Natural peptides coordinated with various metal ions via amide bonds and functional groups on side chains can form various self-assembled structures. For example, ferritin is a natural intracellular protein which takes a specific conformation through interactions between peptide building blocks and Fe\(^{2+}\) ions. Artificial peptides that provide natural or non-natural metal binding sites have been developed to construct metal ion-induced self-assemblies of nanostructures including tubular-, fibre-, vesicle-, spherical-, and rod-coil-type ones. Such metal coordination can initiate intermolecular self-assembly by bringing two or more peptides into close proximity. Furthermore, several metal ions coordinated with peptides have been involved in a redox reaction to induce irreversible peptide cross-linking via covalent bonding, e.g., dityrosine formation.

Based on a peptide template, various types of metal-peptide nanostructures have been designed and utilized as electrochemical sensors, biological scaffolds, and catalysts. In particular, significant effort has been devoted in developing metal nanoparticles (NPs)-incorporated peptide nanostructures which can then be used as catalysts in C–C coupling reaction. To facilitate the reaction, for instance, Knecht group synthesized various shapes of Pd nanostructures with a large surface area by using a self-assembling peptide template composed of R5 peptide. Moreover, peptide amphiphiles possessing both hydrophobic carbon-chain and ionic peptide sequences are promising as bio-inspired-templates for growing PdNPs-incorporated nanofibers. Recently, several groups have demonstrated nanofiber incorporated with PdNPs using a self-assembled peptide amphiphile. The peptide-templated PdNPs showed high catalytic activity for the Suzuki coupling reaction under environmentally-friendly conditions. Although these peptide-templated PdNPs can afford efficient catalytic activities for the C–C coupling reactions, drawbacks originated from the heterogeneous state limits its broad and practical application of the catalyst.

A recent report has revealed that a tyrosine-rich peptide, YYACAYY (YC\(_7\)), can be self-assembled into a two-dimensional peptide nanostructure via interaction of tyrosines and cysteines leading to cross-linking at an air/water interface. Based on this finding, we have successfully designed Pd\(^{2+}\)-ion-mediated sphere-to-bridge-shaped peptide nanostructures (YC\(_7\)@PdNPs) through thermally induced phase transition. During the transition, the Pd\(^{2+}\) ions have interacted with the YC\(_7\) peptide molecules through coordination, which might be a crucial driving force for leading to a distinctive self-assembled sphere-to-bridge peptide nanostructure. More interestingly, the self-assembled YC\(_7\)@PdNPs is dissolved into the aqueous solution via thermal transition during cross-coupling process over phase transition temperature and followed by re-assembly under the critical temperature achieving the PdNP-captured astrocyte-shaped peptide nanostructures (YC\(_7\)@PdNP). This provides a great opportunity to take advantage of YC\(_7\)@PdNPs as a versatile and recyclable catalyst, capitalizing both of its homogeneous characteristic over critical temperature and heterogeneous characteristic under the same temperature. Herein, we demonstrate the feasibility of YC\(_7\)@PdNPs as a new type of catalyst under environmentally friendly conditions: (a) as a nano-catalyst during C–C coupling reactions; and (b) as a heterogeneous catalyst for separation, especially in Suzuki and...
Sonogashira coupling reactions. YC₇@Pd²⁺, this catalytic system via switchable phase enabled reusable catalyst. To the best of our knowledge, this kind of the reassembly process is first demonstrated in this paper.

YC₇ is a random coil-dominant peptide, which self-assembles in an aqueous phase into a two-dimensional nanostructure. From this peptide, we synthesized sphere-to-bridge-type peptide nanostructures (YC₇@Pd²⁺) via thermally controlled and Pd²⁺-ion-mediated ionic interactions (Scheme 1). During heating the peptide up to 90 °C for 1 h, it was allowed to completely dissolve in water. As the peptide solution was gradually cooled to 60 °C, YC₇ underwent a rapid transition into a secondary, α-helix-dominant structure. At this stage, Pd²⁺ ions were injected to induce distinctive Pd-peptide secondary structures via ionic interactions between phenolate anions of tyrosyl residues (or C terminal carboxylate anions) and Pd²⁺ ions. Without Pd²⁺ ions, YC₇ molecules were self-assembled into irregular shaped nanostructures and nanosheets during the thermodynamic transition (90 °C → 60 °C) via interactions between tyrosines and cysteine crosslinking (Fig. S1†). However, the YC₇@Pd²⁺, which was self-assembled by interactions with Pd²⁺ ions, was uniform and spherical with an average diameter of 88 ± 31 nm (count: 100) and further formed linked networks of sphere-to-bridge shapes (Fig. 1a and b). Physicochemical characterization of the nanostructure was performed with several analytical methods. First, the constituent elements of YC₇@Pd²⁺, including Pd, N, O, S and Cl, were analysed by energy-dispersive X-ray microanalysis mapping (Fig. S2†). The results demonstrated that YC₇@Pd²⁺ was composed of Pd²⁺ ions, evenly distributed within the YC₇ matrix.

To analyse the structure of YC₇@Pd²⁺ and the interactions between Pd²⁺ ions and the peptides, it was further characterized by infrared (IR) spectroscopy (Fig. 2). Bands from ν(C=O), ν(CC), δ(COH) of Tyr in YC₇ peptide were observed at 1070–1270 cm⁻¹, which exhibited relatively strong intensity due to its polar character (Fig. 2). These peaks are unique in Tyr not in other residues of YC₇ peptide. When the C–O stretching vibration bands of the self-assembled YC₇ and YC₇@Pd²⁺ were compared, YC₇@Pd²⁺ gave strong peaks at 1232 cm⁻¹ involving two stretching modes of ν(C=C) and ν(C=O) in Tyr–OH, which are attributed to stronger polarity of phenolate (Tyr residue) in the presence of Pd²⁺. These results clearly show that there are strong interactions between Pd²⁺ ions and tyrosine groups of YC₇@Pd²⁺. In addition, a new C=O stretching vibration from the carboxylate of YC₇@Pd²⁺ appeared at 1557 cm⁻¹ which corresponds to the asymmetric stretching vibration of metal carboxylates.

Additionally, the X-ray photoelectron spectroscopy (XPS) data of YC₇@Pd²⁺ clearly revealed Pd peaks (3d⁴/₅ and 3d⁵/₅) at 343.20 and 337.95 eV which corresponded to Pd(II) (Fig. S3†). Taken together, YC₇@Pd²⁺ is a non-crystalline peptide complex coordinated with Pd(II) at tyrosine residues, and has a potential as a Pd catalyst used in C–C coupling reactions. Consequently, Pd²⁺-ion-mediated peptide self-assembly was well characterized with IR and XPS.

Hence, this proves that the phenolate and carboxylate groups of YC₇@Pd²⁺ were primarily involved in coordination with Pd²⁺.
ions leading to the formation of a distinctive Pd-peptide nanostructure. Inductively coupled plasma atomic emission spectroscopy (ICP-OES) analysis revealed that the palladium content of YC7@Pd2+ was calculated to be 1.86 mmol Pd per g catalyst.

The X-ray diffraction (XRD) patterns of self-assembled YC7 exhibited distinctive peaks at 10° and 18° originating from the intersheet reflections of peptide sheets, respectively (Fig. S4†). In contrast, peptide sheet-originated regular sharp peaks of face-centered cubic Pd crystals did not appear in the XRD pattern of YC7@Pd2+ (Fig. S5†). This result suggests that Pd2+ ions were able to collapse the intrinsic YC7 structure, leading to the irregular shaped peptide arrangement inside the sphere-to-bridge-shaped peptide nanostructure.

We investigated the catalytic activity of the YC7@Pd2+ by evaluating the efficiency of C–C coupling reactions including Suzuki, Heck and Sonogashira coupling reactions. Actually, YC7@Pd2+ nanostructures are decomposed into the solution at substituents lowering the yields of the corresponding biaryl coupling reactions gave unfavourable yields (<2%) even in the presence of cetyl trimethyl ammonium bromide (CTAB) (Table 1, entry 1). Electron-donating substituents lowered the yields of the corresponding biaryl compounds (Table 1, entries 2–5). In particular, the oxygen-containing substrates (Table 1, entries 2 (OH) and 3 (OMe)) exhibited more efficient coupling than non-oxygen-containing substrates. These results demonstrated that the hydrogen bonding facilitated the access of YC7@Pd2+ to the substrate molecules under aqueous conditions providing a compatible coupling environment for the Suzuki coupling reaction. Furthermore, the use of CTAB as a phase-transfer catalyst promoted the interphase transfer of substrates, thereby boosting the coupling yields of the non-oxygen containing substrates (Table 1, entries 4 (H) and 5 (Me)). As a control experiment, compared with the coupling reaction catalyzed by YC7@Pd2+, the coupling yields by PdCl2 activation were lower than those of YC7@Pd2+ in the same condition (Table S4†).

Given the successful catalytic activity of YC7@Pd2+ in the Suzuki coupling reactions, we further investigated the catalytic activity of YC7@Pd2+ in the Sonogashira coupling reactions with CuI under aqueous conditions. The Sonogashira coupling reaction catalysed by YC7@Pd2+ exhibited a high coupling yield with a strong electron-withdrawing substrate (Table S3†, entry 1). In contrast to the Suzuki coupling reaction, the hydrogen bonding derived from the electron-donating substrates (Table S5†, entries 3 and 6) was not relatively effective on the catalytic activity in the Sonogashira coupling reaction. CTAB strongly suppressed the cross-coupling reaction, and instead, accelerated homo-coupling reaction with activated aryl iodide. The results indicate that CTAB did not afford a compatible cross-coupling environment between the catalyst and the substrates in the Sonogashira coupling reaction, whereas it stabilized phenylacetylene with Cu+ ion to activate the homo-coupling pathway.

During the coupling reaction at 80 °C in an aqueous solvent, YC7@Pd2+ disassembled into a soluble Pd-peptide complex, which is reduced into the solubilized PdNP catalyst. After cooling down to room temperature, the PdNP-peptide complex was reassembled and transformed into a nanostructure which is similar with a shape of astrocyte (YC7@PdNP, Fig. S6b†). This reversible process between homogeneous and heterogeneous

### Table 1  Suzuki–Miyaura coupling reactions for various aryl iodides in the presence of YC7@Pd2+ catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>COCH3</td>
<td>1</td>
<td>98.7</td>
</tr>
<tr>
<td>2</td>
<td>OH</td>
<td>3</td>
<td>99.6</td>
</tr>
<tr>
<td>3</td>
<td>OCH3</td>
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<tr>
<td>4</td>
<td>H</td>
<td>3/3b</td>
<td>88.8/99.9b</td>
</tr>
<tr>
<td>5</td>
<td>CH3</td>
<td>6/3b</td>
<td>70.8/96.0b</td>
</tr>
<tr>
<td>6</td>
<td>2-Iodophiophene</td>
<td>6/3b</td>
<td>40.0/91.3b</td>
</tr>
</tbody>
</table>

* Conditions: aryl iodine and heterocyclic halides (0.155 mmol), phenylboronic acid (0.186 mmol), YC7@Pd2+ (0.1 mol%), K2CO3 (0.274 mmol) in water (1 mL) at 80 °C.  
  GC yields when 0.5 eq. of CTAB was used.  
  † GC yields.
states facilitated easy isolation and reuse of YC7@PdNP from the reaction mixture. To evaluate the reusability of YC7@PdNP, the catalyst was recycled in subsequent Suzuki coupling reactions with 4-iodophenol or 4-idoacetophenone. While the coupling yields of the activated substrates (idoacetophenone) decreased slightly in the fourth and fifth runs, 4-iodophenol which can form a hydrogen bonding with YC7@PdNP was converted to the corresponding biaryl compound in excellent yields (yield > 98%) even after 5th use (Fig. S7).† These results reconfirm that hydrogen bonding enabled the substrates for easy access to the Pd-peptide complex as well as possibly stabilizing the PdNPs for excellent catalytic activity during a series of Suzuki coupling reactions.

In conclusion, we developed a novel method for the construction of Pd2+ ion-mediated sphere-to-bridge-shaped peptide nanostructures, YC7@PdNP, of which morphology can be controlled by temperature in an aqueous phase. Characterized by the switchable thermally-reversible phase transition, YC7@Pd2+ acted as a solubilized nano-catalyst during C–C coupling reactions and reassembled into a heterogeneous structure for isolation and reuse after each coupling reaction. YC7@Pd2+ showed an excellent activity as a catalyst for the Suzuki and the Sonogashira coupling reactions under aqueous conditions. Especially, in the Suzuki coupling reaction, hydrogen bonding capability of the substrates provided a favourable coupling environment, enhancing the coupling yield and reusability of the catalyst. The morphology controllable self-assembled Pd2+ ion-mediated peptide nanostructure can open a new avenue as a reusable catalyst for C–C coupling reactions under environmentally-friendly conditions.

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Notes and references