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RESEARCH ARTICLE

Roles of Divinylbenzene Co-cross-linker in a Threefold Cross-linked Polystyrene–Phosphine Hybrid Monolith: Impact of Cross-linking Degree on Catalytic Performance

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Abstract: Continuous-flow organic transformations using immobilized catalysts are crucial for green and sustainable chemistry. Cross-linked polymer ligands offer high stability, ease of recovery through filtration, and thus enhance performance in continuous-flow reactions via transition-metal catalysis. Additionally, the cross-linking structure of the polymer support creates a unique reaction platform that controls the coordination behavior of the supported ligands and stabilizes the metal catalysts. However, insights into the material-based design for preparing highly active and durable immobilized metal catalysts are still limited. In this report, we propose a straightforward approach to boost both selective mono-coordination and effective stabilization of metal complexes. We developed threefold cross-linked polystyrene-triphenylphosphine hybrid monoliths with cross-linking structures adjusted by varying the content of divinylbenzene as co-cross-linker. The coordination behaviors and metal-support interactions of these monoliths were evaluated, highlighting the importance of co-cross-linker content in site-isolating phosphine units and stabilizing metal centers via arene-metal interactions on the polystyrene network. By optimizing the cross-linking structure, the monolith catalysts demonstrated exceptionally high catalytic activity and durability in Pd-catalyzed C-Cl transformations, such as Suzuki-Miyaura cross-couplings and Buchwald-Hartwig aminations in continuous flow. This underscores the utility of our monolith system in challenging transition-metal catalysis.

Introduction

With the increasing demand for environmentally benign chemical processes, immobilized catalysts have garnered significant attention for organic transformations.[1] These catalysts offer the advantages of easy separation from products, as well as recovery and reuse, which helps reduce process costs related to waste, energy, and time. Moreover, continuous-flow operation allows for automation, on-demand production, easy scale-up, and safe reaction system.[2] Consequently, continuous-flow organic syntheses using immobilized catalysts are well-suited for green and sustainable chemistry.

Polymer-supported ligands are valuable materials for creating immobilized metal catalysts due to their insolubility in reaction mixtures. From a practical perspective, cross-linking polymeric ligands enhances stability and allows for easy recovery through simple filtration,[3] and also enables application to continuous-flow systems.[4] The cross-linking structure not only creates a heterogenized catalytic system by linking polymer chains but also provides a unique reaction space within the cross-linked network.[5] It has been reported that highly cross-linked polymer chains around Pd catalysts effectively prevented Pd from leaching and aggregating, resulting in high catalytic durability.[6] These studies highlight the critical importance of interactions between

metal centers and polymer supports for metal stabilization and hence high catalytic durability.

Recently, we have developed threefold cross-linked polystyrene-triphenylphosphine hybrid monoliths (**M-PS-TPP**) for applications to Pd-catalyzed cross-couplings of chloroarenes, both in batch[7] and continuous flow.[7] It has been revealed that simply varying cross-linking degree based on the contents of co-cross-linker (divinylbenzene, DVB) significantly modulated the coordination behaviors of the **M-PS-TPP**.[7] Our straightforward, material-based strategy proved effective for creating highly active metal complexes. However, the impact of the cross-linking degree on catalytic durability remained unclear. This prompted us to optimize the **M-PS-TPP** system to boost both controlled coordination and metal stabilization, which would expand its applicability to continuous-flow reactions via challenging transition-metal catalysis.

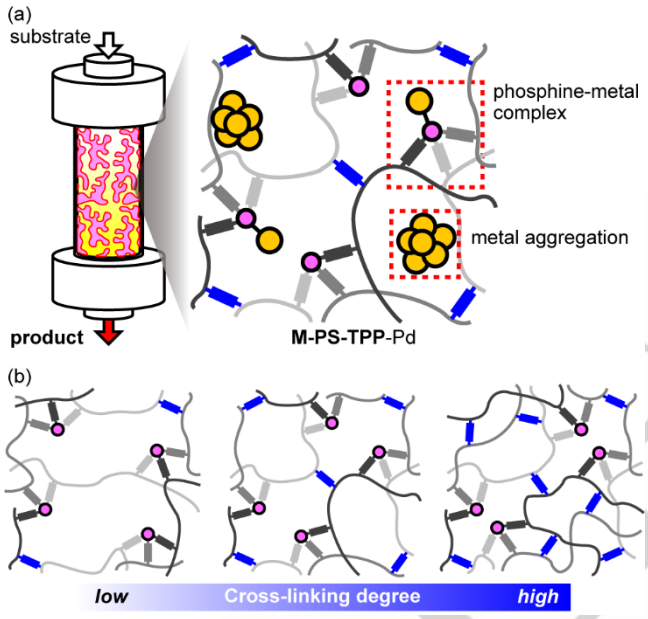


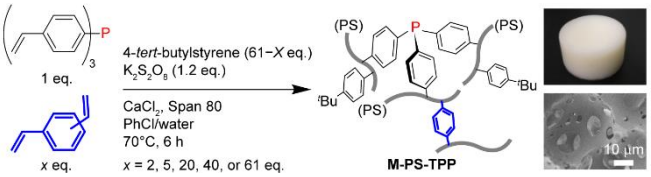
Figure 1. (a) Scheme of the porous polystyrene-phosphine hybrid monolith catalyst (**M-PS-TPP**-Pd) for continuous-flow transition-metal catalysis. The polystyrene chains (gray lines) are connected by threefold cross-linking triphenylphosphine (pink balls) and DVB-co-cross-linker (blue junctions). The supported phosphine coordinates with Pd (yellow balls) to form an active phosphine-metal complex. During catalytic reactions, some metal atoms may aggregate into less active species. (b) The variation of cross-linking structure of the **M-PS-TPP** based on the feed ratio of the DVB-co-cross-linker, which control the coordination behavior and metal aggregation.

Herein, we report a simple strategy for developing polymer-supported phosphine-metal complexes that enables selective coordination and effective stabilization of metal catalysts through modulation of their cross-linking structure (Figure 1). To investigate the effects of cross-linking structure, a series of **M-PS-TPP** was prepared by varying cross-linking degree through changing the feed ratio of the DVB as the co-cross-linker. Coordination of **M-PS-TPP** with Pd^{II} complex was evaluated to assess the selectivity for mono-P-ligation. Continuous-flow cross-couplings were performed using Pd-loaded **M-PS-TPP** (**M-PS-TPP**-Pd) to evaluate their performance in transition-metal catalysis. Through the optimization of the cross-linking degree, we successfully developed a highly active and durable **M-PS-TPP**-Pd system with selective mono-P-ligation behavior and effective stabilization of metal catalysts. In fact, the **M-PS-TPP**-Pd effectively catalyzed challenging transformations such as Suzuki-Miyaura cross-coupling and Buchwald-Hartwig amination in continuous-flow systems. These successful applications demonstrated the utility of our simple strategy based on the cross-linking structure of polymer-supported ligands for continuous-flow organic transformations.

Results and Discussion

Synthesis and Characterization of M-PS-TPP

The highly porous polystyrene-phosphine hybrid monolith (**M-PS-TPP**) was synthesized using a high-internal phase emulsion (HIPE) system, as previously reported (Scheme 1).[7] Organic phase containing threefold cross-linkable triphenylphosphine (1 eq.), DVB (*x* eq.), 4-*tert*-butylstyrene (61−*x* eq.), and Span 80 (surfactant) were emulsified with aqueous phase containing $CaCl_2$ (electrolyte) and $K_2S_2O_8$ (radical initiator). The volume ratio of aqueous phase to organic phase was 90:10 v/v. To control the cross-linking degree of the **M-PS-TPP**s, the feed ratio of DVB as the co-cross-linker was varied to be *x* = 2, 5, 20, 40, and 61 eq. The resulting viscous HIPE was cured in a glass vial at 70°C for 6 h. After curing, the cylindrical solid was obtained and washed successively by immersion in THF/water (2:1 v/v) and THF for more than 1 day each. The resulting **M-PS-TPP**s were swollen and self-standing (Scheme 1, inset (top), and Figure S1, insets, see Supporting Information (SI)). The volume of the swollen **M-PS-TPP**s varied and roughly decreased with increasing DVB contents (Table S1). After drying under vacuum at room temperature, white solid polymers were obtained (91–96% dry yield, Table S1). The amount of phosphine incorporated ([P]) was 0.10–0.12 mmol g^{-1} based on the feed ratio of the monomers (Table S1). We attempted to prepare a DVB-free monolith (i.e., *x* = 0 eq.), however, it failed due to insufficient mechanical strength, resulting in a sol-like material.



Scheme 1. Synthesis of **M-PS-TPP**s, photographic (inset, top), and FE-SEM images (inset, bottom) (DVB contents of 5 eq.).

The dried **M-PS-TPP**s were analyzed by field emission-scanning electron microscopy (FE-SEM). Characteristic void and window structures were observed in the monoliths with DVB

contents of 5–61 eq. (Scheme 1, inset (bottom), and Figure S1b–e, see SI). By contrast, the **M-PS-TPP** with the lowest DVB content of 2 eq. possessed a fractured polymer scaffold (Figure S1a). Mercury intrusion porosimetry analysis revealed that the **M-PS-TPP**s with DVB concents of 5–61 eq. exhibited a bimodal pore size distribution, with 1st- and 2nd-mode pore sizes of 7420–13740 and 2990–4390 nm, respectively (Table S2 and Figure S2b–e). On the other hand, the lowest DVB content of 2 eq. showed a monomodal pore size distribution with a 1st-mode pore size of 4350 nm (Table S2 and Figure S2a). These differences were likely due to the collapse of the porous structure during the drying process, where the lower cross-linking degree resulted in more severe structural fractures due to lower mechanical strength. These observations emphasized the necessity to assess the porous properties of swollen **M-PS-TPP**s and their effect on catalytic performance. This relationship will be explored in more detail in the later section.

The ^{31}P cross polarization/magic angle spinning (CP/MAS) nuclear magnetic resonance (NMR) spectra of the **M-PS-TPP**s were recorded (Figures S3a–S7a). In ^{31}P CP/MAS NMR spectra, peaks were observed at chemical shifts (δ_P) of −7–−4 ppm, corresponding to coordinatively active triphenylphosphine. Additionally, peaks at δ_P of 24–25 ppm were present in some **M-PS-TPP**s, attributed to triphenylphosphine oxide, resulting from partial oxidation of the P atom during preparation.[7] Little differences among the δ_P indicated that cross-linking degree did not potentially influence on the electronic nature of the supported triphenylphosphine.

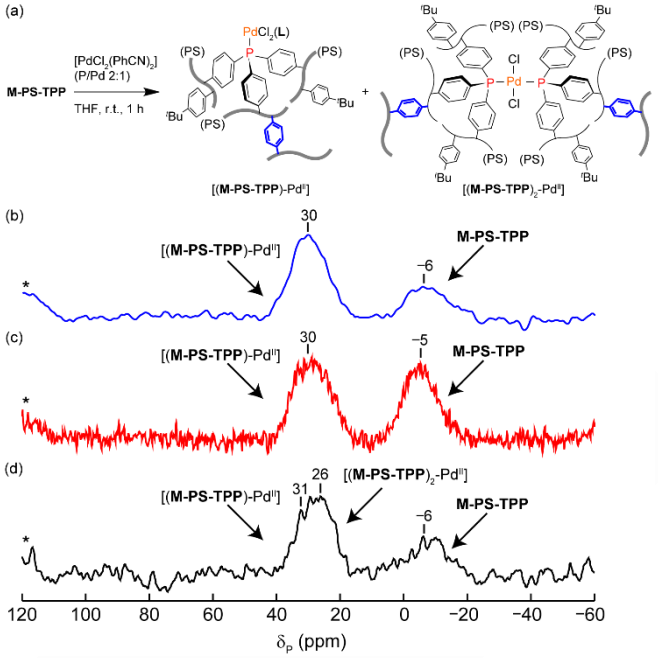


Figure 2. (a) Coordination between **M-PS-TPP** and $[PdCl_2(PhCN)_2]$ (P/Pd 2:1; L = PhCN or solvent). ^{31}P CP/MAS NMR spectra obtained from the **M-PS-TPP**-Pd with the DVB contents of (b) 2, (c) 20,[7] and (d) 61 eq. Asterisks (*) indicate spinning side bands. Some contents of triphenylphosphine oxide on the **M-PS-TPP** were included (δ_P of 24–25 ppm).

Coordination Behavior of M-PS-TPP

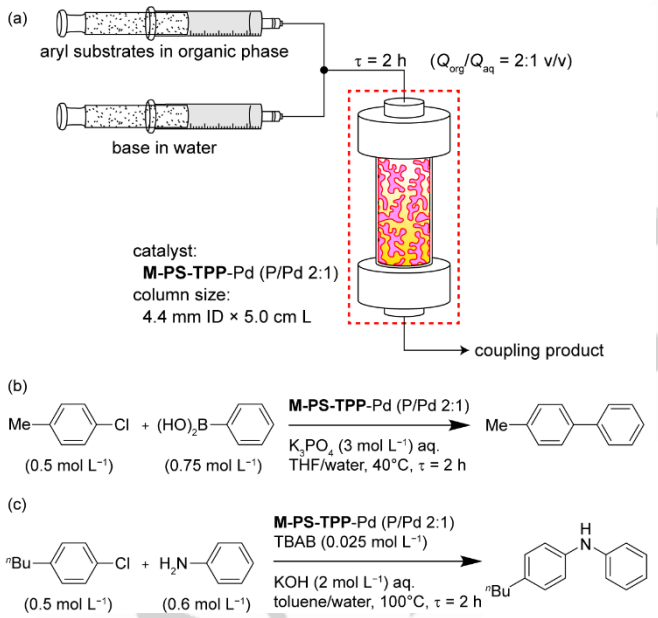
The coordination behaviors of **M-PS-TPP**s toward Pd^{II} were evaluated by ^{31}P CP/MAS NMR analyses. The dried **M-PS-TPP**s were treated with $[PdCl_2(PhCN)_2]$ in THF (P/Pd 2:1) at room temperature for 1 h, resulting in **M-PS-TPP**-Pd as yellow solids (Figure 2a). Inductively coupled plasma-atomic emission spectroscopy (ICP-AES) confirmed no Pd detected in the filtrate of the reaction mixture, corresponding to complete consumption of feed Pd. After the reactions with the Pd^{II} source, new peaks appeared in the ^{31}P CP/MAS NMR spectra of the **M-PS-TPP**-Pd (Figures 2b–d and S3b–S7b, see SI). The **M-PS-TPP**-Pd with DVB contents of 2–20 eq. selectively formulated mono-P-ligated Pd complex (δ_P of 30–32 ppm). By contrast, as the DVB contents increased to 40 eq. or more, peaks attributed to bis-P-ligated Pd complex (δ_P of 24–26 ppm) gradually generated together with that from the mono-ligated complex. The peak intensity for the mono-P-ligation was partially overlapping with that of triphenylphosphine oxide, which was a byproduct formed during the polymerization of the **M-PS-TPP**s. As a result, the ratio of the mono-ligation to the bis-ligation could not be accurately determined due to difficulty in the peak separation.

Successful formation of mono-P-ligated Pd complexes was achieved for **M-PS-TPP**-Pd with lower cross-linking degrees. Previously, we have reported that the mono-P-ligating behaviors of the supported phosphine on polystyrene monoliths were significantly influenced by the cross-linking degree, that is, the existence ratio of mono-coordination to bis-coordination increased with decreasing the DVB contents. This effect was attributed to the differences in site isolation of phosphine units within the heterogeneously cross-linked domains of the polystyrene network.[7] As clearly demonstrated for the DVB contents of 40 and 61 eq., the high cross-linking degree of **M-PS-TPP** resulted in unfavorable domains for the site isolation of the phosphine units. High selectivity for mono-P-ligation consequently would lead to excellent catalytic activity in challenging transition-metal catalysis in continuous-flow conditions.[7]

Catalytic Performance of M-PS-TPP-Pd

A series of **M-PS-TPP** columns was prepared and evaluated for their performance in continuous-flow systems.[8] To evaluate the porosity of the swollen **M-PS-TPP**s ($\varepsilon_{swollen}$), pulse-tracer experiments were performed in a continuous-flow setup (Figures S9–S11, see SI). Notably, the **M-PS-TPP** exhibited a remarkably high $\varepsilon_{swollen}$ (92–99%) with a small tracer (benzene). This suggested that molecular diffusion of reactants through the **M-PS-TPP** was sufficient. Thus, mass transport would not be a limiting factor in the catalytic performance observed in the present study.

To prepare **M-PS-TPP**-Pd columns, $[PdCl_2(PhCN)_2]$ in THF was permeated through the **M-PS-TPP** column (P/Pd 2:1) followed by washing with THF (described in detail in SI). During washing, the concentration of Pd in the eluent was below the detection limit of ICP-AES (< 10 ppb). The Pd loading in the **M-PS-TPP**-Pd was estimated to be 0.05–0.06 mmol g^{-1} (P/Pd 2:1). The catalytic performance of the **M-PS-TPP**-Pd columns was evaluated in Suzuki-Miyaura cross-coupling reaction between 4-chlorotoluene (0.50 mol L^{-1}, 1 eq.) and phenylboronic acid (0.75 mol L^{-1}, 1.5 eq.) under continuous-flow condition (Scheme 2a and b).[7] It should be noted that no Pd leakage was detected in any of the fractions (THF and the aqueous phase) by ICP-AES (Table 1). Initially, the **M-PS-TPP**-Pd columns exhibited high yields (76–93%), which then gradually decreased over time (Figure S12). At a time on stream of 58 h, the turnover numbers (TONs) of the **M-PS-TPP**-Pd columns with DVB contents of 2, 5, 20, 40, and 61 eq. were 874, 1170, 2704,[7] 463, and 420, respectively (Table 1). Increasing the loading ratio of Pd to P (P/Pd 1:1) decreased the catalytic durability of **M-PS-TPP**-Pd (Figure S12). Surprisingly, the cross-linking degree of the **M-PS-TPP**-Pd had a dramatic impact on catalytic performance. A moderate cross-linking degree (DVB of 20 eq.) was essential for achieving the highest TON.



Scheme 2. (a) Continuous-flow setup with **M-PS-TPP**-Pd for (b) Suzuki-Miyaura cross-coupling and (c) Buchwald-Hartwig amination.

Table 1. TONs and Pd leaching in Suzuki-Miyaura cross-couplings with **M-PS-TPP**-Pd columns[a]

x (eq.)	TON (-)[b]	Pd leaching (%)[c]
2	874	n.d.
5	1170	n.d.
20[7]	2704	n.d.
40	463	n.d.
61	420	n.d.

[a] Conditions: 4-chlorotoluene (0.5 mol L^{-1}) and phenylboronic acid (0.75 mol L^{-1}) in THF, K_3PO_4 (3 mol L^{-1}) in water, **M-PS-TPP**-Pd column (P/Pd 2:1), THF phase/water phase 2:1 v/v, residence time (τ) =2.00 h, 40°C. [b] Time on stream = 58 h. [c] Determined by ICP-AES.

The impact of the cross-linking structure on catalytic performance was also assessed in Buchwald-Hartwig amination. The **M-PS-TPP**-Pd column, prepared from **M-PS-TPP** column and $[\{PdCl(\eta^3\text{-allyl})\}_2]$ (P/Pd 2:1), was used for continuous-flow reactions between 1-butyl-4-chlorobenzene (0.5 mol L^{-1}, 1 eq.) and aniline (0.6 mol L^{-1}, 1.2 eq.).[9] Despite reactions under basic and high-temperature condition (KOH and 100°C), all the **M-PS-TPP**-Pd columns demonstrated excellent tolerance to Pd leaching with levels below the detection limit of ICP-AES. Increasing the DVB contents from 2 to 20 eq. markedly improved yield from 45–72% to 92–98%, and TONs reached up to 547 (Figure 3). On the other hand, further increasing DVB contents (40 and 61 eq.) resulted in severe drops in catalytic performance (21–55% yield, up to 314 TONs). This highlighted the critical importance of tuning the cross-linking degree of **M-PS-TPP**-Pd to boost its catalytic performance in challenging C-N cross-couplings.

After 10 h time on stream, the turnover frequency (TOF) for the **M-PS-TPP**-Pd (20 eq. DVB content) was estimated to be 274 h^{-1}, significantly higher than that of polyvinylpyridine-supported NHC-Pd complex (165 h^{-1}), which had a comparable TON (500).[10] To the best of our knowledge, our **M-PS-TPP**-Pd reached the highest TOF reported for immobilized catalysts in continuous-flow Buchwald-Hartwig aminations.

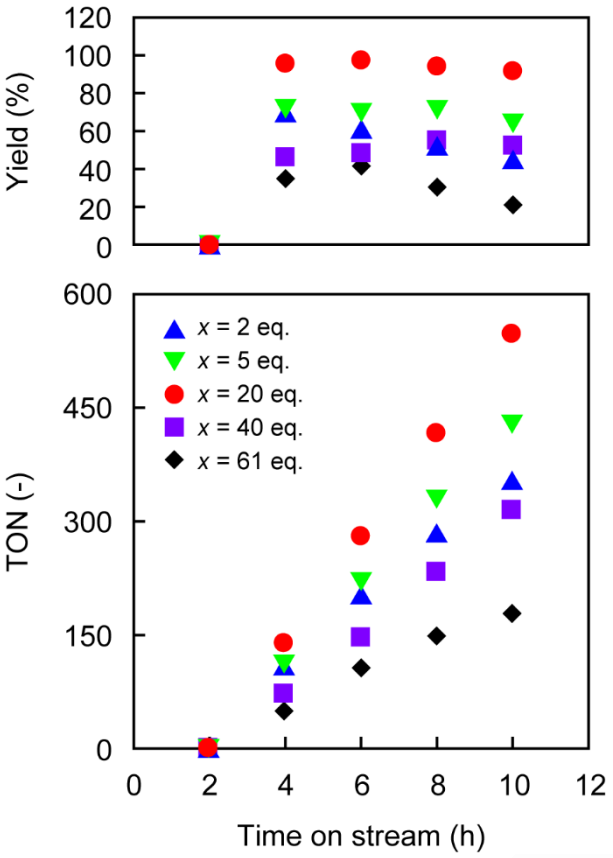


Figure 3. (a) Changes in yields and TONs in the C-N cross-couplings with **M-PS-TPP**-Pd with different cross-linking degree. Conditions: butyl-4-chlorobenzene (0.5 mol L^{-1}) aniline (0.6 mol L^{-1}), tetrabutylammonium bromide (TBAB, 0.025 mol L^{-1}) in toluene, KOH (2 mol L^{-1}) in water, **M-PS-TPP**-Pd column (P/Pd 2:1), organic phase/water phase 2:1 v/v, τ = 2.00 h, 100°C.

Evaluation of the State of Pd on M-PS-TPP-Pd

Transmission electron microscopy (TEM) observations were performed to assess the state of Pd on **M-PS-TPP**-Pd. Notably, Pd aggregation was observed in the spent **M-PS-TPP**-Pd, which was not present before both the C-C (Figure S13, see SI) and C-N cross-couplings (Figures 4 and S14). Particularly, significant Pd aggregation was identified in the spent **M-PS-TPP**-Pd with lower DVB contents (2 and 5 eq.). It is noteworthy that the number of the Pd aggregates decreased with increasing DVB contents to be 20 eq. or more.

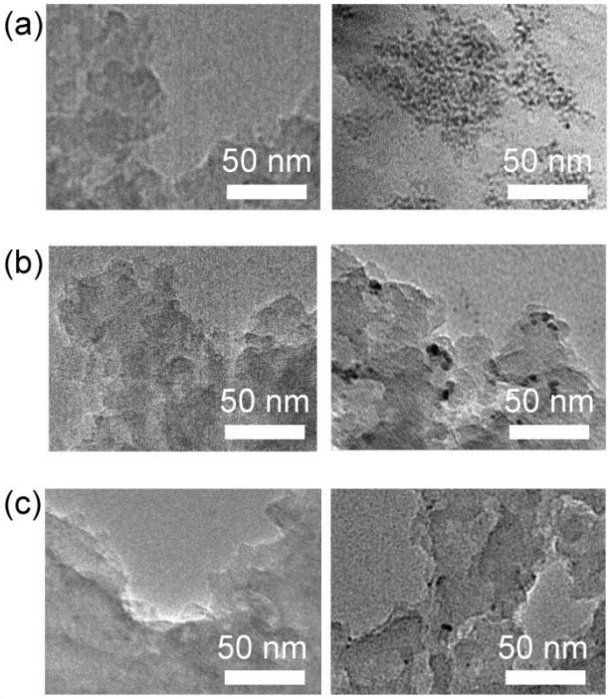


Figure 4. TEM images of **M-PS-TPP**-Pd with DVB contents of (a) 2, (b) 20, and (c) 61 eq. (left) before and (right) after Buchwald-Hartwig aminations.

For successful cross-coupling reactions of chloroarenes, the formation of mono-P-ligated Pd complex was crucial. At the same time, effective prevention of metal aggregation was also required to elongate the catalytic durability of immobilized metal catalysts. As indicated by ^{31}P CP/MAS NMR analyses, the lower cross-linking degree of **M-PS-TPP**-Pd favored the formation of highly active mono-P-ligated Pd over bis-P-ligated Pd (Figures 2b–d and S3b–S7b, see SI). By contrast, the higher cross-linking degree of **M-PS-TPP**-Pd was advantageous for effectively suppressing the formation of less active Pd aggregates during catalytic cycles, as observed in TEM images (Figures 4, S13, and S14). No leaching of Pd into the eluents was confirmed during the run, indicating that all the Pd was likely retained within the cross-linked network of **M-PS-TPP**-Pd. X-ray photoelectron spectroscopy (XPS) analyses for Pd(3d) in fresh **M-PS-TPP**-Pd revealed the presence of Pd^{II}, while some Pd^0 was observed in the spent **M-PS-TPP**-Pd, suggesting reduction of the Pd^{II} into Pd^0 (Figures S15–S19).[11] This indicated that Pd particles in the spent **M-PS-TPP**-Pd were likely formed from the aggregation of in-situ generated Pd^0, which dissociated from the supported phosphine during catalytic cycles of cross-coupling.[12] After all, the selective formation of mono-P-ligated Pd and effective metal stabilization demonstrated a trade-off relationship with the variation in cross-linking degree. In this context, the **M-PS-TPP**-Pd with a DVB content of 20 eq. achieved an optimal balance, resulting in highly active and durable catalysts for transition-metal catalysis.

Interactions between Pd and Polystyrene Network

Previously, we have observed significant interactions between Pd^{II} and the π electrons of styrene pendants on **M-PS-TPP**-Pd, which were related to their catalytic durability.[7] In this system, labile ligands (PhCN or solvent) on Pd^{II} were exchanged with the π-electron system of the aromatic rings while maintaining coordination bonds between the supported phosphine and Pd complex. To directly confirm these interactions between the aromatic rings of polystyrene and Pd, a series of triphenylphosphine-free polystyrene monoliths was fabricated by varying DVB contents (described in detail in SI). Adsorption experiments using the phosphine-free monoliths and Pd^{II} sources were then conducted. The adsorption rate of $[PdCl_2(PhCN)_2]$ increased (from 26 to 70%) with increasing DVB contents (from 3 to 100 mol%) (Figure 5, filled circles). By contrast, the adsorption of $[PdCl_2(PPh_3)_2]$ was negligible (adsorption rate of up to 5%) (Figure 5, blank circles). Surprisingly, the polystyrene monoliths exhibited significant adsorption capability toward $[PdCl_2(PhCN)_2]$ even in the absence of supported phosphine ligand. Moreover, Pd^0 sources such as $[Pd(PPh_3)_4]$ and $[Pd_2(dba)_3]$ did not show meaningful adsorption. These results suggested strong interactions between Pd^{II} and polystyrene chains, which were enhanced increasing cross-linking degree. The modulation of metal-arene interactions thus significantly contributed to the catalytic durability of **M-PS-TPP**-Pd in the present catalytic system.

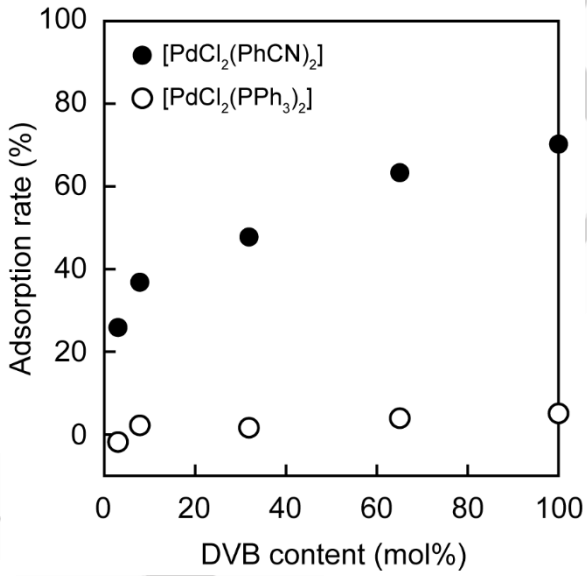


Figure 5. Adsorption rate of $[PdCl_2(PhCN)_2]$ (filled circles) and $[PdCl_2(PPh_3)_2]$ (blank circles) on phosphine-free polystyrene monoliths with different cross-linking degree.

Through comparative experiments with **M-PS-TPP**-Pd, we elucidated insights into the design of cross-linked polymer networks for creating active and durable immobilized catalysts (Figure 6). A lower cross-linking degree favored the formation of mono-P-ligated complexes due to effective site isolation of the phosphine units.[7] Conversely, a higher cross-linking degree provided stabilization of the metal catalyst through π-electron donation from the phenyl rings[13] within the highly cross-linked polystyrene network, where the local concentration of the aromatic rings was elevated. Therefore, achieving a microenvironment that balances selective mono-P-ligation with effective stabilization through arene-metal interactions was pivotal for enhancing the high catalytic durability of immobilized transition-metal complex.

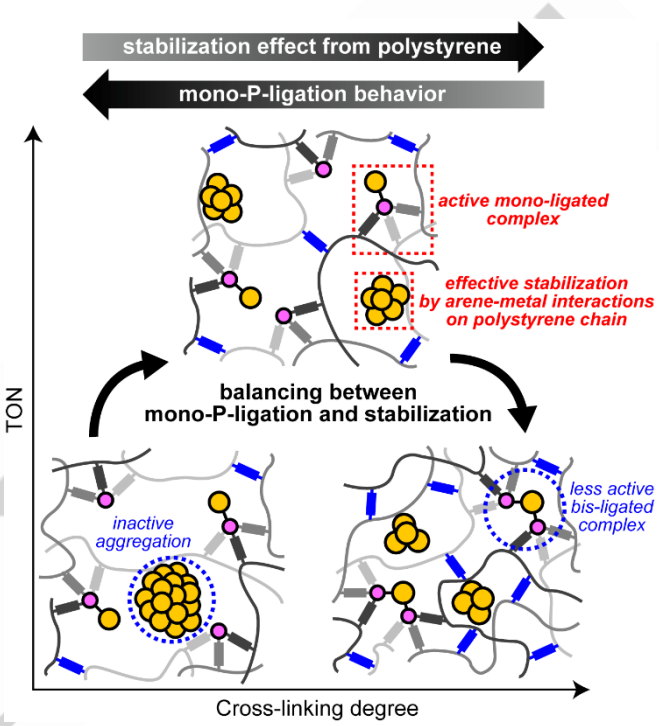


Figure 6. Schematic of **M-PS-TPP**-Pd with polystyrene cross-linking structure for high catalytic performance. Based on the cross-linking degree, coordination behavior of phosphine toward metal and stabilization effect on metal centers were optimized. Cross-linked polystyrene network (gray lines), cross-linking points (blue junctions), triphenylphosphine units (pink balls), and Pd metals (yellow balls) are shown.

Conclusion

In summary, a strategy for immobilized transition-metal complexes that optimizes both selective mono-P-ligation and effective metal stabilization. Comparative experiments demonstrated that the catalytic performance of the threefold cross-linking phosphine-Pd complex on a polystyrene monolith was highly dependent on the cross-linking degree, which was simply controlled by varying the contents of DVB as a co-cross-linker. The DVB units in the monolith played pivotal roles in balancing mono-P-ligation with the stabilization of metal centers for preventing aggregation. The optimized cross-linking structure of the monolith catalyst exhibited superior catalytic durability in challenging C-C and C-N cross-couplings of chloroarenes under continuous-flow conditions. These insights into the design of

polymer-supported metal catalysts contribute to expanding the applicability of immobilized catalyst systems, enhancing their efficiency and sustainability in transition-metal catalysis.

Experimental

Synthesis of M-PS-TPP (Scheme 1)

Typically, a solution of tris(4-vinylphenyl)phosphine (5.5 mg, 0.016 mmol, 1 eq.), 4-*tert*-butylstyrene (106.0 mg, 0.66 mmol, 41 eq.), DVB (42.0 mg, 0.32 mmol, 20 eq.), and Span 80 (0.061 mL) in chlorobenzene (0.19 mL) was placed in a glass vial (21.00 mm inner diameter) equipped with a magnetic stirring bar (20 mm). The organic phase was degassed by three freeze-pump-thaw cycles. Separately, $CaCl_2$ (36.9 mg, 0.33 mmol) and $K_2S_2O_8$ (5.2 mg, 0.019 mmol, 1.2 eq.) were dissolved in water (3.3 mL). The aqueous phase was degassed by N_2 bubbling for more than 0.5 h. Under vigorous stirring of organic phase (500 rpm), the initiator-containing aqueous phase was added dropwise using syringe. The ratio of organic phase to aqueous phase was 10:90 v/v. After addition of aqueous phase, stirring was further continued for 5 min to give HIPE.

For the characterization of the **M-PS-TPP**, the HIPE was cured in the vial at 70°C for 6 h after removing the stirring bar. Carefully crushing the vial, the resulting cylindrical polymer was washed successively by immersion in THF/water (2:1 v/v) and THF for more than 1 day each. The resulting polymer was dried under vacuum at room temperature overnight to give the **M-PS-TPP** as a white solid (141.5 mg, 92%). The amount of phosphine incorporated ([P]) was 0.11 mmol g^{-1} based on the feed ratio of monomers.

For the preparation of the **M-PS-TPP** column, a stainless-steel tube (4.4 mm inner diameter (*d*) × 5.0 cm length) was filled with the HIPE using syringe and sealed at the ends with septa. After curing at 70°C for 6 h, the septa were removed, and the length of the **M-PS-TPP** (*L*) in the column was measured using calipers. The column was provided with fittings and attached to a syringe pump. THF/water (2:1 v/v) and THF were successively permeated through the column for wash (2.5 h each, τ = 0.50 h).

Continuous-Flow Suzuki-Miyaura Cross-Coupling (Scheme 2a and b)

$[PdCl_2(PhCN)_2]$ (0.005 mol L^{-1}) in THF was permeated through the **M-PS-TPP** column (τ = 2.00 h). The molar ratio of Pd to P was 1:2, controlled by total elution volume of the feed solution. After completion of the permeation, the column was washed by permeation of THF (2.5 h, τ = 0.50 h) to afford **M-PS-TPP**-Pd column. 4-Chlorotoluene (0.5 mol L^{-1}, 1 eq.) and phenylboronic acid (0.75 mol L^{-1}, 1.5 eq.) in THF, and K_3PO_4 (3 mol L^{-1}, 2 eq.) in water were separately prepared. These solutions were loaded into syringes and attached to syringe pumps. The two syringe pumps were used to deliver the feed substrate solutions at controlled flow rates of the organic phase and the aqueous phase (τ = 2.00 h). The volume ratio of the organic phase to the aqueous phase was 2:1. The two substrate solutions were pumped and mixed via a T-shaped mixer. The mixture was continuously permeated through the **M-PS-TPP**-Pd column at 40°C. The eluent from the column was continuously collected, and the organic phase was analyzed by HPLC to determine yield and TON. After run, THF/water (2:1 v/v) and THF were successively permeated through the column for washing followed by drying under vacuum.

Continuous-Flow Buchwald-Hartwig Amination (Scheme 2a and c)

$[\{PdCl(h^3\text{-allyl})\}_2]$ (0.0025 mol L^{-1}) in THF was permeated through the **M-PS-TPP** column (τ = 2.00 h). The molar ratio of Pd to P was 1:2, controlled by total elution volume of the feed solution. After completion of the permeation, the column was washed by permeation of toluene (2.5 h, τ = 0.50 h) to afford **M-PS-TPP**-Pd. 1-Butyl-4-chlorobenzene (0.5 mol L^{-1}, 1 eq.), aniline (0.6 mol L^{-1}, 1.2 eq.), TBAB (0.025 mol L^{-1}, 5 mol%) in toluene, and KOH (2 mol L^{-1}, 2 eq.) in water were separately prepared. These solutions were loaded into syringes and attached to syringe pumps. The two syringe pumps were used to deliver the feed substrate solutions at controlled flow rates of the organic phase and the aqueous phase (τ = 2.00 h). The volume ratio of the organic phase to the aqueous phase was 2:1. The two substrate solutions were pumped and mixed via a T-shaped mixer. The mixture was continuously permeated through the **M-PS-TPP**-Pd column at 100°C. The eluent from the column was continuously collected, and the organic phase was analyzed by HPLC to determine yield and TON. After run, MeOH/water (2:1 v/v) and MeOH were successively permeated through the column for washing followed by drying under vacuum.

Supporting Information

The authors have cited additional references within the Supporting Information.[14–17]

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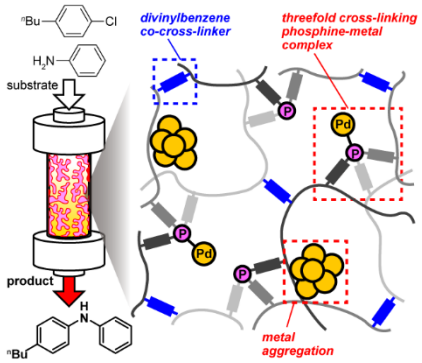
Entry for the Table of Contents



Continuous-Flow Catalysis with Porous Monolith

A series of threefold cross-linked polystyrene-triphenylphosphine hybrid monoliths was prepared to investigate the impact of the divinylbenzene co-cross-linker on coordination behavior and metal stabilization. By adjusting the cross-linking degree by varying the feed ratio of divinylbenzene, selective mono-coordination and effective stabilization of the metal was achieved, facilitating the continuous-flow C–C and C–N cross-couplings of chloroarenes.