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Conjugate addition of arylboronic acids to α,β -unsaturated carbonyl compounds in aqueous medium using Pd(II) complexes with dihydroxy-2,2'-bipyridine ligands: homogeneous or heterogeneous nano-catalysis?†

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The conjugate addition of arylboronic acids to α,β -unsaturated carbonyl compounds in water under air has been studied using a series of palladium(II) derivatives containing symmetrically disubstituted-2,2'-bipyridine ligands. Among them, best results were obtained with complex [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**), which selectively provides the desired addition products in good to high yields under mild conditions. Catalytically active palladium nanoparticles are formed in the course of the reactions. In the presence of sodium dodecyl sulfate (SDS) these nanoparticles can be stabilized and recycled.

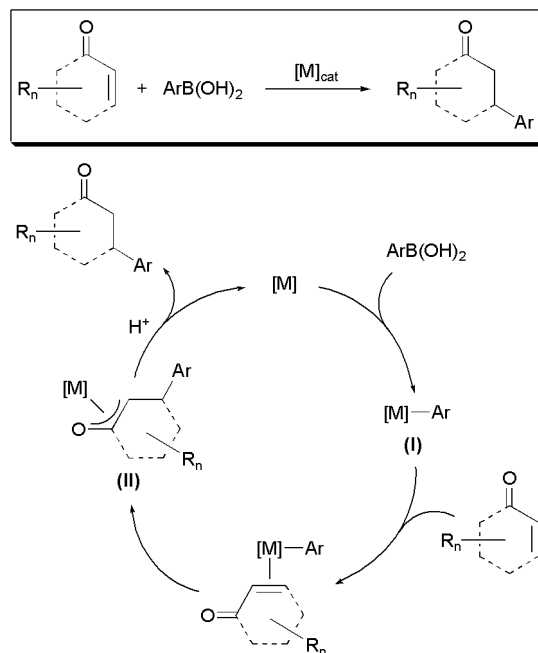
Introduction

The conjugate 1,4-addition of organometallic compounds to electron-deficient olefins represents one of the most powerful tools presently available to create new C–C bonds.¹ In this context, since the pioneering work of Miyaura and co-workers in 1997,² metal-catalyzed conjugated addition of arylboronic acids to α,β -unsaturated carbonyl compounds has attracted considerable attention because of the higher stability of these reagents towards air and moisture, as well as their improved functional group tolerance, as compared to the more classical organocopper, -zinc, -zirconium, -aluminum and -mercury species (Scheme 1).³ In fact, the maturity gained by this reaction in such a short period of time is such that, its asymmetric version, is nowadays considered as the best method for the enantioselective introduction of aryl and alkenyl groups at β -position of these electron-deficient olefins.³

From a mechanistic point of view (Scheme 1),³ these catalytic transformations involve the initial transmetalation of the aryl group from the arylboronic acid to the metal, followed by the insertion of the C=C bond of the enone (or enal) into the metal-carbon bond of intermediate **I**, to give a π -oxa-allyl complex **II**. Final protonolysis of **II** liberates the corresponding conjugated addition product with regeneration of the catalytically active species. To date, these catalytic reactions have been dominated by Rh(I)-based complexes.^{2,3}

Palladium species are also known to promote the conjugate addition of arylboronic acids to α,β -unsaturated carbonyl compounds.⁴ However, despite the lower cost associated with this metal, palladium-based catalysts remain comparatively much less studied due to their propensity to promote the competitive formation of Heck-type coupling products *via* β -hydride elimination pathways (Scheme 2).^{4,5}

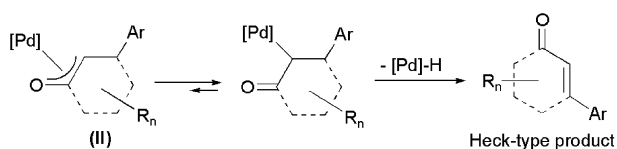
Among the different Pd-based systems able to catalyze the conjugate addition of arylboronic acids to α,β -unsaturated carbonyl compounds selectively,⁶ Pd(OAc)₂/bipy⁷ and the



Scheme 1 The catalytic 1,4-conjugate addition of arylboronic acids to α,β -unsaturated carbonyl compounds.

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† Electronic supplementary information (ESI) available: Characterization data of organic compounds **5aa–5ea** and figures showing the hydrogen bond network in the crystal packing of complex **14**. CCDC reference numbers 828891 and 828892. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cy00214g



Scheme 2 The competitive β -hydride elimination in intermediate **II**.

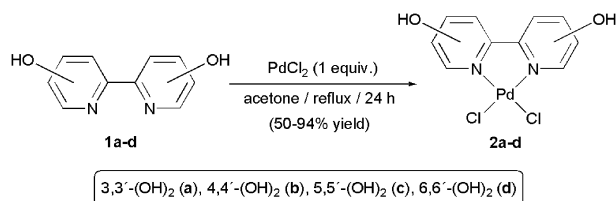
dimeric complex $[\{Pd(\mu-OH)(bipy)\}_2][BF_4]_2$ ⁸ merit to be highlighted due to their outstanding activity under mild conditions. Apparently, the presence of the π -acceptor 2,2'-bipyridine ligand (bipy) coordinated to the active Pd(II) center inhibits the β -hydride elimination and promotes the protonolysis of intermediate **II**.⁹

Remarkably, in the presence of appropriate surfactants, the addition reactions promoted by Pd(OAc)₂/bipy could also be conveniently performed in aqueous media.^{7b} This fact represents a significant advance towards Green Chemistry, since one of its principles is to circumvent the use of hazardous organic solvents as they are responsible for a large part of the waste generated by the chemical processes.¹⁰ In this sense, water is one of the most appealing candidates to replace organic solvents due its abundance, low-cost, and non-toxic and safe nature.¹¹ Indeed, the use of water as solvent in catalytic and stoichiometric organic synthesis has spread throughout the chemical community at a staggering pace during the last two decades.¹²

With all these precedents in mind, and as part of our current research work dealing with the development of catalytic transformations in environmentally friendly aqueous media,¹³ we have investigated the conjugated addition of arylboronic acids to α,β -unsaturated carbonyl compounds in water using well-defined palladium(II) complexes containing symmetrically disubstituted-2,2'-bipyridine ligands functionalized with hydrophilic groups. Our goal was to find palladium catalysts able to promote these addition processes in aqueous medium without the aid of surfactants.¹⁴ As the reader will see, in the course of these studies we have discovered a new example of heterogeneous nanocatalysis involving metallic nanoparticles.

Results and discussion

Introduction of hydrophilic ligands in the coordination sphere of a transition-metal is probably the most popular method for the preparation of water-soluble catalysts.¹⁵ In this context, although scarcely employed in homogeneous catalysis, a large number of 2,2'-bipyridine ligands substituted with hydrophilic groups are known.¹⁶ In particular, our initial efforts focused on the use of the symmetrically substituted dihydroxy-2,2'-bipyridines **1a–d** due to their easy access from commercially available starting materials.¹⁷ We also believed that the ability of the OH groups to establish hydrogen bonds with water would help the solubilization of the resulting complexes in this medium. Thus, by reacting an stoichiometric amount of these dihydroxylated ligands with PdCl₂ in refluxing acetone, we prepared the new complexes **2a–d**, which were isolated as air-stable yellow or brown solids in 50–94% yield (Scheme 3). Alternatively, compounds **2a–d** can be generated in similar yields starting from the soluble precursor [PdCl₂(COD)] (COD = 1,5-cyclooctadiene). In both cases, **2a–d** directly precipitate in the reaction media.



Scheme 3 Preparation of complexes **2a–d**.

Surprisingly, despite the presence of OH groups in their structure, complexes **2a–d** were found to be insoluble in water at room temperature (only in the case of **2a** a solubility of 0.5 mg cm⁻³ could be measured).¹⁸ However, we must note that at high temperature (80 °C), or under strongly basic conditions (pH 14),¹⁹ we were able to prepare aqueous solutions of these compounds of up to 10 mg cm⁻³. Characterization of complexes **2a–d** was straightforward following their analytical and spectroscopic data, with the ¹H and ¹³C{¹H} NMR spectra recorded in DMSO-*d*₆ showing the expected signals for the protons and carbons of the 2,2'-bipyridyl skeletons (details are given in the Experimental Section).²⁰ The presence of the OH units was confirmed by the appearance of a strong absorption band at *ca.* 3400 cm⁻¹ in the IR spectra of these compounds.

To prove the catalytic potential of complexes **2a–d**, we investigated the conjugate addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) as model reaction. Initial exploratory experiments were performed at 80 °C in pure aqueous medium under air, using a **3a**:**4a** molar ratio of 1:3 and a palladium loading of 5 mol%. As shown in Table 1, under these conditions, all the complexes synthesized were able to provide the desired 3-phenylcyclohexanone (**5aa**) as the major reaction product along with variable amounts of the Heck-type product **6aa** and cyclohexanone, the latter resulting from the reduction of the C=C bond of **3a** (entries 1–4).²¹ However, marked differences in activity and selectivity were observed depending on the substitution pattern of the 2,2'-bipyridine

Table 1 Catalytic addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) in water using complexes **2a–d**^a

Entry	Catalyst	Time	Conversion ^b	Yield 5aa ^b	Yield 6aa ^b
1	2a	1 h	> 99%	98%	1%
2	2b	24 h	> 99%	95%	4%
3 ^c	2c	5 h	99%	87%	7%
4 ^d	2d	24 h	35%	18%	3%
5 ^e	PdCl ₂	3 h	51%	37%	8%
6 ^f	2a	1 h	> 99%	98%	1%
7 ^g	2a	1 h	> 99%	98%	1%

^a Reactions performed at 80 °C under air using 0.5 mmol of **3a**, 1.5 mmol of **4a**, 0.025 mmol of the corresponding Pd(II) complex **2a–d** and 1 cm³ of water. Unless otherwise stated, formation of trace amounts of cyclohexanone was in all cases observed (up to 1%). ^b Determined by GC. ^c 5% of cyclohexanone was formed. ^d 14% of cyclohexanone was formed. ^e 6% of cyclohexanone was formed. ^f Reaction performed under N₂ atmosphere. ^g Reaction performed in the presence of 15 mol% of **1a**.

ligand attached to palladium. Thus, higher activities were observed with complexes **2a** and **2c**, substituted with the OH groups in 3,3' and 5,5' positions, as compared to their 4,4' and 6,6'-disubstituted counterparts **2b** and **2d** (entries 1 and 3 vs. 2 and 4). This fact clearly indicates that electronic effects govern the catalytic activity of these complexes, increasing when the electronic density on the metal is lower.²² In particular, the best results were obtained with complex [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) which was able to generate selectively the desired ketone **5aa** in 98% GC-yield after only 1 h of heating (entry 1). As shown in entry 5, under identical reaction conditions, significantly worse results were obtained using PdCl₂ as catalyst, thus confirming the key role played by the dihydroxylated bipy ligand in this catalytic reaction.²³ It is also worth of note that no differences in the activity and selectivity of **2a** were observed when the catalytic reactions were performed under inert atmosphere (entry 6) or in the presence of an excess of the ligand **1a** (entry 7).

A striking feature of all the catalytic reactions listed in Table 1 is the gradual appearance of a black solid suspension. The solid material generated in one of these reactions (entry 1) was isolated by filtration, washed with diethyl ether and acetone, and studied by means of TEM (Transmission Electron Microscopy) and SEM/EDX (Scanning Electron Microscopy/Energy-Dispersive X-ray spectroscopy) techniques. The micrographs obtained (Fig. 1) revealed the formation of aggregates (100–250 nm) of nanoparticles with spherical morphology and a size range of 6–12 nm. SEM/EDX measurements confirmed that the solid was mainly composed of elemental palladium (73.7 wt%).²⁴ The additional presence of carbon (19.2 wt%), oxygen (3.3 wt%) and nitrogen (1.8 wt%) in the sample also evidenced that part of the 3,3'-dihydroxy-2,2'-bipyridine ligand **1a** is “retained” by the nanoparticles. At this point, we must note that decomposition of the Pd(II) complex **2a** into Pd(0) is closely related to the dissociation of the bipy ligand, since a fluorescence phenomenon was observed when the catalytic reaction mixture was exposed to UV light (Fig. 2). Green light emission when irradiated with 365 nm of ultraviolet light is a hallmark of ligand **1a**,^{17b} property that loses when coordinated to a metal center.

Formation of palladium nanoparticles starting from **2a–d** is rather surprising since in previous studies by Lu and Tsai, using related Pd(II)-bipy systems, such a fact was not evidenced.^{7,8,14} That's why, in order to determine whether this

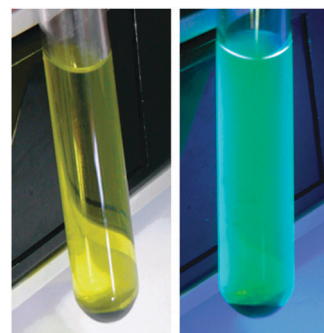


Fig. 2 The fluorescence behaviour observed in the presence of UV-light (right; non-irradiated sample on the left).

property is unique of complexes **2a–d**, we decided to prepare a series of Pd(II) derivatives with different 2,2'-bipy ligands and explore their behaviour under identical reaction conditions. In particular, in addition to the parent compound [PdCl₂(bipy)] (**11**),²⁵ we synthesized the hydrophilic derivatives **12–14** by refluxing an equimolar mixture of PdCl₂ with the appropriate 4,4'-disubstituted-2,2'-bipyridine **8–10** in acetone for 24 h (Scheme 4). These complexes were isolated as air-stable yellow-orange solids in 93–95% yield after a simple filtration of the reaction mixtures since all of them directly precipitate in the medium. Similarly to **2a–d**, the dihydroxymethyl-substituted derivative **13** was found to be insoluble in water at room temperature (a solubility of 5 mg cm⁻³ was observed in basic medium at pH 14).¹⁹ In contrast, the Pd(II) complexes **12** and **14**, substituted with trimethylammonium and carboxylic acid groups, respectively, dissolve in water at neutral pH (10 and 5 mg cm⁻³ at 20 °C).

Complexes **12–14** were characterized by means of standard spectroscopic techniques (IR and multinuclear NMR) and elemental analyses, all data being fully consistent with the proposed formulations (details are given in the Experimental Section).²⁶ In addition, the structures of **13** and **14** could be unambiguously confirmed by means of X-ray diffraction analyses.† X-ray quality crystals were obtained by slow diffusion of methanol into saturated solutions of complexes **13–14** in dimethylsulfoxide. ORTEP views of the molecules are shown in Fig. 3 and 4, respectively (selected bonding parameters are listed in the captions).²⁷ The geometry around the Pd atom is slightly distorted square-planar in both structures, with metal-centered angles between 80.45(10)° and 95.50(8)°. The palladium

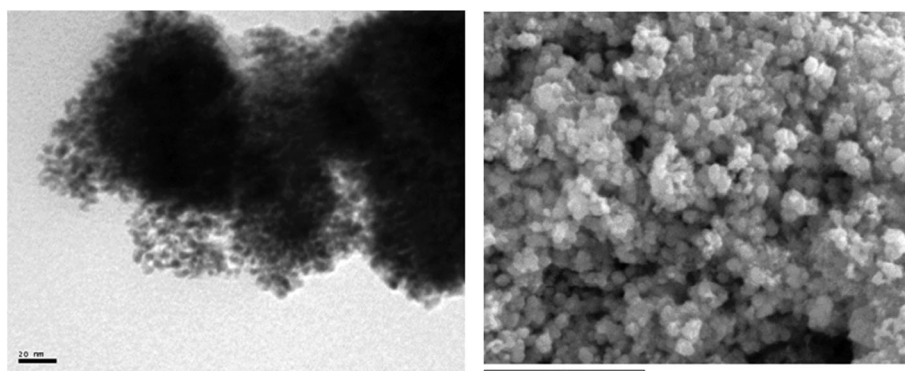
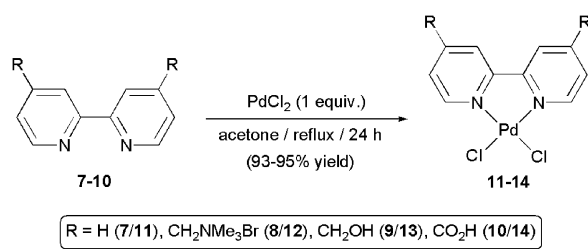


Fig. 1 TEM (left) and SEM (right) images of the agglomerated nanoparticles isolated from the catalytic reaction described in entry 1 of Table 1.



Scheme 4 Preparation of complexes 11–14.

atom is displaced for only 0.0002(3) (**13**) and 0.0064(2) (**14**) Å from the plane defined by the Cl(1), Cl(2), N(1) and N(2) atoms. These data, along with the Pd–N (2.018(3)–2.027(2) Å) and Pd–Cl (2.2752(8)–2.2967(9) Å) bond distances observed, are comparable to those previously reported in the literature for the parent compound [PdCl₂(bipy)] (**11**).²⁸

As shown in Table 2, complexes **11–14** were active in the conjugate addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) in water, delivering all of them 3-phenylcyclohexanone (**5aa**) as the major reaction product. As observed with the dihydroxylated derivatives **2a–d**, minor amounts of the Heck-type coupling product **6aa** and cyclohexanone were also formed in these reactions and, more importantly, the apparition of a black precipitate of palladium metal was in all cases evidenced during the catalytic events. Instability of the Pd(II)/bipy systems seems to be, therefore, a general trend under the aqueous catalytic conditions employed. The result collected in entry 2 deserves some additional comments since the catalytic behaviour of complex **12**, generated *in situ* from [PdCl₂(NH₃)₂] and the cationic 2,2'-bipyridine ligand **8**, has been recently described by Tsai and co-workers.¹⁴ In their work, in which the addition reaction of **4a** to **3a** was studied in the pH range 1–12, there is no feedback on the formation of palladium black and a very poor yield of **5aa** was reached when the catalytic reaction was conducted at neutral pH (6% *vs.* our 72%). In contrast, under extreme acidic conditions (pH 1) almost quantitative formation of **5aa** was observed and the catalytic system could be recycled several times. Note that, as shown in entries 5–6 of Table 2, complexes *cis*-[PdCl₂(PTA)] (**15**) and *cis*-[PdCl₂(DAPTA)] (**16**) containing the water-soluble phosphine ligands 1,3,5-triaza-7-phosphatricyclo[3.3.1.1^{3,7}]decane (PTA) and 3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (DAPTA) were almost inoperative in this catalytic transformation.

From this general catalyst screening, and despite its tendency to decompose into elemental palladium, the dihydroxylated derivative [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) emerged as the top choice due to its selectivity and efficiency (entry 1 in Table 1). In this regard, additional studies showed that this complex (5 mol%) is also able to promote efficiently the addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) at room temperature, even when a 1:1 molar ratio of the reactants was employed.²⁹ Under this challenging reaction conditions, ketone **5aa** was quantitatively generated after 5 h, and could be isolated in analytically pure form (86% yield) by extraction from the aqueous phase with hexanes and subsequent chromatographic purification (entry 1 in Table 3). It is

† CCDC-828891 (**13**) and 828892 (**14**) contain the supplementary crystallographic data for this paper.

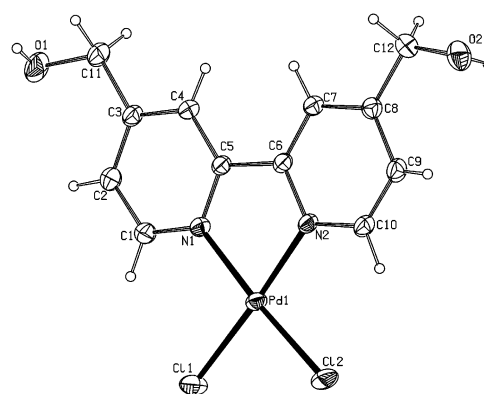


Fig. 3 ORTEP-type view of the structure of compound **13** showing the crystallographic labelling scheme. Thermal ellipsoids are drawn at 20% probability level. Selected bond distances (Å): Pd–Cl(1) 2.2967(9); Pd–Cl(2) 2.2869(8); Pd–N(1) 2.022(2); Pd–N(2) 2.018(3); C(11)–O(1) 1.398(5); C(12)–O(2) 1.410(5). Selected bond angles (°): Cl(1)–Pd–Cl(2) 89.33(3); Cl(1)–Pd–N(1) 95.50(8); Cl(1)–Pd–N(2) 175.85(7); Cl(2)–Pd–N(1) 175.10(8); Cl(2)–Pd–N(2) 94.74(7); N(1)–Pd–N(2) 80.45(10); C(3)–C(11)–O(1) 113.8(3); C(8)–C(12)–O(2) 113.9(3).

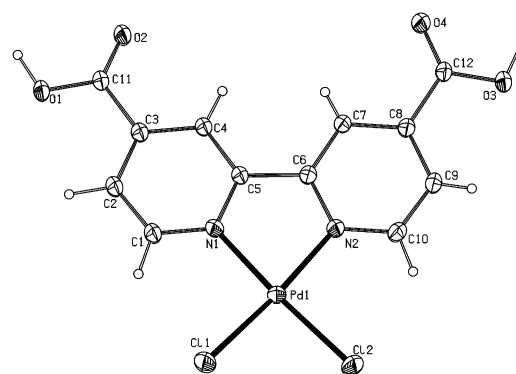
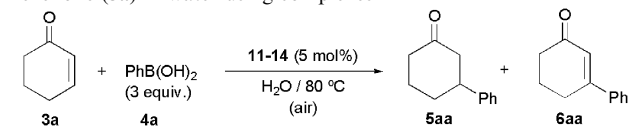


Fig. 4 ORTEP-type view of the structure of compound **14** showing the crystallographic labelling scheme. Thermal ellipsoids are drawn at 20% probability level. Selected bond distances (Å): Pd–Cl(1) 2.2752(8); Pd–Cl(2) 2.2771(8); Pd–N(1) 2.027(2); Pd–N(2) 2.023(2); C(11)–O(1) 1.306(3); C(11)–O(2) 1.201(3); C(12)–O(3) 1.312(3); C(12)–O(4) 1.202(4). Selected bond angles (°): Cl(1)–Pd–Cl(2) 90.01(3); Cl(1)–Pd–N(1) 94.98(7); Cl(1)–Pd–N(2) 174.66(7); Cl(2)–Pd–N(1) 174.42(7); Cl(2)–Pd–N(2) 94.41(7); N(1)–Pd–N(2) 80.75(9); C(3)–C(11)–O(1) 113.7(2); C(3)–C(11)–O(2) 122.5(2); O(1)–C(11)–O(2) 123.8(3); C(8)–C(12)–O(3) 113.0(2); C(8)–C(12)–O(4) 123.0(2); O(3)–C(12)–O(4) 124.1(3).

also worth mentioning that the activity of complex **2a** is retained at lower catalyst loadings. Thus, using only 3 mol% of **2a**, quantitative formation of **5aa** was observed by GC after 8 h of stirring at r.t. (incomplete reactions after 24 h were observed with palladium loadings of 0.5 and 0.005 mol%).

To further define the scope of this green catalytic system, the addition of a number of other arylboronic acids to 2-cyclohexenone (**3a**), 2-cyclopentenone (**3b**) and 2-cyclohexenone (**3c**), was explored using 5 mol% of **2a**. Thus, as shown in Table 3 (entries 2–13), the expected addition products **5ab–5ca** could be selectively prepared in good to excellent yields (82–99% GC yields; 73–88% isolated yields), regardless of the electronic nature of the aromatic ring of the boronic acid.

Table 2 Catalytic addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) in water using complexes **11–14**^a

Entry	Catalyst	Time	Conversion ^b	Yield 5aa ^b	Yield 6aa ^b
1	11	3 h	> 99%	91%	7%
2	12	32 h	79%	72%	6%
3	13	5 h	> 99%	92%	6%
4	14	24 h	> 99%	86%	11%
5	15	24 h	4%	3%	1%
6	16	24 h	12%	11%	1%

^a Reactions performed at 80 °C under air using 0.5 mmol of **3a**, 1.5 mmol of **4a**, 0.025 mmol of the corresponding Pd(II) complex **11–14** and 1 cm³ of water. Formation of trace amounts of cyclohexanone was in all cases observed. ^b Determined by GC.

Only trace amounts of the corresponding Heck-type products **6ab–6ca** were detected by GC in the crude reaction mixtures ($\leq 1\%$), thus confirming the remarkable selectivity of **2a**. Although all these processes were operative at r.t. employing equimolar ratios of the reactants, in some cases the use of high temperature (80 °C) and/or excess of the boronic acid was required to achieve good conversions. The generality of the process was further demonstrated by using the acyclic substrates **3d–e** (entries 14–15), which also led to the addition products **5da–5ea** in high yields.

Again, in all the reactions listed in Table 3 extensive formation of palladium nanoparticles was observed. This fact raised the question on the real nature of the catalytically active species in these aqueous 1,4-addition reactions.³⁰ Thus, in order to determine whether the process is really homogeneous, the conjugate addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) promoted by [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) was performed in the presence of mercury.³¹ As shown in Fig. 5, although the reaction works in the presence of Hg(0), a remarkably lower conversion was attained after 5 h as compared to that performed in its absence (64% vs. > 99%), thus suggesting that the palladium nanoparticles play a role in this catalytic transformation.

In line with this, an interesting observation was made when the same catalytic reaction was carried out, in the absence of Hg(0), under more dilute conditions (graphs (b), (c) and (d) in Fig. 6). The irregularities in the curves at short times (20–40 min) visually match with the progressive change of color of the aqueous solution from yellow to orange and finally to dark green, a color change that is accompanied by a turbidity. TEM images recorded from a sample collected at this moment (reaction (c)) confirmed the appearance of the first nanoparticles (Fig. 7).

Moreover, as shown in Fig. 8, addition of mercury at this stage almost completely suppressed the catalysis. All these facts strongly support that, only at the early stages of the catalytic events, molecular Pd(II) species are the real active species and that, once formed, palladium(0) nanoparticles are the responsible to drive the catalytic reactions to completion.³²

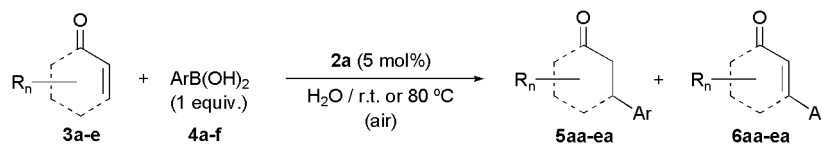
Finally, recycling of the nanoparticles was also investigated using again the addition of phenylboronic acid (**4a**) to 2-cyclo-

hexenone (**3a**) as model reaction. Thus, we observed that the solid material generated from [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) shows, after filtration and washing with diethyl ether and acetone (Fig. 1), a very poor activity and a low selectivity towards the formation of the desired 1,4-addition product **5aa**. In particular, 40 h of heating at 80 °C were required to achieve the complete consumption of **3a**, the catalytic reaction leading to **5aa** in only 40% GC yield, along with 20% of the Heck product **6aa** and 39% of the reduced cyclohexanone. This result is not surprising since agglomeration of metal-nanoparticles is known to have a negative impact on the activity and selectivity of several catalytic transformations.^{33,34}

In order to avoid the agglomeration of the catalytically active Pd nanoparticles, and facilitate their possible recycling, some experiments were performed in the presence of surfactants. This type of additives are known to confer an “electrosteric” stabilization to nanoparticles, thus preventing the formation of bulk metal.^{35,36} Among the different surfactants employed,³⁷ best results were obtained with sodium dodecyl sulfate (SDS; 0.01 M aqueous solution).³⁸ Thus, as shown in Fig. 9, performing the catalytic addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) with [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) in this medium, the aqueous phase containing the stabilized nanoparticles could be effectively reused in at least six consecutive runs after simple extraction of the reaction product **5aa** with hexanes. Remarkably, compared to the use of pure water, no differences in activity were observed in SDS_(aq) during first cycle. TEM images recorded from the aqueous phase after extraction of **5aa** confirmed the formation of micelles (size range 40–150 nm) in which the palladium nanoparticles remain embedded (Fig. 10). Only after the fifth run agglomeration of the nanoparticles was observed. Interestingly, we must also note that the use of SDS-stabilized palladium nanoparticles generated in the absence of the 3,3'-dihydroxy-2,2'-bipyridine ligand **1a** led, under the same reaction conditions, to only 9% conversion after 24 h.³⁹ This fact clearly indicates that the ligand **1a** “retained” by the nanoparticles plays a key role during the catalytic event.

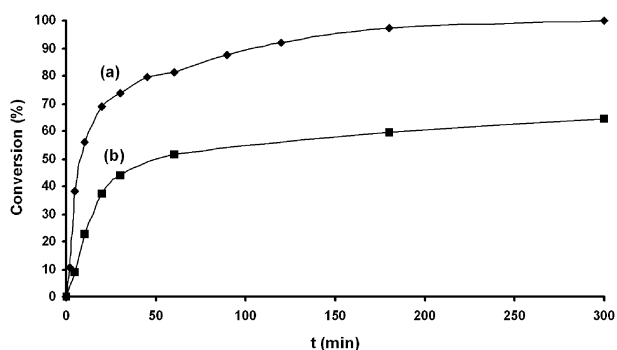
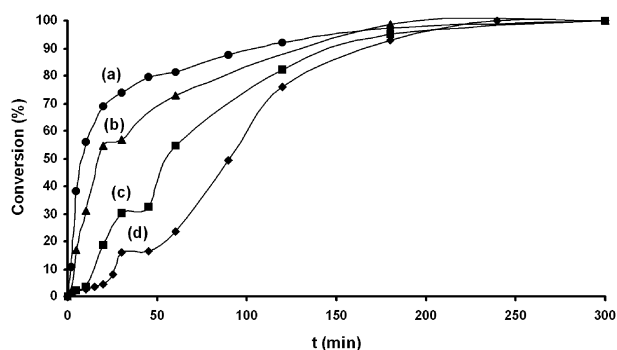
Conclusions

In summary, we have found that the readily accessible Pd(II) complex [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) is an excellent precatalyst for the selective conjugate addition of arylboronic acids to α,β -unsaturated carbonyl compounds under challenging reactions conditions, *i.e.* in environmentally friendly aqueous media under air. Moreover, we have demonstrated that such a catalytic transformation, which usually proceeds under homogeneous conditions, is in fact a new example of a heterogeneous process involving metallic nanoparticles. Thus, we have evidenced that only at the early stages of the catalytic events are molecular Pd(II) species responsible for the catalysis, with nanoparticles of elemental palladium, generated by decomposition of [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**), being the true active species at the end of the catalytic reactions. Interestingly, in the presence of the surfactant SDS (sodium dodecyl sulfate) these metal nanoparticles can be stabilized by the micelles thus allowing their effective recycling, a key factor for practical applications of this heterogeneous catalytic system.⁴⁰

Table 3 Catalytic addition of arylboronic acids to α,β -unsaturated carbonyl compounds in water using complex **2a**: Generality of the process^a

Entry	Substrate 3	ArB(OH) ₂ 4	Temperature	Time	Conversion ^b	Yield of 5 ^b	Yield of 6 ^b
1	2-cyclohexenone (3a)	Ar = Ph (4a)	r.t.	5 h	>99%	5aa ; > 99% (86%)	6aa ; < 1%
2	2-cyclohexenone (3a)	Ar = 4-C ₆ H ₄ Me (4b)	r.t.	24 h	98%	5ab ; 97% (78%)	6ab ; 1%
3	2-cyclohexenone (3a)	Ar = 4-C ₆ H ₄ OMe (4c)	r.t.	48 h	99%	5ac ; 98% (77%)	6ac ; 1%
4	2-cyclohexenone (3a)	Ar = 4-C ₆ H ₄ Cl (4d)	r.t.	24 h	99%	5ad ; 98% (76%)	6ad ; 1%
5	2-cyclohexenone (3a)	Ar = 4-C ₆ H ₄ Br (4e)	80 °C	1 h	>99%	5ae ; > 99% (80%)	6ae ; < 1%
6 ^c	2-cyclohexenone (3a)	Ar = 2-C ₆ H ₄ Me (4f)	80 °C	15 h	99%	5af ; 98% (77%)	6af ; 1%
7	2-cyclopentenone (3b)	Ar = Ph (4a)	r.t.	4 h	97%	5ba ; 96% (80%)	6ba ; 1%
8	2-cyclopentenone (3b)	Ar = 4-C ₆ H ₄ Me (4b)	r.t.	24 h	93%	5bb ; > 92% (86%)	6bb ; < 1%
9 ^c	2-cyclopentenone (3b)	Ar = 4-C ₆ H ₄ OMe (4c)	r.t.	48 h	>99%	5bc ; > 98% (90%)	6bc ; < 1%
10 ^c	2-cyclopentenone (3b)	Ar = 4-C ₆ H ₄ Cl (4d)	r.t.	24 h	>99%	5bd ; > 98% (82%)	6bd ; < 1%
11 ^c	2-cyclopentenone (3b)	Ar = 4-C ₆ H ₄ Br (4e)	80 °C	24 h	83%	5be ; 82% (73%)	6be ; 1%
12 ^c	2-cyclopentenone (3b)	Ar = 2-C ₆ H ₄ Me (4f)	r.t.	48 h	99%	5bf ; 98% (79%)	6bf ; 1%
13	2-cycloheptenone (3c)	Ar = Ph (4a)	r.t.	16 h	>99%	5ca ; > 98% (88%)	6ca ; < 1%
14	3-buten-2-one (3d)	Ar = Ph (4a)	80 °C	1 h	99%	5da ; 83% (69%)	6da ; 16%
15	cinnamaldehyde (3e)	Ar = Ph (4a)	80 °C	26 h	75%	5ea ; 75% (60%)	6ea ; not observed

^a Reactions performed under air using 0.5 mmol of the corresponding α,β -unsaturated carbonyl compound **3a-e** and arylboronic acid **4a-f**, 0.025 mmol of complex **2a** and 1 cm³ of water. ^b Determined by GC (isolated yields after chromatographic work-up are given in brackets). ^c Reaction performed using 3 equivalents of the arylboronic acid.

**Fig. 5** Catalytic addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) using [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) in the absence (a) or presence (b) of mercury. Conditions: Reactions performed at r.t. under air using 0.5 mmol of **3a**, 0.5 mmol of **4a**, 0.025 mmol of **2a** and 1 cm³ of water.**Fig. 6** Effect of the concentration in the catalytic addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) using [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**). Conditions: Reactions performed at r.t. under air using 0.5 mmol of **3a**, 0.5 mmol of **4a**, 0.025 mmol of **2a** and 1 (a), 1.25 (b), 2 (c) or 3.3 (d) cm³ of water.

Experimental section

General methods

All reagents were obtained from commercial suppliers and used as received with the exception of the disubstituted 2,2'-bipyridine ligands **1a-d**,¹⁷ **8**,⁴¹ **9**⁴² and **10**,⁴³ and the Pd(II) complex **11**,²⁵ **15**⁴⁴ and **16**⁴⁴ which were prepared by following the methods reported in the literature. Flash chromatography was performed using Merck silica gel 60 (230-400 mesh). Infrared spectra were recorded on a Perkin-Elmer 1720-XFT spectrometer. NMR spectra were recorded on a Bruker DPX-300 instrument at 300 MHz (¹H) or 75.4 MHz (¹³C). The chemical shift values (δ) are given in parts per million and are referred to the residual peak of the deuterated solvent employed. DEPT experiments have been carried out for all the compounds reported. GC measurements were made on a Hewlett-Packard

HP6890 equipment using a Supelco Beta-Dex™ 120 column. GC-MS measurements were performed on a Agilent 6890N equipment coupled to a 5973 mass detector (70eV electron impact ionization) using a HP-1MS column. Elemental analyses were provided by the Analytical Service of the Instituto de Investigaciones Químicas (IIQ-CSIC, Seville) and performed with a Leco-CHNS microanalyzer. TEM (Transmission Electron Microscopy) and SEM/EDX (Scanning Electron Microscopy-Energy/Dispersive X-ray spectroscopy) measurements were provided by the Analytical Service of the University of Oviedo and recorded on MET-JEOL 2000 EX-II and MEB JEOL-6610LV equipments, respectively.

Synthesis of complexes 2a-d. A suspension of PdCl₂ (0.100 g, 0.56 mmol) in acetone (20 cm³) was treated with the appropriate dihydroxy-2,2'-bipyridine ligand **1a-d** (0.105 g, 0.56 mmol) under refluxing conditions for 24 h. Then, the reaction mixture

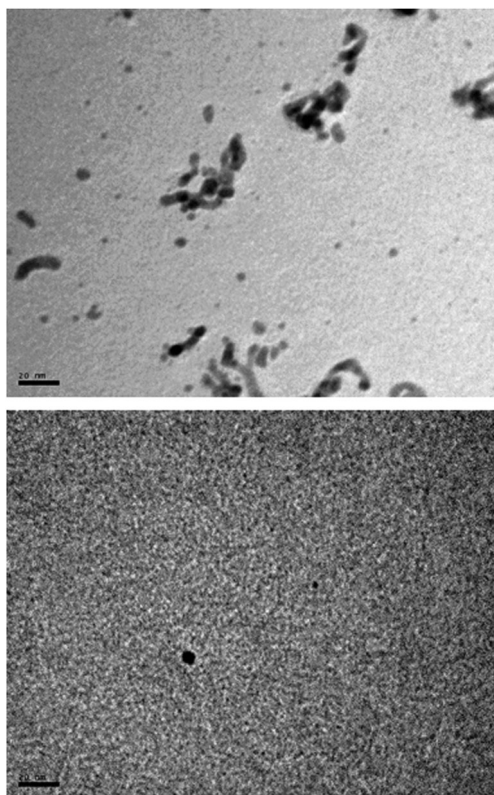


Fig. 7 TEM images of the sample taken from the reaction medium when the turbidity begins to appear (the sample corresponds to the reaction denoted as (c) in Fig. 6).

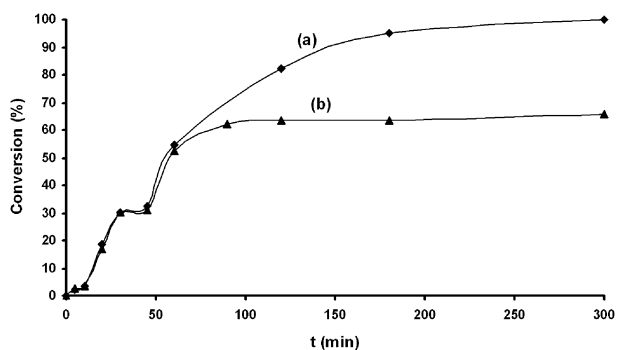


Fig. 8 Catalytic addition of phenylboronic acid (**4a**) to 2-cyclohexenone (**3a**) using [PdCl₂{3,3'-(OH)₂-2,2'-bipy}] (**2a**) without addition of Hg(0) (a) and with addition of Hg(0) after 60 min of reaction (b). Conditions: Reactions performed at r.t. under air using 0.5 mmol of **3a**, 0.5 mmol of **4a**, 0.025 mmol of **2a** and 2 cm³ of water.

was allowed to reach the room temperature and the resulting solid precipitate filtered, washed with acetone (2 × 5 cm³) and vacuum-dried. Characterization data are as follows: (**2a**): Yellow solid; Yield: 94% (0.192 g); IR (KBr): ν 709 (s), 798 (s), 1200 (m), 1329 (s), 1445 (s), 1653 (m), 3083 (w), 3446 (s) cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 8.22 (m, 4H, H₄, H_{4'}, H₅ and H_{5'}), 8.49 (dd, ³J_{HH} = 4.2 Hz, ⁴J_{HH} = 2.2 Hz, 2H, H₆ and H_{6'}) ppm (signal for OH protons not observed); ¹³C{¹H} NMR (DMSO-*d*₆): δ 125.2 (C₅ and C_{5'}), 131.0 (C₄ and C_{4'}), 138.3 (C₆ and C_{6'}), 146.7 (C₂ and C_{2'}), 160.1 (C₃ and C_{3'}) ppm; Elemental analysis calcd (%) for C₁₀H₈Cl₂N₂O₂Pd: C, 32.86;

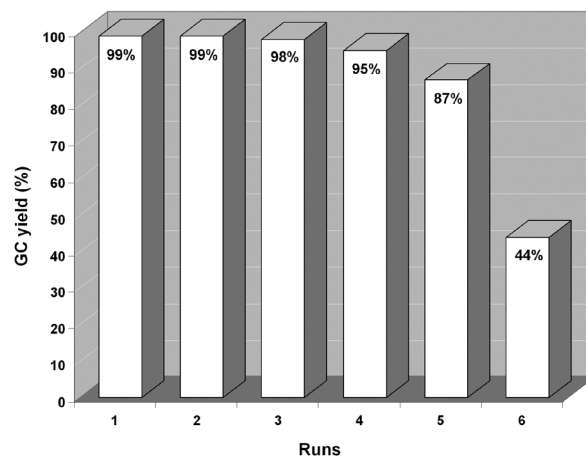
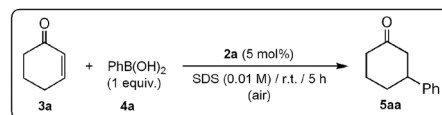


Fig. 9 Catalyst recycling by stabilization of the catalytically active nanoparticles with SDS. GC-yields are in all cases given after 5 h of reaction.

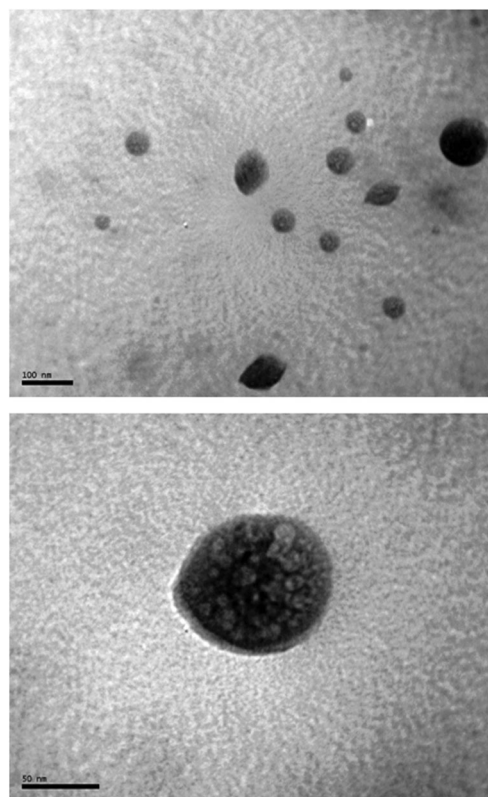


Fig. 10 TEM images of the micelles generated in the presence of SDS. Sample taken after the first catalytic cycle.

H, 2.21; N, 7.66; found: C, 32.89; H, 2.14; N, 7.34. (**2b**): Yellow solid; Yield: 83% (0.170 g); IR (KBr): ν 871 (m), 1038 (m), 1225 (m), 1262 (m), 1349 (m), 1456 (m), 1624 (s), 3051 (m), 3435 (m) cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 7.09 (dd, ³J_{HH} = 6.6 Hz, ⁴J_{HH} = 2.6 Hz, 2H, H₅ and H_{5'}), 7.73 (d, ⁴J_{HH} = 2.6 Hz, 2H, H₃ and H_{3'}), 8.73 (dd, ³J_{HH} = 6.6 Hz,

2H, H₆ and H_{6'}), 12.24 (br, 2H, OH) ppm; ¹³C{¹H} NMR (CDCl₃): δ 112.3 (C₅ and C_{5'}), 115.0 (C₃ and C_{3'}), 150.2 (C₆ and C_{6'}), 158.8 (C₂ and C_{2'}), 169.0 (C₄ and C_{4'}) ppm; Elemental analysis calcd (%) for C₁₀H₈Cl₂N₂O₂Pd: C, 32.86; H, 2.21; N, 7.66; found: C, 32.90; H, 2.36; N, 7.26. (**2c**): Beige solid; Yield: 50% (0.102 g); IR (KBr): ν 548 (w), 708 (w), 829 (m), 1063 (m), 1198 (s), 1303 (s), 1482 (s), 1576 (s), 1617 (m), 3064 (w), 3366 (s) cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 7.61 (dd, ³J_{HH} = 8.8 Hz, ⁴J_{HH} = 2.6 Hz, 2H, H₄ and H_{4'}), 8.18 (d, ³J_{HH} = 8.8 Hz, 2H, H₃ and H_{3'}), 8.70 (dd, ⁴J_{HH} = 2.6 Hz, 2H, H₆ and H_{6'}), 11.33 (br, 2H, OH) ppm; ¹³C{¹H} NMR (CDCl₃): δ 123.5 (C₃ and C_{3'}), 126.8 (C₄ and C_{4'}), 137.6 (C₆ and C_{6'}), 148.1 (C₂ and C_{2'}), 154.9 (C₅ and C_{5'}) ppm; Elemental analysis calcd (%) for C₁₀H₈Cl₂N₂O₂Pd: C, 32.86; H, 2.21; N, 7.66; found: C, 32.88; H, 2.54; N, 7.65. (**2d**): Light brown solid; Yield: 82% (0.168 g); IR (KBr): ν 800 (s), 1011 (m), 1021 (m), 1162 (s), 1218 (m), 1293 (m), 1326 (m), 1425 (s), 1480 (s), 1574 (m), 1616 (s), 3099 (w), 3434 (m) cm⁻¹; ¹H NMR (CD₃NO₂): δ 6.94 (dd, ³J_{HH} = 8.2 Hz, ⁴J_{HH} = 3.2 Hz, 2H, H₅ and H_{5'}), 7.76 (dd, ³J_{HH} = 8.2 Hz, ⁴J_{HH} = 3.2 Hz, 2H, H₃ and H_{3'}), 8.04 (dd, ³J_{HH} = 8.2 and 8.2 Hz, 2H, H₄ and H_{4'}) ppm (signal for OH protons not observed); Elemental analysis calcd (%) for C₁₀H₈Cl₂N₂O₂Pd: C, 32.86; H, 2.21; N, 7.66; found: C, 33.01; H, 2.15; N, 7.69.

Synthesis of complex 12. Complex **12**, isolated as an orange solid, was prepared as described for **2a–d** starting from PdCl₂ (0.100 g, 0.56 mmol) and the cationic 2,2'-bipyridine ligand **8** (0.258 g, 0.56 mmol). Yield: 94% (0.335 g); IR (KBr): ν 843 (m), 904 (w), 1095 (w), 1244 (w), 1419 (s), 1490 (s), 1559 (s), 2967 (m), 3021 (m) cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 3.22 (s, 18H, CH₃), 4.83 (s, 4H, CH₂), 8.01 (d, ³J_{HH} = 5.8 Hz, 2H, H₅ and H_{5'}), 9.21 (d, ³J_{HH} = 5.8 Hz, 2H, H₆ and H_{6'}), 9.29 (s, 2H, H₃ and H_{3'}) ppm; ¹³C{¹H} NMR (DMSO-*d*₆): δ 53.2 (CH₃), 65.9 (CH₂), 128.5 (C₅ and C_{5'}), 131.7 (C₃ and C_{3'}), 142.2 (C₄ and C_{4'}), 150.7 (C₆ and C_{6'}), 157.0 (C₂ and C_{2'}) ppm; Elemental analysis calcd (%) for C₁₈H₂₈N₄Br₂Cl₂Pd: C, 33.91; H, 4.43; N, 8.79; found: C, 34.09; H, 4.30; N, 8.87.

Synthesis of complex 13. Complex **13**, isolated as a yellow solid, was prepared as described for **2a–d** starting from PdCl₂ (0.100 g, 0.56 mmol) and 4,4'-bis(hydroxymethyl)-2,2'-bipyridine **9** (0.121 g, 0.56 mmol). Yield: 93% (0.205 g); IR (KBr): ν 837 (m), 1061 (m), 1420 (s), 1616 (s), 2916 (w), 3062 (m), 3446 (m) cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 4.75 (d, ³J_{HH} = 5.6 Hz, 4H, CH₂), 5.83 (t, ³J_{HH} = 5.6 Hz, 2H, OH), 7.74 (d, ³J_{HH} = 5.9 Hz, 2H, H₅ and H_{5'}), 8.44 (s, 2H, H₃ and H_{3'}), 9.03 (d, ³J_{HH} = 5.9 Hz, 2H, H₆ and H_{6'}) ppm; ¹³C{¹H} NMR (DMSO-*d*₆): δ 62.4 (CH₂), 121.6 (C₅ and C_{5'}), 125.1 (C₃ and C_{3'}), 150.4 (C₄ and C_{4'}), 157.0 (C₆ and C_{6'}), 159.0 (C₂ and C_{2'}) ppm; Elemental analysis calcd (%) for C₁₂H₁₂Cl₂N₂O₂Pd: C, 36.62; H, 3.07; N, 7.12; found: C, 36.55; H, 3.15; N, 7.23.

Synthesis of complex 14. Complex **14**, isolated as a yellow solid, was prepared as described for **2a–d** starting from PdCl₂ (0.100 g, 0.56 mmol) and 2,2'-bipyridine-4,4'-dicarboxylic acid **10** (0.137 g, 0.56 mmol). Yield: 95% (0.222 g); IR (KBr): ν 663 (s), 810 (m), 1210 (s), 1262 (m), 1411 (s), 1733 (s), 2521 (w), 2967 (w), 3082 (m), 3201 (m), 3299 (m) cm⁻¹; ¹H NMR (DMSO-*d*₆): δ 8.22 (dd, ³J_{HH} = 6.0 Hz, ⁴J_{HH} = 1.6 Hz, 2H, H₅ and H_{5'}), 9.02 (d, ⁴J_{HH} = 1.6 Hz, 2H, H₃ and H_{3'}),

9.32 (d, ³J_{HH} = 6.0 Hz, 2H, H₆ and H_{6'}) ppm (signal for CO₂H protons not observed); ¹³C{¹H} NMR (DMSO-*d*₆): δ 124.8 (C₅ and C_{5'}), 127.8 (C₃ and C_{3'}), 143.5 (C₄ and C_{4'}), 152.0 (C₆ and C_{6'}), 158.0 (C₂ and C_{2'}), 165.7 (CO₂H) ppm; Elemental analysis calcd (%) for C₁₂H₈O₄Cl₂N₂Pd: C, 34.19; H, 1.91; N, 6.65; found: C, 34.36; H, 2.08; N, 6.90.

General procedure for the catalytic addition of arylboronic acids to α,β-unsaturated carbonyl compounds promoted by complex 2a. Under aerobic atmosphere, the corresponding arylboronic acid **4a–f** and α,β-unsaturated carbonyl compound **3a–e** (0.5 mmol of each), the palladium complex [PdCl₂(3,3'-(OH)₂-2,2'-bipy)] (**2a**; 0.009 g, 0.025 mmol; 5 mol%), and water (1 cm³) were introduced into a sealed tube and the resulting reaction mixture stirred at room-temperature (or 80 °C) for the indicated time (see Table 3). The course of the reaction was monitored by taking regularly samples of ca. 20 μL which, after extraction with hexanes (3 cm³), were analyzed by GC. Once the reaction finished, the crude was extracted with hexanes (5 × 2 cm³) and purified by flash chromatography (silica gel; hexanes as eluent). The identity of the resulting carbonyl compounds **5aa–5ea** was assessed by comparison of their ¹H and ¹³C{¹H} NMR spectroscopic data with those reported in the literature and by their fragmentation in GC/MSD (details are given in the ESI file).

Nanoparticles recycling. In a sealed tube, 2-cyclohexenone (**3a**; 48 μL, 0.5 mmol), phenylboronic acid (**4a**; 0.061 g, 0.5 mmol) and complex [PdCl₂(3,3'-(OH)₂-2,2'-bipy)] (**2a**; 0.009 g, 0.025 mmol; 5 mol%) were suspended in 0.01 M SDS_(aq) (1 cm³) under aerobic conditions. The resulting reaction mixture was stirred at room-temperature for 5 h and controlled by GC to determine the conversion and yield of the process. Then, the reaction product was extracted with hexanes (5 × 2 cm³) and traces of the organic solvent eliminated at reduced pressure. Substrates **3a** and **4a** (0.5 mmol of each) were added to the aqueous phase and the mixture stirred again at room temperature for 5 h.

X-Ray crystal structure determination of compounds 13 and 14. Crystals suitable for X-ray diffraction analysis were obtained by slow diffusion of methanol into a saturated solution of the corresponding complex in dimethylsulfoxide. The most relevant crystal and refinement data are collected in Table 4.

In both cases data collection was performed on a Oxford Diffraction Xcalibur Nova single crystal diffractometer, using Cu-Kα radiation (λ = 1.5418 Å). Images were collected at a 65 mm fixed crystal-to-detector distance using the oscillation method, with 1° oscillation and a variable exposure time per image of 10–15 s for **13** and 2–6 s for **14**. Data collection strategy was calculated with the program CrysAlis Pro CCD.⁴⁵ Data reduction and cell refinement were performed with the program CrysAlis Pro RED.⁴⁵ An empirical absorption correction was applied using the SCALE3 ABSPACK algorithm as implemented in the program CrysAlis Pro RED.⁴⁵

In all cases the software package WINGX was used for space group determination, structure solution and refinement.⁴⁶ Both structures were solved by direct methods using SIR2004.⁴⁷ Isotropic least-squares refinement on *F*² using SHELXL97 was performed.⁴⁸ During the final stages of the refinements, all the positional parameters and the anisotropic temperature factors of all the non-H atoms were refined. The H atoms were

Table 4 Crystal data and structure refinement for compounds **13** and **14**

	13	14
Empirical formula	C ₁₂ H ₁₂ Cl ₂ N ₂ O ₂ Pd·2DMSO	C ₁₂ H ₈ O ₄ Cl ₂ N ₂ Pd·DMSO
Formula weight	549.79	499.63
Temperature/K	293(2)	293(2)
Wavelength/Å	1.5418	1.5418
Crystal system	Triclinic	Triclinic
Space group	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$
Crystal size/mm	0.214 × 0.079 × 0.034	0.064 × 0.031 × 0.018
<i>a</i> /Å	8.4783(3)	7.6738(3)
<i>b</i> /Å	11.6061(4)	10.4974(4)
<i>c</i> /Å	13.1535(5)	12.5545(4)
α (°)	67.125(4)	112.689(3)
β (°)	89.797(3)	90.017(3)
γ (°)	68.971(4)	108.646(3)
<i>Z</i>	2	2
Volume/Å ³	1099.10(7)	875.20(6)
Calculated density/g cm ⁻³	1.661	1.896
μ /mm ⁻¹	11.034	12.748
<i>F</i> (000)	556	496
θ range/°	3.69 to 73.88	3.85 to 73.97
Index ranges	-9 ≤ <i>h</i> ≤ 10 -14 ≤ <i>k</i> ≤ 14 -16 ≤ <i>l</i> ≤ 16	-9 ≤ <i>h</i> ≤ 9 -12 ≤ <i>k</i> ≤ 13 -15 ≤ <i>l</i> ≤ 15
Completeness to θ_{\max}	94.3%	94.5%
No. of reflns. collected	11501	9900
No. of unique reflns.	4216 (<i>R</i> _{int} = 0.0217)	3365 (<i>R</i> _{int} = 0.0247)
No. of parameters/restraints	349/8	292/2
Refinement method	Full-matrix least-squares on <i>F</i> ²	
Goodness-of-fit on <i>F</i> ²	1.060	1.039
Weight function (<i>a</i> , <i>b</i>)	0.0507, 0.7398	0.0347, 0.5458
<i>R</i> ₁ [<i>I</i> > 2 σ (<i>I</i>)] ^a	0.0313	0.0251
<i>wR</i> ₂ [<i>I</i> > 2 σ (<i>I</i>)] ^a	0.0816	0.0640
<i>R</i> ₁ (all data)	0.0335	0.0288
<i>wR</i> ₂ (all data)	0.0839	0.0662
Largest diff. peak and hole/e Å ⁻³	0.345 and -0.712	0.549 and -0.385

$$^a R_1 = \frac{\sum(|F_o| - |F_c|)}{\sum|F_o|}; wR_2 = \frac{\{\sum[w(F_o^2 - F_c^2)^2]\}}{\{\sum[w(F_o^2)^2]\}}^{1/2}$$

found from different Fourier maps and included in a refinement with isotropic parameters. In the crystal of **13** two DMSO molecules of solvation per formula unit of the complex were found. One of them is disordered, with the sulphur atom being located in two positions with occupancy of 50%. In the crystal of **14** a DMSO molecule per formula unit of the complex was also found with the sulphur atom equally disordered. The function minimized was $[\sum wFo^2 - Fc^2]/\sum w(Fo^2)^{1/2}$ where $w = 1/[\sigma^2(Fo^2) + (aP)^2 + bP]$ (*a* and *b* values are collected in Table 4) with $\sigma^2(Fo^2)$ from counting statistics and $P = (\text{Max}(Fo^2 + 2Fc^2))/3$. Atomic scattering factors were taken from the International Tables for X-ray Crystallography.⁴⁹ Geometrical calculations were made with PARST.⁵⁰ The crystallographic plots were made with PLATON.⁵¹

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