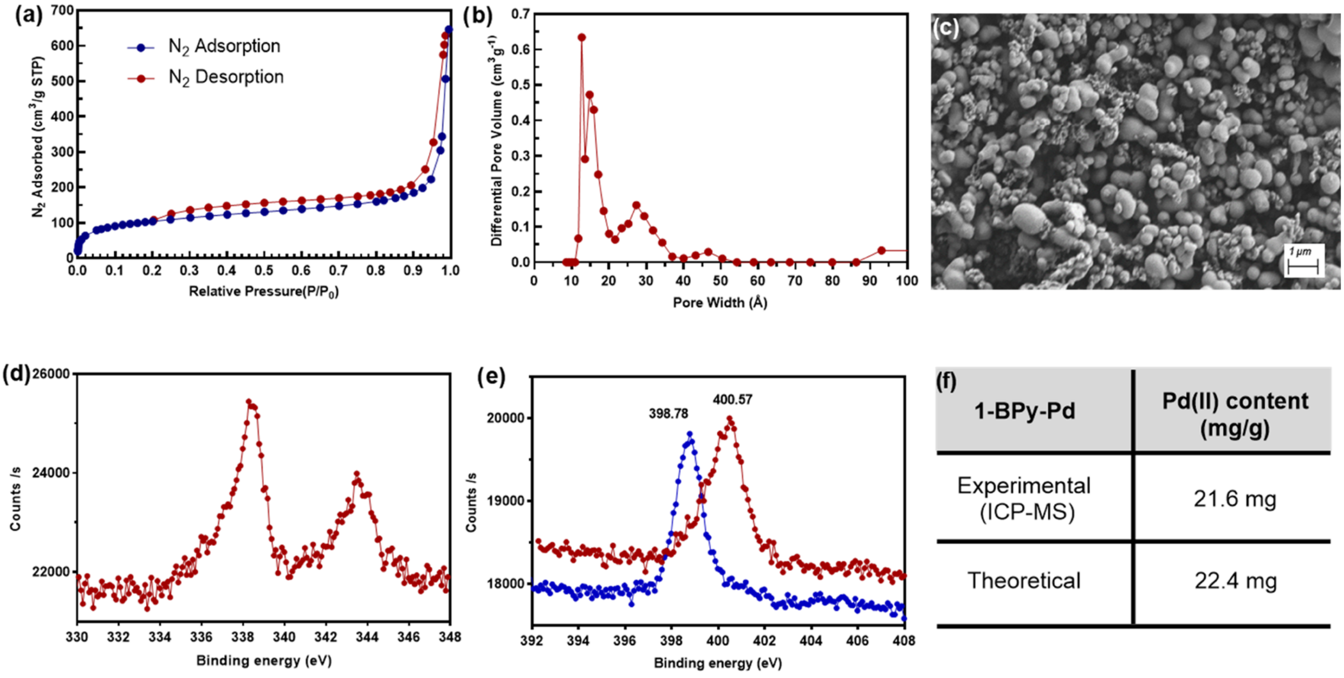


Figure 2. (a) N_2 adsorption−desorption isotherm of **1-BPy-Pd**, BET surface area: 376 m^2/g; (b) pore size distribution of **1-BPy-Pd;** (c) SEM image of the **1-BPy-Pd** powder; (d) Pd 3d XPS spectra of **1-BPy-Pd;** (e) N 1s XPS spectra of **1-BPy-Pd** (red) and **1-BPy** (blue); and (f) Pd content of **1-BPy-Pd**.

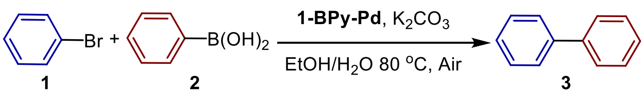
triethylamine (140 μL, 1,0 mmol, 1 equiv), and anhydrous dimethylformamide (DMF) (2 mL) were added sequentially. The reaction tube was placed in an oil bath preheated to 120 °C. After 3 h, the reaction mixture was removed from the oil bath and allowed to cool to rt. To the reaction mixture was added 5 mL water. The mixture was extracted with diethyl ether (20 mL × 3). The combined organic layer was dried by Na_2SO_4 and concentrated under vacuum. The crude product was further purified by flash column chromatography on silica gel to afford the desired product **3m** as a white solid (88 mg, 98% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 8.3, 1.3 Hz, 4H), 7.40 (t, *J* = 7.7 Hz, 4H), 7.32−7.28 (m, 2H), 7.15 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.5, 128.8, 127.8, 126.7.

Procedure for Reduction of Nitroarenes. **1-Bpy-Pd** (6.0 mg, 0.12 mol %) was added to a mixture of nitrobenzene (103 μL, 1 mmol, 1 equiv) in water (2.0 mL). Then, $NaBH_4$ (114 mg, 3 mmol, 3 equiv) was added to the mixture. The reaction mixture was allowed to stir at room temperature for 24 h. The polymer catalyst was recycled by filtration. The final mixture was extracted with diethyl ether (20 mL × 3). The combined organic layer was dried by Na_2SO_4 and concentrated under vacuum. The crude product was further purified by flash column chromatography on silica gel to afford the desired product **3n** as a colorless oil (93 mg, 99% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.19 (td, *J* = 7.5, 3.7 Hz, 2H), 6.79 (dt, *J* = 7.6, 5.1 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 2H), 3.62 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 146.5, 129.4, 118.6, 115.2.

■ RESULTS AND DISCUSSION

Synthesis and Characterization of the Nanoporous Polymer Catalyst. The synthesis of the nanoporous organic polymer was achieved by a previously reported Pd-catalyzed C−O polycondensation reaction.[45,46] The rigid three-dimensional *t*-Bu-triptycene (**TBTrip**) hydroquinone **1-A** and siprobifluorene (**SBF**) dibromide **1-B** provide a nanoporous poly(arylene ether) with high molecular weight, high porosity, good film forming capacity, and excellent chemical and physical stability.[45,46] The 15 mol % bipyridine dibromide **1-C** comonomer was used in the polycondensation process for the synthesis of bipyridine-based poly(arylene ether) **1-Bpy**, and treatment with $PdCl_2$ generates **1-BPy-Pd** (Figure 1a). Each bipyridine-ligated Pd is surrounded by 7−8 **SBF-TBTrip** repeating units (Figure 1b), ensuring a confined nanospace for each Pd center. We find **1-BPy-Pd** is insoluble in DMF, dimethyl sulfoxide (DMSO), methanol, and acetonitrile, which are typically employed for the SMC reaction. However, it is soluble in tetrahydrofuran (THF), $CHCl_3$, and DCM, which allows for solution processing (Figure 1c). Nitrogen adsorption analyses at 77K were used to investigate the surface area and pore size distribution of **1-Bpy-Pd**. The Brunauer−Emmett−Teller (BET) surface area of **1-BPy-Pd** was determined to be 376 m^2g^{-1} (Figure 2a).[45,46] The pore size distribution was in the microporous range (1−2 nm), as calculated by nonlocal density functional theory (NLDFL) (Figure 2b). 15 mol % bipyridine-$PdCl_2$ was chosen as a compromise between Pd content and porosity. The incorporation of more bipyridine-Pd

Table 1. Catalytic Activity Test of 1-BPy-Pd for the Suzuki−Miyaura Coupling Reaction

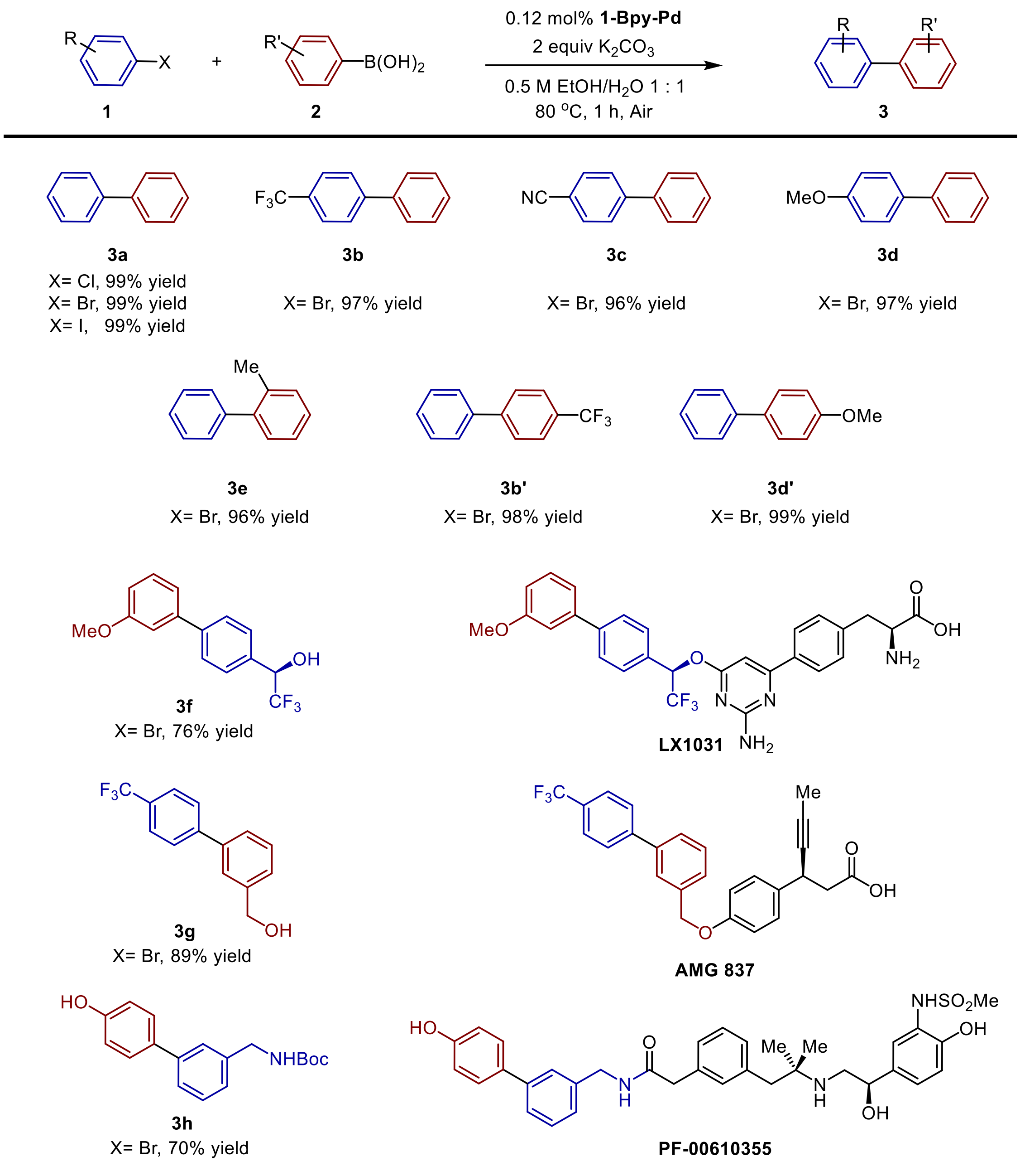


entry	catalyst	reaction scale (mmol)	yield (%)	TON (10^3)
1	**1-BPy-Pd**	1	99[a]	0.8
2	**1-BPy**	1	0	
3	none	1	0	
4	**1-BPy-Pd**	400	98[b]	**200**

[a]Reaction conditions: **1-BPy-Pd** (6 mg, 0.12 mol %), phenylboronic acid (1.5 mmol), aryl bromide (1 mmol), and K_2CO_3 (2 mmol), $EtOH/H_2O$ (1/1) 2 mL, 80 °C, 1 h; **1-BPy-Pd** was used as a powder which can be well dispersed in methanol or ethanol. The morphology of **1-BPy-Pd** particles produced from dispersions in methanol is shown in the SEM image (Figure 2c). The ^{1}H NMR yield and catalytic activity of **1-BPy-Pd** were maintained for up to five cycles tested. [b]Isolated yield.

https://doi.org/10.1021/acsanm.2c04393
ACS Appl. Nano Mater. 2022, 5, 18603−18611

Table 2. Substrate Scope Screening for the Suzuki−Miyaura Coupling Reaction with 1-BPy-Pd as a Catalyst[a]



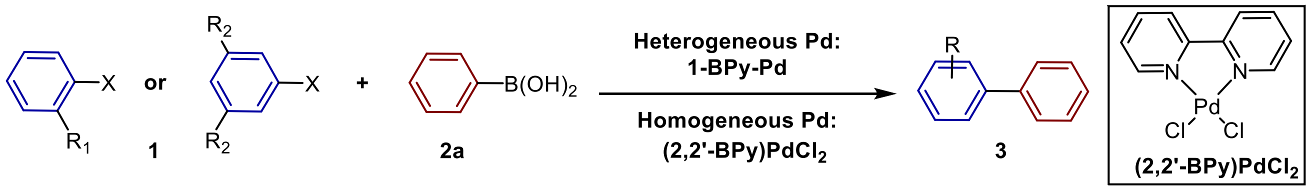
[a]Reaction conditions: **1-BPy-Pd** (6 mg, 0.12 mol %), aryl boronic acid (1.5 mmol), aryl halide (1 mmol), and K_2CO_3 (2 mmol), $EtOH/H_2O$ (1/1) 2 mL, 80 °C, 1−1.5 h, isolated yield.

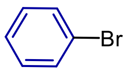
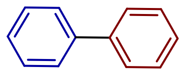
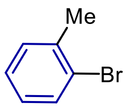
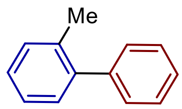
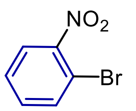
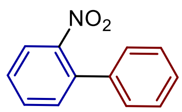
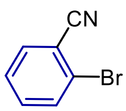
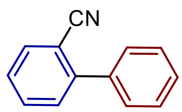
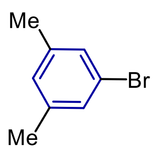
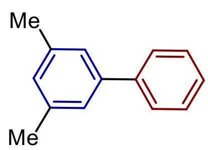
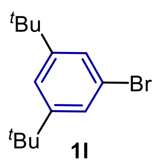
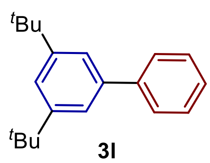
units into the scaffold of the polymer leads to a significant decrease in the surface area and porosity. The morphology of **1-BPy-Pd** particles deposited from methanol was also analyzed by scanning electron microscopy (SEM), and the results in Figure 2c reveal a globular structure.

The oxidation state of palladium and its ligand environment in **1-BPy-Pd** was probed by X-ray photoelectron spectroscopy (XPS). The XPS analysis of Pd 3d binding energy (Pd $3d_{5/2}$ and $3d_{3/2}$) revealed the presence of two intensive doublets at 338.1 and 343.4 eV (Figure 2d), indicating that the valence state of Pd in **1-BPy-Pd** is +2.[47] As detailed in Figure 2e, the binding energy of N 1s in the catalyst precursor **1-BPy** was 398.8 eV. However, the binding energy of N 1s of **1-Bpy-Pd** was shifted to 400.6 eV (Figure 2e), which is attributed to the formation of the Pd-BPy complex.[44,48] The Pd content of **1-BPy-Pd** was determined by inductively coupled plasma mass spectroscopy (ICPMS), and the values are listed in Figure 2f. The loading amount of Pd is consistent with a 96% occupancy of the bipyridine binding sites of the host polymer **1-BPy**.

Catalytic Activity of 1-BPy-Pd for the Suzuki−Miyaura Cross-Coupling Reaction. The catalytic activity of **1-BPy-Pd** was evaluated in the SMC coupling of aryl halides and aryl boronic acids. The Suzuki coupling of phenylboronic acid and aryl bromide in the presence of K_2CO_3 in $EtOH/H_2O$ (1:1) at 80 °C with **1-Bpy-Pd** (0.12 mol %) produced biphenyl in 99% (Table 1, Entry 1). The catalyst was recovered by filtering, washing with methanol and acetone, and drying in a vacuum. The Pd concentration of the recycled catalyst was

Table 3. Size-Selective Suzuki–Miyaura Coupling Reaction Enabled by 1-BPy-Pd as a Heterogeneous Catalyst[a]



Entry	Aryl Bromide	Product	Heterogeneous Catalysis 0.5 mol% **1-BPy-Pd**	Homogeneous Catalysis 0.5 mol% **(2,2'-BPy)PdCl$_2$**
1	 **1a**	 **3a**	99% yield[a]	96% yield[a]
2	 **1e**	 **3e**	**1**% yield[b]	93% yield[a]
3	 **1i**	 **3i**	**2**% yield[b]	69% yield[a]
4	 **1j**	 **3j**	64% yield[a]	90% yield[a]
5	 **1k**	 **3k**	63% yield[a]	91% yield[a]
6	 **1l**	 **3l**	17% yield[a]	71% yield[a]

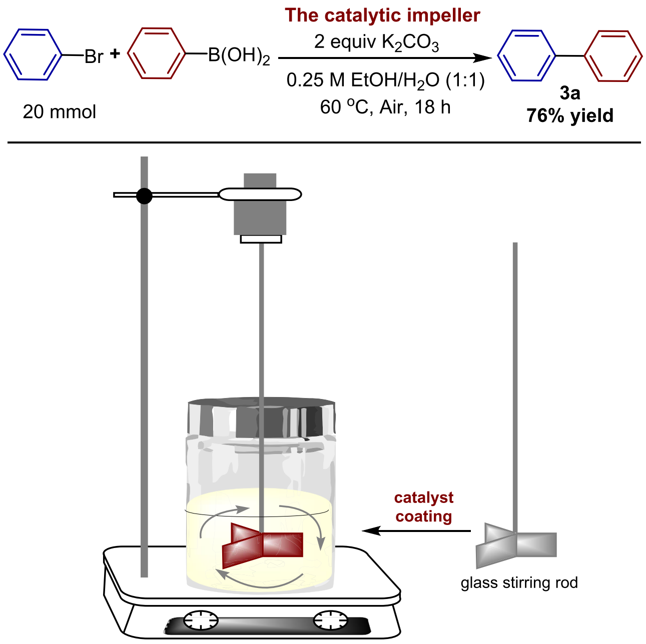
[a]Reaction conditions: **1-BPy-Pd** or **(2,2′-BPy)PdCl$_2$** (0.5 mol %), aryl boronic acid (1.5 mmol), aryl bromide (1 mmol), and K_2CO_3 (2 mmol), $EtOH/H_2O$ (1/1) 2 mL, 80 °C, 1.5 h; (a) isolated yield; (b) GC yield.

then determined by ICPMS and found to be the same as the freshly prepared catalyst. After five consecutive coupling reactions, **1-BPy-Pd** was still capable of promoting the SMC reaction, affording a biphenyl product in 98–99% yield.

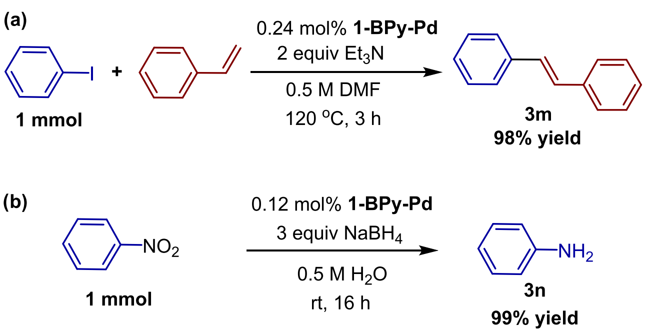
To further confirm the role of this polymer catalyst, a control experiment using the catalyst precursor **1-BPy** was carried out. Even though **1-Bpy** contains a trace amount of Pd from its synthesis (102 ppm by weight), the SMC reaction using this catalyst precursor failed to provide any biphenyl product (Table 1, Entry 2). Another control experiment without using any polymer or Pd resulted in a 0% yield of the biphenyl product. (Table 1, Entry 3). These results prove that bipyridine-Pd complexes embedded into the nanoporous poly(arylene ether) are the catalytic species. To further evaluate the catalytic activity and stability of **1-Bpy-Pd**, a larger-scale SMC reaction was carried out using a 400-fold quantity of reagents employed. The 400 mmol reaction can provide 60.2 g (98% yield) of the biphenyl product only using 10 mg of **1-Bpy-Pd** (Table 1, Entry 4). The turnover number of this polymer catalyst was calculated to be 200k. Compared to the previously reported polymer-immobilized Pd catalyst shown in Supporting Information Table S2, our heterogeneous catalyst has superior TON values. **1-BPy-Pd** has a copolymer support that contains 85 mol % noncatalytic units that provide

https://doi.org/10.1021/acsanm.2c04393
ACS Appl. Nano Mater. 2022, 5, 18603–18611

Scheme 1. Suzuki−Miyaura Cross-Coupling Reaction Using a Catalytic Impeller and Mechanical Stirrer



Scheme 2. 1-Bpy-Pd-Catalyzed (a) Heck Reaction and (b) Reduction of Nitroarenes



nanoporous cavities for the catalytic region. The confined cavities surrounding the catalytic metal centers may contribute to the high catalytic activity and stability.[49−51]

Having identified **1-BPy-Pd** as an efficient heterogeneous SMC catalyst, we set out to examine the substrate scope (Table 2). The results are summarized in Table 2 (**3b-e**, **3b′**, and **3d′**). This heterogeneous SMC reaction displayed good functional group tolerance, and benzyl alcohol (**3f**, **g**), phenol (**3h**), and amide (**3h**) groups were tolerated under the reaction conditions. Coupled units were produced that are intermediates in the synthesis of drugs. LX1031 is a tryptophan hydroxylase inhibitor for the treatment of irritable bowel syndrome.[52] AMG837 is a therapeutic agent that is being investigated for the treatment of type II diabetes.[53] PF-00610355 was developed as a novel inhaled β_2-adrenoreceptor agonist for the treatment of asthma and chronic obstructive pulmonary disease (COPD).[54] This heterogeneous SMC reaction employing easily recyclable **1-Bpy-Pd** as a catalyst provides a practical synthetic route for the preparation of the key intermediates for these pharmaceutical agents. Our heterogeneous Pd catalyst also minimizes the Pd contamination in pharmaceutical manufacturing, which is often a problem for the homogeneous metal-catalyzed reactions.[55,56]

Size-Selective Suzuki−Miyaura Cross-Coupling Reaction. The size-selectivity effects of **1-BPy-Pd** were investigated using several aryl bromides with different size substitutes. **1-BPy-Pd** was used as a heterogeneous catalyst, and (2,2′-BPy)$PdCl_2$ was set as a control (Table 3). The cross-coupling reaction of phenyl bromide and phenylboronic acid affords the biphenyl product in an excellent yield regardless of the Pd catalyst (Table 3, Entry 1). 2-Bromotoluene (**1e**) is considered to be a simple and reactive reactant for the homogeneous SMC reaction.[38] The homogeneous reaction of **1e** using 0.5 mmol % (2,2′-BPy)$PdCl_2$ as a homogeneous catalyst can produce the desired product in 93% yield. However, when 0.5 mmol % **1-BPy-Pd** as a heterogeneous catalyst was used, the reaction of **1e** and phenylboronic acid only produced the desired product in only 1% yield (Entry 2). The recycled **1-BPy-Pd** from the reaction of **1e** maintained high catalytic activity and can be used in the reaction of phenyl bromide to produce the biphenyl product in excellent yield. These results indicate that **1-BPy-Pd** was not deactivated by **1e** and aryl bromides with *ortho*-substitutes are unreactive in this heterogeneous SMC reaction. We reason that the steric hindrance of the *ortho*-substituted methyl group blocks the contact between **1e** and the pore-confined Pd species.

To further identify the size-selective effect of **1-BPy-Pd**, phenyl bromide derivatives with different *ortho*- or *meta*-substitutes were tested in SMC reactions. 1-Bromo-2-nitrobenzene (**1i**) is a highly reactive substrate for the oxidative addition to Pd (0) as a result of the electron-withdrawing nitro group. However, the heterogeneous SMC reaction of **1i** produced the desired product in only a 2% yield, which was much lower than the 69% yield of the homogeneous reaction (Entry 3). When 1-bromo-2-cyanobenzene (**1j**), which contains a smaller *ortho*-substitute than the methyl and nitro groups, was used, the heterogeneous reaction provided the corresponding product **3j** in 63% yield. Hence phenyl bromide derivatives having a bulky *ortho*-substitute have less accessibility to the pore-confined Pd catalyst than those with smaller *ortho*-substitutes. To further investigate the substitution pattern effects, 1-bromo-3,5-dimethylbenzene (**1k**) was used in heterogeneous and homogeneous SMC reactions. A slightly lower isolated yield was obtained in the heterogeneous reaction (Entry 5). In the case of the replacement of **1k** to much bulkier 1-bromo-3,5-di-*tert*-butylbenzene (**1l**), the yield dropped from 71 to 17% for homogeneous (2,2′-BPy)$PdCl_2$ to heterogeneous **1-BPy-Pd**, respectively (Entry 6). These results implied that *meta*-substituted aryl bromides with large-size substitutes are also blocked from the pores containing Pd in the heterogeneous catalyst.

Preparation of the Catalytic Impeller Using Solution-Processable 1-BPy-Pd. We previously reported that solution-processible nanoporous polymers as heterogeneous photocatalysts can be easily processed to be a wide range of known morphologies, including dispersions, films, coatings, textiles, and magnetic nanoparticles.[44] As a demonstration of this utility, **1-BPy-Pd** was coated on the surface of the impeller of the glass stir rod that can be driven by a mechanical stirrer (Supporting Information: 3.2 Suzuki−Miyaura Cross-Coupling Reaction by Using a Catalytic Impeller). A 20 mmol scale SMC reaction was carried out using this mechanical stirrer catalytic impeller to produce the biphenyl product in a good yield (Scheme 1). The catalytic impeller can be removed, and the stirrer can be cleaned easily. The processing of this

https://doi.org/10.1021/acsanm.2c04393
ACS Appl. Nano Mater. 2022, 5, 18603−18611

"semiheterogeneous" catalyst simplifies the use and recovery of heterogeneous catalysts.

Catalytic Activity of 1-BPy-Pd for the Heck Reaction and Reduction of Nitroarenes. To further extend the utility of **1-BPy-Pd**, heterogeneous Heck and nitroarene reactions were investigated. The reaction of iodobenzene with styrene using **1-BPy-Pd** as a heterogeneous catalyst produced the desired product **3m** in 98% yield (Scheme 2a). In addition, nitrobenzene can be reduced to aniline in an excellent yield in the presence of a low-loading polymer catalyst and $NaBH_4$ (Scheme 2b). This heterogeneous reduction can be operated under air at room temperature and in water and thereby conforms to green chemistry principles.[57−59]

■ CONCLUSIONS

In summary, we developed a solution-processable nanoporous poly(arylene ether) (**1-Bpy-Pd**) as a heterogeneous catalyst for the Suzuki−Miyaura coupling (SMC) reaction. The high surface area, covalently linked catalytic sites, good dispersion, and high chemical and physical stability endow this catalyst with excellent catalytic activity and good recyclability for SMC reactions. Turnover numbers of **1-Bpy-Pd** in the SMC reaction up to 200K were observed. In addition, the polymer catalyst enables the size-selective C−C cross-coupling reactions. The aryl bromides with bulky substitution on the *ortho-* or *meta-*positions of the aromatic rings prohibited heterogeneous SMC reactions even though they are good substrates for homogeneous catalytic reactions. A catalytic impeller prepared using solution-processable **1-Bpy-Pd** further facilitated the use and recovery of the heterogeneous catalyst. This work sets the stage for additional advances in size-selective heterogeneous catalysis development.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsanm.2c04393.

Detailed experiment procedures; characteristics of the synthesized biaryl compounds; ^{1}H, ^{13}C, and ^{19}F NMR spectra of the synthesized biaryl compounds; XPS spectra of freshly prepared and recycled 1-BPy-Pd; and SEM images of 1-BPy-Pd (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Timothy M. Swager − *Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States;* orcid.org/0000-0002-3577-0510; Email: tswager@mit.edu

Authors

Sheng Guo − *Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States;* orcid.org/0000-0002-2542-0525

Yifan Wu − *Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States*

Shao-Xiong Lennon Luo − *Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States;* orcid.org/0000-0001-5308-4576

Complete contact information is available at: https://pubs.acs.org/10.1021/acsanm.2c04393

Author Contributions

‡S.G. and Y. W. contributed equally to this work. The manuscript was written through contributions of all authors.

Notes

The authors declare the following competing financial interest(s): A patent has been filed.

■ ACKNOWLEDGMENTS

This research was supported by the National Science Foundation DMR-2207299. The authors thank a core center grant P30-ES002109 from the National Institute of Environmental Health Sciences and the National Institutes of Health for ICPMS equipment.

■ REFERENCES

(1) Ludwig, J. R.; Schindler, C. S. Catalyst: Sustainable Catalysis. *Chem* **2017**, *2*, 313−316.

(2) Ganesh, K. N.; Zhang, D.; Miller, S. J.; Rossen, K.; Chirik, P. J.; Kozlowski, M. C.; Zimmerman, J. B.; Brooks, B. W.; Savage, P. E.; Allen, D. T.; Voutchkova-Kostal, A. M. Green Chemistry: A Framework for a Sustainable Future. *Environ. Sci. Technol. Lett.* **2021**, *8*, 487−491.

(3) Kate, A.; Sahu, L. K.; Pandey, J.; Mishra, M.; Sharma, P. K. Green catalysis for chemical transformation: The need for the sustainable development. *Curr. Opin. Green Sustainable Chem.* **2022**, *5*, No. 100248.

(4) García-Serna, J.; Piñero-Hernanz, R.; Durán-Martín, D. Inspirational perspectives and principles on the use of catalysts to create sustainability. *Catal. Today* **2022**, *387*, 237−243.

(5) Friend, C. M.; Xu, B. Heterogeneous Catalysis: A Central Science for a Sustainable Future. *Acc. Chem. Res.* **2017**, *50*, 517−521.

(6) Török, B.; Schäfer, C.; Kokel, A. Chapter 1 - Heterogeneous catalysis for organic synthesis: Historical background and fundamentals. In *Heterogeneous Catalysis in Sustainable Synthesis*; Török, B.; Schäfer, C.; Kokel, A., Eds.; Elsevier, 2022; pp 1−21.

(7) Piermatti, O.; Abu-Reziq, R.; Vaccaro, L. Strategies to Immobilized Catalysts. *Catal. Immobilization* **2020**, 1−22.

(8) Itsuno, S.; Haraguchi, N. Catalysts Immobilized onto Polymers. *Catal. Immobilization* **2020**, 23−75.

(9) Zhang, Y.; Riduan, S. N. Functional porous organic polymers for heterogeneous catalysis. *Chem. Soc. Rev.* **2012**, *41*, 2083−2094.

(10) Osako, T.; Ohtaka, A.; Uozumi, Y. Development of Polymer-Supported Transition-Metal Catalysts and Their Green Synthetic Applications. *Catal. Immobilization* **2020**, 325−368.

(11) Zhou, Y.-B.; Zhan, Z.-P. Conjugated Microporous Polymers for Heterogeneous Catalysis. *Chem. Asian J.* **2018**, *13*, 9−19.

(12) Bhanja, P.; Sharma, S. K.; Chongdar, S.; Paul, B.; Bhaumik, A. Bifunctional crystalline microporous organic polymers: Efficient heterogeneous catalysts for the synthesis of 5-hydroxymethylfurfural. *Mol. Catal.* **2021**, *515*, No. 111877.

(13) Li, H.; Xu, B.; Liu, X.; A, S.; He, C.; Xia, H.; Mu, Y. A metallosalen-based microporous organic polymer as a heterogeneous carbon−carbon coupling catalyst. *J. Mater. Chem. A* **2013**, *1*, 14108−14114.

(14) Li, B.; Guan, Z.; Yang, X.; Wang, W. D.; Wang, W.; Hussain, I.; Song, K.; Tan, B.; Li, T. Multifunctional microporous organic polymers. *J. Mater. Chem. A* **2014**, *2*, 11930−11939.

(15) Xu, W.; Liu, C.; Xiang, D.; Luo, Q.; Shu, Y.; Lin, H.; Hu, Y.; Zhang, Z.; Ouyang, Y. Palladium catalyst immobilized on functionalized microporous organic polymers for C−C coupling reactions. *RSC Adv.* **2019**, *9*, 34595−34600.

(16) Kaur, P.; Hupp, J. T.; Nguyen, S. T. Porous Organic Polymers in Catalysis: Opportunities and Challenges. *ACS Catal.* **2011**, *1*, 819−835.

(17) Lu, S.; Hu, Y.; Wan, S.; McCaffrey, R.; Jin, Y.; Gu, H.; Zhang, W. Synthesis of Ultrafine and Highly Dispersed Metal Nanoparticles Confined in a Thioether-Containing Covalent Organic Framework and Their Catalytic Applications. *J. Am. Chem. Soc.* **2017**, *139*, 17082−17088.
(18) Zhang, F.; Liang, C.; Wu, X.; Li, H.; Nanospherical, A. Ordered Mesoporous Lewis Acid Polymer for the Direct Glycosylation of Unprotected and Unactivated Sugars in Water. *Angew. Chem., Int. Ed.* **2014**, *53*, 8498−8502.
(19) Wei, Y.; Mao, Z.; Li, Z.; Zhang, F.; Li, H. Aerosol-Assisted Rapid Fabrication of a Heterogeneous Organopalladium Catalyst with Hierarchical Bimodal Pores. *ACS Appl. Mater. Interfaces* **2018**, *10*, 13914−13923.
(20) Das, P.; Linert, W. Schiff base-derived homogeneous and heterogeneous palladium catalysts for the Suzuki−Miyaura reaction. *Coord. Chem. Rev.* **2016**, *311*, 1−23.
(21) Ding, S.-Y.; Gao, J.; Wang, Q.; Zhang, Y.; Song, W.-G.; Su, C.-Y.; Wang, W. Construction of Covalent Organic Framework for Catalysis: Pd/COF-LZU1 in Suzuki−Miyaura Coupling Reaction. *J. Am. Chem. Soc.* **2011**, *133*, 19816−19822.
(22) Esteban, N.; Ferrer, M. L.; Ania, C. O.; de la Campa, J. G.; Lozano, A. E.; Alvarez, C.; Miguel, J. A. Porous Organic Polymers Containing Active Metal Centers for Suzuki-Miyaura Heterocoupling Reactions. *ACS Appl. Mater. Interfaces* **2020**, *12*, 56974−56986.
(23) Wang, Z.; Reddy, C. B.; Zhou, X.; Ibrahim, J. J.; Yang, Y. Phosphine-Built-in Porous Organic Cage for Stabilization and Boosting the Catalytic Performance of Palladium Nanoparticles in Cross-Coupling of Aryl Halides. *ACS Appl. Mater. Interfaces* **2020**, *12*, 53141−53149.
(24) Kim, S.; Kim, B.; Dogan, N. A.; Yavuz, C. T. Sustainable Porous Polymer Catalyst for Size-Selective Cross-Coupling Reactions. *ACS Sustainable Chem. Eng.* **2019**, *7*, 10865−10872.
(25) Zhuang, Q.; Gao, R.; Shi, M.; Lin, X.; Xie, A.; Dong, W. Confining Palladium Nanoparticles in Microporous Tetrastyrene Polymer Enables Efficient Size-Selective Heterogeneous Catalysis. *ACS Appl. Nano Mater.* **2021**, *4*, 3869−3876.
(26) Wang, Z. J.; Ghasimi, S.; Landfester, K.; Zhang, K. A. I. Photocatalytic Suzuki Coupling Reaction Using Conjugated Microporous Polymer with Immobilized Palladium Nanoparticles under Visible Light. *Chem. Mater.* **2015**, *27*, 1921−1924.
(27) Zhang, C.; Wang, J.-J.; Liu, Y.; Ma, H.; Yang, X.-L.; Xu, H.-B. Main-Chain Organometallic Microporous Polymers Based on Triptycene: Synthesis and Catalytic Application in the Suzuki−Miyaura Coupling Reaction. *Chem. − Eur. J.* **2013**, *19*, 5004−5008.
(28) Zhang, Q.; Yang, Y.; Zhang, S. Novel Functionalized Microporous Organic Networks Based on Triphenylphosphine. *Chem. − Eur. J.* **2013**, *19*, 10024−10029.
(29) Li, B.; Guan, Z.; Wang, W.; Yang, X.; Hu, J.; Tan, B.; Li, T. Highly Dispersed Pd Catalyst Locked in Knitting Aryl Network Polymers for Suzuki−Miyaura Coupling Reactions of Aryl Chlorides in Aqueous Media. *Adv. Mater.* **2012**, *24*, 3390−3395.
(30) Song, Q.; Jia, Y.; Luo, B.; He, H.; Zhi, L. Covalently Stabilized Pd Clusters in Microporous Polyphenylene: An Efficient Catalyst for Suzuki Reactions Under Aerobic Conditions. *Small* **2013**, *9*, 2460−2465.
(31) Wang, C.-A.; Zhao, W.; Li, Y.-W.; Han, Y.-F.; Zhang, J.-P.; Li, Q.; Nie, K.; Chang, J.-G.; Liu, F.-S. The bulky Pd-PEPPSI-embedded conjugated microporous polymer-catalyzed Suzuki−Miyaura cross-coupling of aryl chlorides and arylboronic acids. *Polym. Chem.* **2022**, *13*, 1547−1558.
(32) Ogasawara, S.; Kato, S. Palladium Nanoparticles Captured in Microporous Polymers: A Tailor-Made Catalyst for Heterogeneous Carbon Cross-Coupling Reactions. *J. Am. Chem. Soc.* **2010**, *132*, 4608−4613.
(33) Xu, S.; Song, K.; Li, T.; Tan, B. Palladium catalyst coordinated in knitting N-heterocyclic carbene porous polymers for efficient Suzuki−Miyaura coupling reactions. *J. Mater. Chem. A* **2015**, *3*, 1272−1278.
(34) Wen, Q.; Zhou, T.-Y.; Zhao, Q.-L.; Fu, J.; Ma, Z.; Zhao, X. A Triptycene-Based Microporous Organic Polymer Bearing Tridentate Ligands and Its Application in Suzuki−Miyaura Cross-Coupling Reaction. *Macromol. Rapid Commun.* **2015**, *36*, 413−418.
(35) Dong, W.; Zhang, L.; Wang, C.; Feng, C.; Shang, N.; Gao, S.; Wang, C. Palladium nanoparticles embedded in metal−organic framework derived porous carbon: synthesis and application for efficient Suzuki−Miyaura coupling reactions. *RSC Adv.* **2016**, *6*, 37118−37123.
(36) Zhang, L.; Feng, C.; Gao, S.; Wang, Z.; Wang, C. Palladium nanoparticle supported on metal−organic framework derived N-decorated nanoporous carbon as an efficient catalyst for the Suzuki coupling reaction. *Catal. Commun.* **2015**, *61*, 21−25.
(37) Zhang, L.; Dong, W.-H.; Shang, N.-Z.; Feng, C.; Gao, S.-T.; Wang, C. N-Doped porous carbon supported palladium nanoparticles as a highly efficient and recyclable catalyst for the Suzuki coupling reaction. *Chin. Chem. Lett.* **2016**, *27*, 149−154.
(38) Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457−2483.
(39) Beletskaya, I. P.; Alonso, F.; Tyurin, V. The Suzuki-Miyaura reaction after the Nobel prize. *Coord. Chem. Rev.* **2019**, *385*, 137−173.
(40) Chen, D.; Wei, L.; Yu, Y.; Zhao, L.; Sun, Q.; Han, C.; Lu, J.; Nie, H.; Shao, L.-X.; Qian, J.; Yang, Z. Size-Selective Suzuki−Miyaura Coupling Reaction over Ultrafine Pd Nanocatalysts in a Water-Stable Indium−Organic Framework. *Inorg. Chem.* **2022**, *61*, 15320.
(41) Saggiomo, V. 3D Printed Devices for Catalytic Systems. *Catal. Immobilization* **2020**, 369−408.
(42) Biniaz, P.; Makarem, M. A.; Rahimpour, M. R. Membrane Reactors. *Catal. Immobilization* **2020**, 307−324.
(43) Zhou, X.; Wang, Z.; Yu, B.; Kuang, S.; Sun, W.; Yang, Y. Highly efficient Markovnikov hydroaminocarbonylation of alkenes and alkynes catalyzed by a "soluble" heterogeneous Pd catalyst. *Green Chem.* **2022**, *24*, 4463−4469.
(44) Liu, R. Y.; Guo, S.; Luo, S.-X. L.; Swager, T. M. Solution-processable microporous polymer platform for heterogenization of diverse photoredox catalysts. *Nat. Commun.* **2022**, *13*, No. 2775.
(45) Guo, S.; Swager, T. M. Versatile Porous Poly(arylene ether)s via Pd-Catalyzed C−O Polycondensation. *J. Am. Chem. Soc.* **2021**, *143*, 11828−11835.
(46) Guo, S. Y.; Benedetti, J.; Syar, F.; Swager, D.; Smith, T.; Z A Microporous Poly(arylene ether) Platform for Membrane-Based Gas Separation. In *ChemRxiv* Apr 18 2022 DOI: 10.26434/chemrxiv-2022-2496w-v2 (accessed 2022-6-30).
(47) Guan, Z.; Hu, J.; Gu, Y.; Zhang, H.; Li, G.; Li, T. $PdCl_2(Py)_2$ encaged in monodispersed zeolitic hollow spheres: a highly efficient and reusable catalyst for Suzuki−Miyaura cross-coupling reaction in aqueous media. *Green Chem.* **2012**, *14*, 1964−1970.
(48) Muniz-Miranda, M.; Muniz-Miranda, F.; Caporali, S.; Calisi, N.; Pedone, A. SERS, XPS and DFT investigation on palladium surfaces coated with 2,2′-bipyridine monolayers. *Appl. Surf. Sci.* **2018**, *457*, 98−103.
(49) Jin, Y.; Zhang, Q.; Zhang, Y.; Duan, C. Electron transfer in the confined environments of metal−organic coordination supramolecular systems. *Chem. Soc. Rev.* **2020**, *49*, 5561−5600.
(50) Hong, C. M.; Bergman, R. G.; Raymond, K. N.; Toste, F. D. Self-Assembled Tetrahedral Hosts as Supramolecular Catalysts. *Acc. Chem. Res.* **2018**, *51*, 2447−2455.
(51) Zhao, L.; Jing, X.; Li, X.; Guo, X.; Zeng, L.; He, C.; Duan, C. Catalytic properties of chemical transformation within the confined pockets of Werner-type capsules. *Coord. Chem. Rev.* **2019**, *378*, 151−187.
(52) Zhao, M. M.; Zhang, H.; Iimura, S.; Bednarz, M. S.; Kanamarlapudi, R. C.; Yan, J.; Lim, N.-K.; Wu, W. Process Development of Tryptophan Hydroxylase Inhibitor LX1031, a Drug Candidate for the Treatment of Irritable Bowel Syndrome. *Org. Process Res. Dev.* **2020**, *24*, 261−273.
(53) Walker, S. D.; Borths, C. J.; DiVirgilio, E.; Huang, L.; Liu, P.; Morrison, H.; Sugi, K.; Tanaka, M.; Woo, J. C. S.; Faul, M. M.

Development of a Scalable Synthesis of a GPR40 Receptor Agonist. *Org. Process Res. Dev.* **2011**, *15*, 570−580.
(54) de Koning, P. D.; Castro, N.; Gladwell, I. R.; Morrison, N. A.; Moses, I. B.; Panesar, M. S.; Pettman, A. J.; Thomson, N. M. Development of a Potential Manufacturing Route to PF-00610355: A Novel Inhaled β_2-Adrenoreceptor Agonist. *Org. Process Res. Dev.* **2011**, *15*, 1256−1265.
(55) Balaram, V. Recent advances in the determination of elemental impurities in pharmaceuticals – Status, challenges and moving frontiers. *TrAC, Trends Anal. Chem.* **2016**, *80*, 83−95.
(56) Pagliaro, M.; Pandarus, V.; Ciriminna, R.; Béland, F.; DemmaCarà, P. Heterogeneous versus Homogeneous Palladium Catalysts for Cross-Coupling Reactions. *ChemCatChem* **2012**, *4*, 432−445.
(57) Chen, T.-L.; Kim, H.; Pan, S.-Y.; Tseng, P.-C.; Lin, Y.-P.; Chiang, P.-C. Implementation of green chemistry principles in circular economy system towards sustainable development goals: Challenges and perspectives. *Sci. Total Environ.* **2020**, *716*, No. 136998.
(58) Anastas, P.; Eghbali, N. Green Chemistry: Principles and Practice. *Chem. Soc. Rev.* **2010**, *39*, 301−312.
(59) Zimmerman, J. B.; Anastas, P. T.; Erythropel, H. C.; Leitner, W. Designing for a green chemistry future. *Science* **2020**, *367*, 397−400.

https://doi.org/10.1021/acsanm.2c04393
ACS Appl. Nano Mater. 2022, 5, 18603−18611