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Synthesis of cycloparaphenylene under spatial nanoconfinement

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ABSTRACT

Suzuki coupling reactions between symmetrical monomers were conducted in various mesoporous silica nanoreactors grafted with palladium catalysts, enabling the selective formation of [12]cycloparaphenylene precursor with separate yield up to 25% in one-pot reactions, much higher than that in homogeneous reaction. The spatial nanoconfinement of the nanoreactors promotes the macrocyclization while limits the concomitant linear oligomer formation, offering more possibilities for the synthesis of macrocycles from symmetrical monomers in one-pot reaction.

Enzymes are biological catalysts with multiple compartmentalized cavities where chemical and biological reactions take place efficiently and selectively. Great scientific efforts have been attracted to mimic this process by conducting various kinds of reactions in nanocavities [1–3]. Rebek *et al.* reported a molecular container with deep cavity [4], where the guest molecules have curved conformations and end groups closer together [5]. This molecular container has been successfully used in many selective macrocyclizations [6–8]. Recently, Buchmeiser *et al.* reported that the immobilization of catalysts inside mesoporous silica allows the full utilization of confinement effect in olefin ring-closing metathesis (RCM), which is similar to the selectivity of enzymes in improving macrocyclization and suppressing oligomerization [9–11].

[n]Cycloparaphenylenes ([n]CPP, where n is the number of phenylene group) can be envisioned as the smallest macrocyclic slices of carbon nanotubes and have attracted significant scientific interests in recent years [12,13]. The conception of [n]CPP was proposed by Parekh and Guha in 1934 [14]. More than seventy years passed until Jasti and Bertozzi synthesized [9]CPP, [12]CPP, and [18]CPP from the less-strained macrocyclic precursors in 2008 (Scheme 1, top) [15]. The key to success is that the L-shaped cyclohexadiene unit is able to alleviate ring strain and serves as masked benzene units. This method however suffers from lack of control over the ring size and rather low yields of the desired CPPs. Alternative strategies were reported to resolve these issues, relying on large excess monomer ratio [16,17] and stepwise macrocyclization [18,19].

In the past few years, our group synthesized various kinds of confined nanoreactors, which were supported by mesoporous silica, such as SBA-15, MCM-41 and DMSNs. These nanoreactors showed good control over the size of conjugated polymer nanoparticles and molecular weight (and distribution) of linear conjugated polymers [20–23]. Similar to enzymes, in such nanoreactors, the confined space can create highly substrate specific reaction sites and controlled substrate conformation [4,10,24,25].

Herein we report a new method of selective synthesis of CPP with [12]macrocycle yield of up to 25% (Scheme 1, below), an increase of 150% in the yield from homogenous catalysis with $Pd(PPh_3)_4$ as the catalyst. The synthesis is based on Suzuki coupling reactions using tailored catalyst which was prepared by selective loading of palladium(II) *N*-heterocyclic carbene complex (NHC-Pd) [23] in the internal surface of mesoporous SBA-15 channels. The preparation of the nanoreactor is depicted in Scheme S1 (Supporting information). Briefly, the mesopores of SBA-15 was firstly filled with a PEO-PPO-PEO triblock copolymer (P123) to protect the internal hydroxyl groups. The external hydroxy groups were then capped with 1,1,1,3,3,3-hexamethyldisilazane (HMDS). After removal of the P123 protection and exposure of the internal hydroxy groups by Soxhlet extraction, the Pd species were introduced into the nanopores in two ways. For NHC-Pd@SBA-15, it was obtained by direct coupling reaction between NHC-Pd (with siloxy group) and hydroxyl groups in the nanopores. On the other hand, amino groups were introduced into the nanopores to further bind palladium complexes followed by reduction, resulted in Pd@SBA-15-NH_2 (Scheme 2). For comparison, SBA-15 was replaced by two

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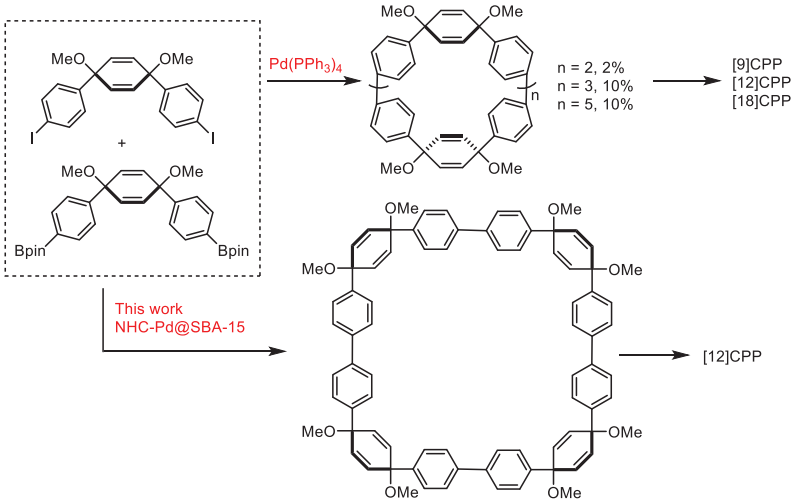
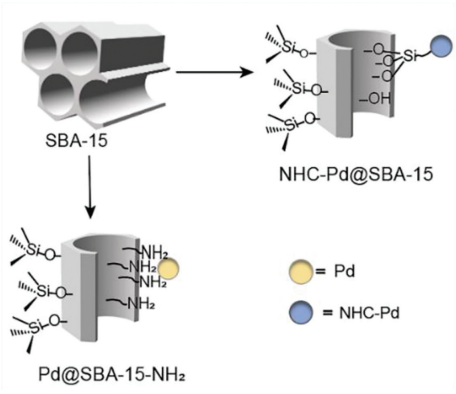


Scheme 1. Synthetic routes used to access [n]CPPs.



Scheme 2. Schematic illustration of the preparation of NHC-Pd@SBA-15 and Pd@SBA-15-NH_2.

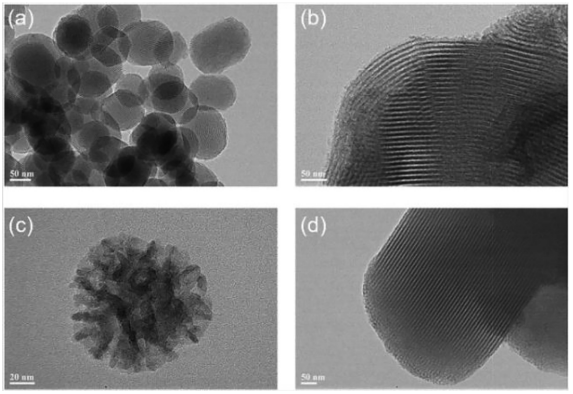


Fig. 1. TEM images of (a) Pd@MCM-41-NH_2; (b) Pd@SBA-15-NH_2; (c) Pd@DMSNs-NH_2 and (d) NHC-Pd@SBA-15.

mesoporous silicon materials with different morphologies, namely MCM-41 with smaller cylindrical pores and DMSNs with semi-open dendritic pores. Following similar preparation processes, using MCM-41 and DMSNs as supporting materials, four kinds of nanoreactors including NHC-Pd@MCM-41, Pd@MCM-41-NH_2, NHC-Pd@DMSNs and Pd@DMSNs-NH_2 were prepared to investigate the effect of pore size and morphology on the confined Suzuki coupling reaction.

The pore sizes, determined by Brunner–Emmet–Teller (BET) method, were 3 nm, 7 nm and 12 nm for MCM-41, SBA-15 and DMSNs supported mesoporous palladium nanoreactors, respectively (Table S1 in Supporting information). The Pd loadings determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES) were between 0.25% and 1.4 wt% (Table S1). This difference is caused by the difference in morphology and preparation processes. Negligible Pd leaching and good recycling and reusing characteristics have been demonstrated by our previous studies [20,22,23].

Fig. 1 shows the transmission electron microscopy (TEM) images of the catalysts. The regular lattice fringes and the hexagonal channels of SBA-15 and MCM-41 remained intact after the reaction. Semi-open dendritic structures of DMSNs also remained intact. The palladium in the pore is well-dispersed and no palladium was found on the outer surface of the mesoporous silicon. A verification experiment by Suzuki cross-coupling reaction between highly reactive difunctional and tetrafunctional monomers (A2 + B4) combinations was designed to further validate the exclusive embedding of Pd on the internal surface of the mesoporous silica supports. If any palladium species presents on the outer surface of these catalysts, the formation of insoluble polymeric gel would be observed. Encouragingly, with all of these nanoreactors as catalyst, soluble polymeric products were obtained even after prolonged reaction time with complete monomer conversion (see Supporting information), suggesting that the palladium species were embedded in the confined nanochannles selectively.

The Suzuki cross-coupling/macrocyclization between the symmetrical diiodo- and diboronate monomers were performed in *N,N*-dimethylacetamide (DMAc) with K_2CO_3 as the base and the above 6 nanoreactors as the catalysts, respectively. [12]Macrocycle as the major product was separated by column chromatography. Encouragingly, using 2.5 mol% NHC-Pd@SBA-15 as the catalyst, the yield of [12]macrocycle was 25% (Table 1, entry 3), much higher than that in a homogenous reaction (8% under the same condition). Meanwhile, Pd@SBA-15-NH_2 gave an increased yield of 17%. The reaction time of heterogeneous reactions is longer than that of homogeneous reactions as the localization of catalysts on the porous support resulted in less chance of the monomers to collide with the reactive catalyst [26]. In the case of Pd@SBA-15-NH_2 as the catalyst, the monomers were completely consumed in seven days, slightly longer than that of NHC-Pd@SBA-15, suggesting that the catalytic activity of NHC-Pd complex was higher than that of Pd nanoparticles in confined nanoreactor.

Table 1
Comparison of the catalytic performances of different nanoreactors.

Catalyst	Time	Yield of [12]macrocycle (%)
$Pd(PPh_3)_4$	16 h	8 (10)*
Pd@SBA-15-NH_2	7 days	17
NHC-Pd@SBA-15	5 days	25
Pd@MCM-41-NH_2	7 days	5
NHC-Pd@MCM-41	6 days	5
Pd@DMSNs-NH_2	7 days	9
NHC-Pd@DMSNs	5 days	10

* Reported by Bertozzi *et al.* [15].

It should be noted that high monomer concentration (125 mmol/L in this work) is typically considered as detrimental to macrocyclization [27]. We speculate that the higher yield of [12]macrocycle obtained with NHC-Pd@SBA-15 is due to the confinement effect that affects the configuration and diffusion rate of the substrate [11,28]. In the competition between macrocyclization and linear polymerization, confined space is favorable for the macrocyclization and unfavorable for the linear growth. The diameters of the optimized structures of [6]macrocycle, [12]macrocycle and [18]macrocycle were calculated to be 1.35, 2.22 and 3.21 nm, respectively (Fig. S8 in Supporting information). According to the reconstruction−simulation of SBA-15, diffusion is hindered when the molecular size is larger than one third of the pore size of SBA-15 [26]. Altogether, the pore size of the nanoreactors matched well with the size of [12]macrocycle and favored the selective formation of [12]macrocycle. Compared with the homogeneous catalyst, the Pd catalysts embedded in MCM-41 support gave reduced yield of [12]macrocycle. It is reasonable since the pore size of MCM-41 (3 nm) is only slightly larger than the diameter of [12]macrocycle, which is not conducive to the diffusion of the precursor to the catalytic site and further backfolding for the macrocyclization. On the other hand, the DMSNs supported nanoreactors showed similar [12]macrocycle selectivity as that in a homogenous reaction, probably due to the large pore size (12 nm) showing no confinement effect during the competition between linear chain formation and macrocyclization.

In summary, the Suzuki macrocyclization was promoted for the synthesis of [12]CPP precursor with much higher yield by selective introduction of catalysts into size-tailored nanoreactors, allowing for the full utilization of nanoconfinement effect. This approach offers a direct, highly selective strategy for the synthesis of macrocyclic molecules from symmetrical monomers in one-pot reaction.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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