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<td><strong>Author(s)</strong></td>
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A supramolecular recyclable catalyst for aqueous Suzuki–Miyaura coupling†

Miao Qi,ab Pei Zi Tan,ab Fei Xue,ab Haripal Singh Malhi,ac Zhong-Xing Zhang,*a David J. Young*acd and T. S. Andy Hor*ab

A water-soluble, supramolecular catalytic system has been designed based on inclusion complexation between a hydrophobic palladium(II)–dipyrzole complex bearing an adamantyl (Ad) molecular recognition moiety and a complementary, hydrophilic β-cyclodextrin (β-CD) derivative. The single-crystal molecular structure of the Pd(II) complex was determined and its host–guest inclusion complexation with heptakis(2,6-di-O-methyl)-β-CD (dmβ-CD) in an aqueous medium was confirmed by 2D NOESY 1H NMR spectroscopy. The catalyst showed high activity for Suzuki–Miyaura coupling of hydrophilic aryl bromides with aryl boronic acids in aqueous organic solvents. In the presence of n-Bu4NB as a stabilizer, the catalyst-containing reaction solution can be recycled and reused multiple times to catalyze the coupling reaction of fresh substrates once the product has been removed by centrifugation. This work demonstrates a supramolecular complex approach, non-covalently modifying a water insoluble metal complex to provide a water-soluble inclusion system to serve as a recyclable catalyst for potential application in green chemical synthesis.

Introduction

Green chemistry addresses the environmental impact of both chemical products and the processes by which they are produced.1–4 Water is an ideal green solvent and may offer additional benefits such as improved reactivities, selectivities, simplified workup procedures and recycling of an expensive metal catalyst.5,6

The development of novel water soluble catalysts has elicited interest from both industrial and academic researchers.7,8 Designing catalytically active metal species to operate in an aqueous phase has primarily focused on ligands with suitable hydrophilic groups in addition to their functionality necessary to support the stability, activity, and selectivity of the metal center. Most commonly, ionic substituents such as sulfonate, carboxylate, phosphonate, or ammonium are employed, but neutral hydrophilic polysols, carbohydrates, and polyethylene glycols have also been successfully used.9

We herein present a new approach to the design and preparation of water-soluble metal catalysts by utilizing non-covalent rather than covalent bonding. This strategy makes use of host–guest inclusion complexation to reversibly tether a hydrophilic moiety to the hydrophobic ligand of the metal complex thereby enhancing its solubility in aqueous media.

Cyclodextrins (CDs) are well-known cyclic oligosaccharides formed from the enzymatic degradation of starch.10 Their partial water solubility, homochirality and ability to form inclusion complexes makes them among the most studied hosts in supramolecular chemistry,11–16 with a wide range of applications from drug delivery,17–19 to resolution of enantiomers20 and as catalysts.21–23 The supramolecular structures formed between CDs and polymers have also inspired interesting supramolecular biomaterials. Some of us have recently constructed a series of supramolecular hydrogels, non-covalently connected micelles, nano-capsules and pseudo-block copolymers based on the inclusion complexation between β-CD moieties and adamantyl (Ad) groups.24–27

On the basis of this experience with the self-assembling behavior of β-CD/Ad pairs and of transition metal complexes bearing pyrazole-derived ligands,28 we have now designed a bidentate dipyrzole ligand tethered to an Ad group as the molecular recognition moiety (Ad-L). This ligand then reacted with the Pd(n) precursor PdCl2(NCCH3)2 to form an Ad-L
containing complex (Ad-L–PdCl₂) that is insoluble in water because of the bulky hydrophobic group. Upon host-guest inclusion complexation of Ad-L–PdCl₂ with heptakis(2,6-di-O-methyl)-β-CD (dmβ-CD) in aqueous media, however, the Pd(n) complex dissolves completely at room temperature to form a water-soluble supramolecular assembly (Ad-L–PdCl₂ ⊂ β-CD) that efficiently catalyzes Suzuki–Miyaura coupling between hydrophilic aryl bromides with aryl boronic acid at room temperature. By comparison, the Pd(II) complex (Ad-L–PdCl₂), that is present heterogeneously in the aqueous reaction mixture exhibits much lower catalytic efficiency under similar conditions.

Results and discussion

Synthesis and characterization of Ad-L and Ad-L–PdCl₂

The ligand Ad-L was synthesized by the nucleophilic substitution reaction of one equivalent of 1-adamantanolmethylamine with two equivalents of (3,5-dimethyl-1H-pyrazol-4-yl)methanol in anhydrous acetonitrile at room temperature over 24 h (Scheme 1). This facile procedure resulted in good yields with little side products. The central amine and the two pyrazolyl nitrogen atoms of this ligand are potential ligand donors to the metal centre and hence this hybrid molecule can possibly bind to a metal in a \( \kappa^2(N,N) \) or \( \kappa^2(N',N) \) fashion depending on the electronic state and steric constraints around the metal. The co-presence of a tertiary amine and pyrazolyl nitrogen donors in proximity also enhances the hemilability which gives it coordinative freedom and conformational freedom to adapt to the coordination and geometry changes of the metal during the catalytic cycle.

The adamantyl-containing Pd(n) complex (Ad-L–PdCl₂) was quantitatively prepared by reacting Ad-L with an equal amount of PdCl₂(NCC(CH₃)₂)₂ in dry CH₂Cl₂ at room temperature. The \(^1\)H NMR spectrum of the ligand showed a 0.1–0.4 ppm downfield shift upon coordination. Most affected was the –CH₂– group bridging the central amine and the pyrazolyl group. From a singlet in the free ligand, this signal became two doublets at 7.11 and 5.23 ppm with a geminal coupling constant of 15 Hz (see ESI, Fig. S1†).

Single crystals of adamantyl-containing Pd(n) complex suitable for single-crystal X-ray diffraction analysis (Fig. 1) were obtained by slow diffusion of diethyl ether into a solution of complex in CH₂Cl₂ at –20 °C. Selected bond lengths and bond angles are summarized in Table 1.

The Pd(n) centre in Ad-L–PdCl₂ is slightly distorted from the ideal square planar geometry that is typically found in a d⁸ metal centre. The bidentate chelating ligand binds the Pd(n) centre through the two pyrazolyl nitrogen atoms N3 and N1. The non-coordinating [N5–Pd] distance is 3.683 Å. This \( \kappa^2(N,N) \) coordination gives rise to a puckered 8-membered metallocyclic ring –Pd1–N1–N2–C6–N5–C12–N4–N3– which is best described as a boat–chair like conformation. The Pd–N (pyrazolyl) bond lengths are 2.019(2) Å and 2.024(2) Å which are consistent with literature values as are the Pd–Cl distances of 2.2777(6) Å and 2.2858(6) Å.

Host–guest inclusion complexation between Ad-L–PdCl₂ and β-CD derivative

The adamantyl (Ad) group and β-CD moiety is a well-known host–guest pair with a stability constant (log \( K \)) up to 5 at room temperature. To confirm the host–guest inclusion complexation of the adamantyl-containing Pd(n) complex with heptakis(2,6-di-O-methyl)-β-CD (dmβ-CD), 2D-NOESY \(^1\)H NMR measurements were made in aqueous DMSO. Dmβ-CD was chosen for this analysis because of its enhanced solubility in water relative to β-CD.

The sample was prepared by adding a solution of Ad-L–PdCl₂ (guest) in DMSO–\( d_6 \) into a solution of dmβ-CD (host) in D₂O. The final host–guest mixture (molar ratio 1 : 1) in D₂O–DMSO–\( d_6 \) (1 : 1, v/v) was filtered before measurement. It can be seen in the 2D NOESY spectrum (Fig. 2, left) that the peaks of the Pd(n) complex were only present at low intensity compared to the peaks belonging to dmβ-CD. This is most likely due to longer proton relaxation times and the high hydrophobicity of the former. This is a common phenomenon for amphiphilic materials like copolymers in aqueous solution. The C(3)–H and C(5)–H of dmβ-CD (3.6 to 3.7 ppm) point into the hydrophobic cavity of β-CD and exhibit correlation signals with the

![Scheme 1 Synthesis of Ad-L and Ad-L–PdCl₂.](image)

![Fig. 1 ORTEP diagram of adamantyl-containing Pd(n) complex shown with 50% probability ellipsoids (hydrogen atoms are omitted for clarity).](image)

<table>
<thead>
<tr>
<th>Table 1 Selected bond lengths (Å) and bond angles (°)</th>
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<tr>
<td>Bond length (Å)</td>
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<tr>
<td>Pd(1)–N(3) 2.019(2)</td>
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<tr>
<td>Pd(1)–N(1) 2.024(2)</td>
</tr>
<tr>
<td>Pd(1)–Cl(1) 2.2777(6)</td>
</tr>
<tr>
<td>Pd(1)–Cl(2) 2.2858(6)</td>
</tr>
<tr>
<td>Cl(1)–Pd(1)–Cl(2) 92.33(3)</td>
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protons (1.6 to 2.0 ppm) on the guest Ad group (Fig. 2, right), indicating that the Ad moiety has inserted into the β-CD cavity. This observation is in agreement with literature reports by us and by other groups.26,27,39

Suzuki–Miyaura coupling reaction

Selection of solvent. The Suzuki–Miyaura coupling reaction is one of the most important synthetic methodologies for the formation of carbon–carbon bonds.40,41 These reactions are generally catalyzed by soluble palladium complexes with various Pd(0) stabilizing ligands in organic media. A number of protocols have also been developed by us42,43 and other groups44–48 using water or aqueous mixed solvents as the reaction media to reduce the negative environmental impact of conducting this reaction on an industrial scale.

In this work, Suzuki–Miyaura cross coupling of 4-bromo-benzoic acid and phenylboronic acid was used to evaluate the catalytic performance of our supramolecular catalyst (Ad-L–PdCl₂ × dmβ-CD) (Scheme 2) in a series of water–organic solvent mixtures (3/1, v/v). These reactions were carried out in air at room temperature with a 0.5 mol% catalyst loading. The supramolecular pre-catalyst and the substrates dissolved in the water–organic solvent reaction media to form a homogeneous reaction mixture. Product yields after 2 hours are given in Table 2.

It can be seen from Table 2 that the yield of the Suzuki–Miyaura coupling product after 2 hours decreased in the order H₂O–CH₃OH > H₂O–DMF > H₂O–acetone > H₂O–CH₃CN. Fortuitously, the H₂O–CH₃OH mixture is also the ‘greenest’ of these water–organic solvent mixtures.49

Contribution of host–guest inclusion complexation to Suzuki–Miyaura coupling reaction. Next, the efficacy of host dmβ-CD was evaluated in the optimal solvent (Fig. 3). The presence of dmβ-CD resulted in a very high product yield (>98%) after 4 hours. In the absence of dmβ-CD, the reaction

Table 2 Yield of Suzuki–Miyaura coupling reaction in different aqueous solvent mixtures after 2 hours

<table>
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<th>Entry</th>
<th>Reaction media</th>
<th>Yield (%)</th>
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<tr>
<td>1</td>
<td>H₂O–CH₃OH</td>
<td>&gt;97</td>
</tr>
<tr>
<td>2</td>
<td>H₂O–DMF</td>
<td>87.7</td>
</tr>
<tr>
<td>3</td>
<td>H₂O–CH₃CN</td>
<td>31.3</td>
</tr>
<tr>
<td>4</td>
<td>H₂O–acetone</td>
<td>61.2</td>
</tr>
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Entry a Reaction conditions: 0.5 mol% supramolecular catalyst (Ad-L–PdCl₂ complexed with an equal amount of dmβ-CD), 0.5 mmol of 4-bromobenzoic acid, 0.6 mmol of phenylboronic acid, 1.2 mmol of Na₂CO₃, 4 mL of water-organic mix solvent (3/1, v/v), room temperature for 2 h in air. b Yields were determined by ¹H NMR analysis in d₆-acetone using an internal standard (hexadecane) and calculated using a product calibration plot with R² = 0.998 (see ESI).

Scheme 2 Suzuki–Miyaura coupling reaction of 4-bromobenzoic acid and phenylboronic acid in aqueous media catalyzed by supramolecular inclusion complex catalyst (Ad-L–PdCl₂ × dmβ-CD).

Fig. 2 (Left) 2D NOESY ¹H NMR spectrum of Ad-L–PdCl₂ and dmβ-CD in D₂O–DMSO-d₆ (1 : 1, v/v) with water suppression (500 MHz, 25 °C); (right) expanded 2D NOESY ¹H NMR spectrum.

Fig. 3 (Top) Comparison of Suzuki–Miyaura coupling reactions performed in H₂O–CH₃OH (3/1, v/v) with and without dmβ-CD in air at room temperature over 4 h. Each point represents the mean value ± SD of 2 runs; (bottom) photographs comparing the homogeneity of catalyst and catalyst mixed with 4-bromobenzoic acid/Na₂CO₃ in H₂O–CH₃OH (3/1, v/v), as well as the turbidity of the reaction mixtures after adding phenylboronic acid in 30 min with (a1–a3) and without (b1–b3) the host dmβ-CD, respectively.

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proceeded in a slightly reduced yield (ca. 93%) over the same period. Importantly, the reaction was significantly faster over the first two hours in the presence of the solubilizing host (Fig. 3, curve a and b). The series of photographs in Fig. 3 illustrates the improved solubility of Ad-L–PdCl₂ in the presence of dmβ-CD. The presence of the latter resulted in the Pd(u) complex dissolving completely to result in a clear yellow solution (Fig. 3, bottom a1). The solution remained clear on addition of the 4-bromobenzoic acid and the base Na₂CO₃ (Fig. 3, bottom a2). Subsequently, when the water soluble phenylboronic acid was added and the coupling reaction initiated, the reaction mixture became increasingly turbid on the generation of water insoluble product (Fig. 3, bottom a3). Without the host dmβ-CD, the Pd(u) complex was not dissolved in the reaction medium H₂O–CH₃OH (3/1, v/v) but dispersed in a light yellow suspension. The reaction mixture was also less turbid over the same reaction period suggesting a slower reaction rate (Fig. 3, bottom b1–b3).

The influence of solubility was further investigated by varying the proportion of organic solvent in the presence and absence of the host dmβ-CD (Fig. 4). The reactions in the presence of dmβ-CD always afforded the product in higher yields (94–99%) over a volume ratio of H₂O–CH₃OH ranging from 0.5 to 5. The reactions in the absence of dmβ-CD also afforded the product in good yields (94–98%), but only when the volume ratio of H₂O–CH₃OH was below 3. Interestingly, when the volume ratio of H₂O–CH₃OH was higher than 3, the yields dropped to around 50% because of poor aqueous solubility of the catalyst. When the volume ratio of H₂O–CH₃OH was in the range 0.5–2, the Pd(u) complex either dissolved or was well dispersed in the reaction medium, even in the absence of dmβ-CD. Therefore the yields in both cases (i.e. with and without dmβ-CD) were similar. When the volume ratio of H₂O–CH₃OH was 3, the Pd(u) complex was kept soluble in the reaction medium by the dmβ-CD. However, when dmβ-CD was absent, the Pd(u) complex dissolved poorly resulting in a lower yield (around 86%) and this was exacerbated by increasing the volume ratio of H₂O–CH₃OH to 4 and 5 (yield around 50%).

**Recycling of the catalyst**

High precious metal prices and toxicity make recycling of the Pd catalyst attractive from an economic and environmental perspective. Recycling experiments were performed using the standard Suzuki–Miyaura coupling reaction of 4-bromobenzoic acid and phenylboronic acid in water–MeOH (3 : 1, v/v). The coupling product was easily isolated by centrifugation. The aqueous filtrate was recovered and investigated for its ability to catalyze the reaction of freshly added substrates (Table 3).

It has been reported that pH strongly influences catalyst activity for Suzuki–Miyaura cross coupling reactions conducted in aqueous media⁵⁰ and that a pH of around 11 is optimal.⁵⁰,⁵¹

In this work, the pH value of the original reaction mixture was measured to be ca. 11.0 at the beginning of the coupling reaction. However, by the end of the reaction, the pH value of the recycled filtrate dropped to be ca. 10.0 and then ca. 9.0 after the second reaction. Therefore, the pH of the reaction mixture was adjusted back to 11.0 with dilute aqueous NaOH before each recycling experiment.

The Suzuki–Miyaura coupling reaction of 4-bromobenzoic acid and phenylboronic acid in water–MeOH was quantitative after 2 h (Table 3, entry 1). However, this high catalytic activity was not maintained using the recycled catalyst. The yield dropped to ca. 60% at the first recycle (i.e. step 1) and was less than 10% by the 4th recycling step. Palladium black was observed in these reactions, thus suggesting catalyst decomposition.

Pd(0) intermediates are the catalytically active species in Suzuki–Miyaura cross coupling reactions.⁵²–⁵⁴ Catalyst decomposition to form palladium black is also frequently observed. This phenomenon is usually explained by assuming that the oxidative addition step which starts the catalytic cycle is in competition with an ill-defined sequence of reactions leading to palladium nanoparticles (Pd-NPs) that eventually aggregate irreversibly to form larger, catalytically inactive, palladium metal particles (palladium black).⁵⁵ Obviously a low conversion will result if the aggregation is faster than the cross coupling. Catalyst decomposition also hampers recycling. A simple and effective approach to prevent the catalyst from losing activity is to use quaternary ammonium salts which stabilize Pd-NPs and slow the aggregation process.⁵⁶–⁵⁸ Stabilization of Pd-NPs can increase the catalytic activity because dispersible Pd-NPs are themselves active catalysts⁵⁷ or act as a reservoir of soluble, catalytically active Pd(0).⁵⁷,⁵⁸ Both the cation and anion of ammonium salt play a combined role in stabilizing Pd-NPs, the anion being coordinated to the electrophilic metal nanoparticles with the cation surrounding the negatively-charged anion-metal sphere.⁵⁵

In our work, a suitable amount of tetrabutylammonium bromide (TBAB) was found to be effective to stabilize the catalyst against decomposition and made recycling feasible. Experiments carried out using different TBAB–4-bromobenzoic acid molar ratios showed that the catalytic performance for each recycling step increased significantly with increasing the stabilizer until a maximum was reached at the TBAB–4-bromobenzoic acid molar ratio of 0.15 : 1 (Table 3, entries 2–6).

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**Legend:**

**Fig. 4**. Comparison of Suzuki–Miyaura coupling performed in various proportions of H₂O and CH₃OH, with and without dmβ-CD (conditions: room temperature, 2 h in air). Each point represents the mean value ± SD of 2 runs.
When higher amounts of stabilizer were used, the substrate conversion decreased. When TBAB in recycling reaction (1) was increased from 0 to 0.15 equiv., the yield increased from ca. 60% (entry 1) to 100% (entry 3). When the TBAB was further increased to 0.25 equiv., the yield decreased from 100% to ca. 80% (entry 5) and to ca. 25% when 1.0 equivalents of TBAB were employed (entry 6). No catalyst decomposition was observed in these TBAB stabilized reactions. These results indicate that the optimal molar ratio of TBAB to substrate was 0.15 and that high loadings of TBAB actually inhibited the reaction, presumably at the oxidative addition step. By contrast, NaBr did not stabilize the catalyst and slight inhibition was observed (entry 7).

Although 0.15 equiv. of TBAB significantly enhanced the catalytic performance in subsequent recycling steps (Table 3, entry 3, step 1–4), this was not the case for the initial run (Table 3, entry 3, step 0). The yield for this step was quantitative without stabilizer and approximately 80% with stabilizer. It is possible that the higher stability gained from the TBAB stabilization leads to longer catalytic induction period. Further, a series of catalytic reactions and recycling experiments was carried out for 5 h and 24 h, and compared with those performed at 2 h in the presence of 0.15 equiv. of TBAB (Fig. 5). At a reaction time of 5 h (red bars), the aqueous solution with supramolecular catalyst can be recycled and reused twice before the yield dropped to below 90% and three times for a reaction time of 24 h (blue bars).

**Experimental**

**Synthesis of bis[[3,5-dimethyl-1H-pyrazolyl)methyl][1-adamantyl]methyl]amine (Ad-L)**

The synthesis of Ad-L was modified from a previous report by our group.28 (3,5-Dimethyl-1H-pyrazolyl)methanol (0.252 g, 2 mmol) was dissolved in anhydrous CH3CN (30 mL). 1-Adamantanemethanamine (0.166 g, 1 mmol) was added and the solution stirred in a closed vessel for 24 h at room temperature. The solvent was removed under reduced pressure and the resultant white solid re-dissolved in 10 mL of n-hexane, filtered and the clear solution cooled overnight at 4 °C, yielding white crystals (0.26 g, yield 68%). 1H NMR (300 MHz, CDCl3): 1.21 (s, 6H, Ad-CH2–), 1.54 (d, 3H, J = 16.3 Hz, Ad-CH2CH3), 1.61 (d, 3H, J = 12.3 Hz, Ad-CH2CH3), 1.84 (s, 3H, Ad-CH3), 2.19 (s, 6H, Pz-CH3), 2.27 (s, 6H, Pz-CH3), 2.37 (s, 2H, Ad-CH2–), 4.91 (s, 4H, Pz-CH2–N–), 5.79 (s, 2H, Pz-CH3). 13C NMR (75.5 MHz, CDCl3): δ (ppm) 12.1 (Pz-CH3), 14.2 (Pz-CH3), 29.1 (Ad-CH3), 35.4 (Ad-C), 37.7 (Ad-CH2), 41.1 (Ad-CH), 62.2 (Ad-CH2–N–), 69.0 (N-CH2-Pz), 106.3 (Pz-CH), 140.2 (Pz-C), 147.9 (Pz-C). ESI-MS (in CH3Cl2, m/z (%)): [M + H]+ = 381 (100), [2M + Na]+ = 784 (30). Anal. calcd for C33H33N3: C, 72.40; H, 9.25; N, 18.35. Found: C, 72.35; H, 8.38; N, 18.12%.

**Synthesis of adamantyl-containing Pd(n) complex (Ad-L–PdCl2)**

PdCl2(NCCH3)2 was synthesized following a literature procedure.44 A suspension of PdCl2 (1.00 g, 5.65 mmol) was heated under reflux in CH3CN (50 mL) with vigorous stirring for 10 h under N2. The resultant wine-red colored solution was cooled for 16 h at 4 °C and a yellow-orange solid was filtered, washed with Et2O and dried in vacuo at room temperature.
PdCl₂(NCCH₃)₂ (0.070 g, 0.27 mmol) in dry CH₂Cl₂ (10 mL) and Ad-L (0.103 g, 0.27 mmol) in dry CH₂Cl₂ (5 mL) were mixed and stirred at room temperature for 12 h (ref. 62) and then concentrated under vacuum. Et₂O (5 mL) was added to induce precipitation. A yellow-orange solid was obtained, washed with Et₂O, and dried under vacuum. The product was crystallized from a CH₂Cl₂–Et₂O mixture to give bright orange crystals (0.14 g, yield 92%).

1H NMR (500 MHz, CDCl₃); 1.64 (s, 6H, Ad-CH₂–), 1.70 (d, 3H, J = 18.9 Hz, Ad-CH–), 1.78 (d, 3H, J = 11.9 Hz, Ad-CH₂–), 2.07 (s, 3H, Ad-CH₃), 2.14 (s, 2H, Ad-CH₂–), 2.36 (s, 6H, Ad-CH₃), 2.78 (s, 6H, Pz-CH₃), 5.23 (d, 2H, J = 15.1 Hz, Pz-CH₃), 5.87 (s, 2H, Pz CH), 7.11 (d, 2H, J = 15.7 Hz, Pz-CH₂–). 13C NMR (125 MHz, CDCl₃); δ (ppm) 13.6 (Pz CH₃), 15.8 (Pz-CH₃), 28.8 (Ad-CH₂), 37.2 (Ad-C), 37.4 (Ad-CH₂), 41.8 (Ad-CH), 57.6 (Ad-CH₃–), 70.7 (N–CH₂–Pz), 108.8 (Pz-CH), 143.7 (Pz-C), 151.9 (Pz-C). ESI-MS (in CH₂Cl₂/m/z (%)); [M + Cl]⁺ = 524 (100), [M + Na]⁺ = 576 (20). Analytical calc. for C₃₂H₄₅Cl₂N₅Pd: C, 49.43; H, 6.31; N, 12.53. Found: C, 48.66; H, 5.71; N, 11.91%.

### Measurements and experimental methods

**General procedure for Suzuki–Miyaura coupling reaction**

**Method 1.** Palladium[a] complex (Ad-L–PdCl₂) (1.4 mg, 0.0025 mmol) was dissolved in 0.5 mL of MeOH and 0.03 mL of acetone in a clean vial with stirring at 40 °C for a bright yellow solution resulted. The acetone assists complete dissolution of the complex. This solution was then added dropwise to dmβ-CD (3.5 mg, 0.0025 mmol) in deionized water (1.5 mL) at stirring at room temperature. The pH was adjusted to 11.0 with water and dried under vacuum at 50 °C. The reaction mixture was neutralized with dilute aqueous HCl and a white coupling product was isolated by centrifugation (6000 rpm, r.t.). The clear filtrate was transferred to a clean vial, and measured amounts of fresh substrate were added with stirring at room temperature. The pH was adjusted to 11.0 using dilute aqueous NaOH. After the required time had elapsed, the white coupling product was isolated by centrifugation, and the clear filtrate was recycled and reused for the next coupling reaction.

**Yield calculation for Suzuki–Miyaura coupling reaction**

Yields were calculated by 1H NMR spectroscopy based on the 4-bromobenzoic acid used as hexadecane as an internal standard. After the Suzuki–Miyaura coupling reaction, the reaction mixture was neutralized with dilute aqueous HCl and a measured amount of hexadecane (usually 14 mg) in ethyl acetate (4 mL) was added. The organic phase was separated, and the reaction mixture extracted with fresh ethyl acetate (3 × 3 mL). The organic extracts were combined, washed twice with water (5 mL), dried over anhydrous Na₂SO₄, and a 0.9 mL aliquot was filtered, evaporated at room temperature and re-dissolved in deuterated solvent (acetone-δ). The yield of the product was calculated from a calibration curve (Fig. S2, † R² = 0.998).

**Catalyst recycling**

After a standard Suzuki–Miyaura coupling reaction of 4-bromobenzoic acid and phenylboronic acid in water–methanol (3 : 1, v/v), the white coupling product was isolated by centrifugation (6000 rpm, r.t.). The clear filtrate was transferred to a clean vial, and measured amounts of fresh substrate were added with stirring at room temperature. The pH was adjusted to 11.0 using dilute aqueous NaOH. After the required time had elapsed, the white coupling product was isolated by centrifugation, and the clear filtrate was recycled and reused for the next coupling reaction.

### Conclusions

A key catalytic design in this system is the incorporation of an adamantyl tether onto the ligand backbone that does not interfere with the catalytic process but activating its inclusion property to capture a β-cyclodextrin moiety and uses that to solubilise the entire supramolecular hybrid in an aqueous or aqueous–organic mixed media. The main challenge in this design is the chemical and thermal stability of the supramolecular hybrid catalysts and, very importantly, introduction of the inclusion pair (adamantyl and cyclodextrin here) must not interfere with the catalytic site thereby curtailing the catalytic efficacy. The crystal and molecular structure of the adamantyl-tethered complex reported herein gives clear evidence that the bulky pendant is pointing away from the metal center and that its introduction does not interfere with the coordination sphere of the Pd(n). It also does not impose undesirable bonding of the amine with the metal, which has been witnessed in other functional hybrid ligand systems. Encouraged by these results, we are actively applying this simple yet powerful design to a range of other metal catalysts and catalytic reactions.

### Acknowledgements

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### Notes and references
