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ARTICLE TYPE

Bis(imino)acenaphthene (BIAN)-supported palladium(II) carbene complexes as effective C–C coupling catalysts and solvent effects in organic and aqueous media

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The synthesis and catalytic properties of two new 1,2-acenaphthenyl *N*-heterocyclic carbene-supported palladium(II) catalysts are presented. The acenaphthenyl carbene has been prepared with mesityl or 1,5-diisopropyl *N*-aryl substituents. Comprehensive catalytic studies for the Suzuki coupling of aryl halides with aryl boronic acids have been conducted. In general, the diisopropyl-functionalised catalyst showed superior selectivity and reactivity. A comparison of the catalytic performances in dichloromethane, toluene and water at low temperatures (30–40 °C) is also presented. Both catalysts were proficient in the homogeneous Suzuki coupling of aryl iodides, bromides and chlorides with boronic acids in dichloromethane. Similar reactions in water led to the formation of insoluble colloidal catalytic species that still exhibited high activity in the Suzuki reaction with aryl chlorides. Reactions performed in toluene showed intermediate results; partial catalyst decomposition led to concomitant homogeneous and heterogeneous catalysis. The heterogeneous palladium precipitates could be easily recovered by filtration and reactivated for subsequent use. Activation energies determined for aryl bromide-based Suzuki reactions were found to be in the range of 159–171 kJ mol⁻¹ in organic solvents and 111–116 kJ mol⁻¹ in water. The corresponding activation energy for the aryl chloride was found to be 322 kJ mol⁻¹ in water.

Introduction

20 The Suzuki-Miyaura cross-coupling reaction is used extensively in industrial processes for the formation of carbon-carbon bonds.¹ This reaction plays an important industrial-scale role for the production of natural products, pharmaceuticals, and agrochemicals.^{2–4} Typically, Suzuki coupling is performed in an organic solvent using homogeneous catalysts that are designed to generate exclusively the *hetero*-coupled biaryl product. The C–C coupled products are obtained by the treatment of an aryl halide with an organoborane in the presence of a suitable base (Scheme 1).⁵ Complexes based on Group X metals are the most proficient in this task and can be rendered soluble in appropriate organic solvents using a range of spectator ligands such as 3-chloropyridine, triethylamine, and allyl moieties.^{6–9} Suzuki catalysts often employ bulky phosphine ligands that result in optimal catalytic activity and selectivity. However, phosphine ligands are typically susceptible to oxidation and metal-ligand degradation.^{10–12} As a consequence, *N*-heterocyclic carbenes (NHCs) have attracted interest as more stable supporting ligands. NHCs feature a significantly stronger electron donating character than phosphines, which enhances the stability of resulting complexes towards heat, air and moisture. The strong σ -donating ability of the NHCs also promotes oxidative addition of aryl halides and can assist in reductive elimination of biaryl products.^{13,14}

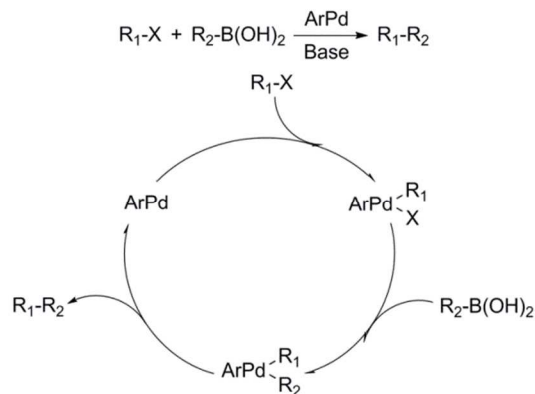
Recent advances in ‘green’ Suzuki coupling have focused on developing catalysts that are easily recoverable and can operate in environmentally benign solvents. Some pertinent examples in-

clude, heterogenised catalysts (*e.g.*, nanoparticles),^{15–17} metallo-polymers,^{18–20} and single-site catalysts grafted onto insoluble support media (*e.g.*, silica or alumina).^{21–23} For example, Sekar *et al.* generated active catalysts for Suzuki, Heck, and Sonogashira cross-coupling reactions using covalently-bonded Pd-C_(binaphthyl) nanoparticles.¹⁵ These nanoparticles formed quantitatively C–C bonds even after several cycles of catalyst use and recovery.¹⁵ Meanwhile, Ma *et al.* have prepared active Pd(II) Suzuki catalysts by direct anchoring to SBA-16-type silica, which afforded an easily recoverable and recyclable heterogeneous composite catalyst that showed excellent activity even after prolonged recycling.²¹

The pursuit of greener Suzuki catalysts has also resulted in the development of molecular complexes that are catalytically active in environmentally-benign and renewable solvents, such as water. Morales-Morales *et al.* utilized water-soluble pincer ligands in aqueous media to convert *p*-substituted aryl bromides to the corresponding *hetero*-coupled biphenyl products in appreciable yields.²⁴ Such aqueous reactions raise an important question: do homogeneous molecular catalysts remain intact during Suzuki reaction conditions, or do the catalysts decompose to generate new (presumably heterogeneous) catalyst species? A technique that is commonly employed to address this question involves the injection of excess Hg(0) into the reaction mixture to poison any leached Pd(0) species.^{25,26} Alternatively, the likely identity of the active Suzuki cross-coupling species can be determined *via* a filtration test, in which the reaction is interrupted and separated into a supernatant layer and a precipitate; both phases are then independently probed for the presence of trace metal species and

catalytic reactivity.^{27–28}

In the present work, two new 1,2-acenaphthenyl *N*-heterocyclic carbene-supported palladium(II) catalysts have been synthesized with the objective of assessing their comparative performance in the Suzuki reaction, when conducted in polar and nonpolar organic solvents, and in aqueous media. In general, it was found that these catalysts consistently behaved as stable homogeneous catalysts in organic solvents, and decomposed to give less well-defined, but still highly active heterogeneous catalyst species in water. In fact, reactions performed in water significantly enhanced the activity of the original Pd(II) catalysts, based on measured rate constants and activation energies. In addition, both catalysts studied here were able to activate aryl chloride feedstocks in all solvents. Consideration of the trend in activation energies for the aryl halides (C–Cl > C–Br > C–I; 407, 346, 280 kJ mol⁻¹, respectively) reveals that aryl chlorides are significantly the least reactive, yet they are industrially the most attractive because heavy halogenated by-products can be avoided.²⁹ In this study, appreciable yields of cross-coupled products were obtained using aryl chlorides at temperatures as low as 40 °C.



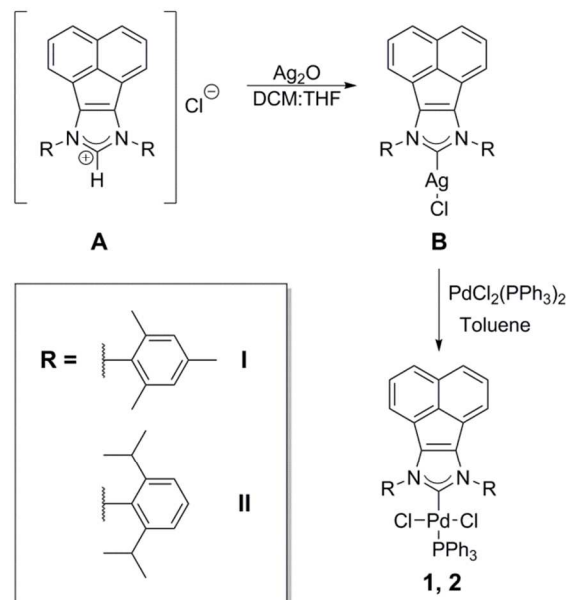
Scheme 1. Generic mechanism for the Suzuki-Miyaura coupling reaction

Results and Discussion

1. Catalyst synthesis and structures.

The present work has focused on the catalytic activities of two related Pd(II)-carbene complexes with the objective of expanding the scope of this family of catalysts. The carbene ligands in question (A-I and A-II) were prepared using the previously reported route for B-II (Scheme 2).³⁰ The silver(I)-carbene complexes B-I and B-II were treated directly with PdCl₂(PPh₃)₂ in toluene to give the corresponding Pd(II) complexes, (IMes)PdCl₂PPh₃ (1) and (IPr)PdCl₂PPh₃ (2) by transmetalation and elimination of AgCl (Scheme 2; see ESI for further synthetic details). The single crystal X-ray diffraction structure of 2 was obtained by growing suitable crystals by slow evaporation of CH₂Cl₂ in air (Fig. 1 and Table 1).[‡] The metal site Pd1 in 2 displays a somewhat distorted square-planar environment, most likely imposed by the steric bulk of the *N*-diisopropyl aryl groups that are rotated approximately perpendicular to the C₃N₂ ring plane, which is commonly observed for such Brookhart-type complexes.³¹ The Pd1–C1

bond distance is 2.04, Å while the *trans*-oriented phosphine Pd1–P1 bond is 2.32 Å. The average Pd–P bond length obtained from a survey of similar NHC-Phosphine Pd(II) structures in the CCDC is somewhat shorter, at 2.267 Å. This may be indicative of a particularly strong *trans*-influence exerted by the acenaphthene carbene ligand. As expected, the fused five- and six-membered aromatic acenaphthene structure in 2 displays a distinct curvature with a maximum out-of-plane displacement of 0.18(2) Å degrees with respect to the C1–N1–C2–C3–N2 mean plane.



Scheme 2. Syntheses of palladium catalysts 1 and 2

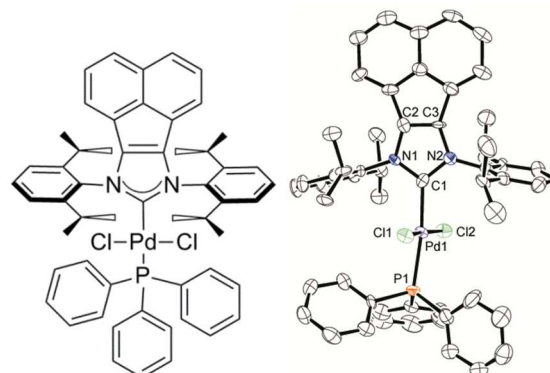


Figure 1. Crystal structure of 2

Table 1 Selected bond distances and angles for 2.

Length (Å)		Angles (°)	
Pd1–Cl1	2.295(2)	Cl1–Pd1–Cl2	172.82(10)
Pd1–Cl2	2.321(2)	C1–Pd1–Cl1	92.2(2)
Pd1–C1	2.041(7)	C1–Pd1–Cl2	90.4(2)
Pd1–P1	2.324(2)	C1–Pd1–P1	173.3(2)
C2–C3	1.356(12)	N1–C1–N2	107.3(7)

Tu *et al.* recently reported the synthesis of a related NHC complex that was shown to be an active catalyst for Buchwald-Hartwig aminations^{32,33} and Suzuki-Miyaura coupling reactions.^[34] Merino *et al.* have developed a similar Ru-based

complex that is capable of ring closing metathesis.³⁵ The catalytic activities of **1** and **2** with respect to Suzuki-Miyaura cross-coupling reactions were initially explored with aryl iodides (0.216 mmol), phenylboronic acid (0.259 mmol) and K₂CO₃ (0.647 mmol) in toluene, CH₂Cl₂, or H₂O (3.0 cm³). These solvents were chosen as examples of nonpolar and polar aprotic solvents, and polar protic solvents, respectively. Prior to injection of the catalyst, all reaction mixtures were stirred at 40 °C until all solids had dissolved.

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2. Suzuki coupling by catalysts **1** and **2** with aryl iodide, bromide and chloride precursors.

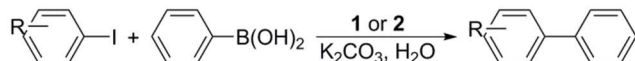


Table 2 Suzuki-Miyaura biaryl coupling of aryl iodides by **1** and **2**

Substrate	Catalyst	Entry	Conversion (%)	S ^{hetero} (%)
	1	1a	81.5	99.7
		1b	4.6	91.2
		1c	100	97.1
	2	2a	77.3	99.6
		2b	23.3	97.3
		2c	100	98.9

¹⁵ ^a Reaction conditions: aryl iodide (0.216 mmol), phenylboronic acid (0.259 mmol), K₂CO₃ (0.647 mmol), **1** or **2** (1.0 mol% Pd), solvent (a-toluene, b-CH₂Cl₂, c-H₂O; 3.0 mL), 40 °C, 20 h; all reactions were monitored by GC.

The catalyst loadings were determined using UV-vis spectrophotometry (Figs. S1 & S2), and **1** or **2** was rapidly injected into the reaction mixture at $t = 0$. The reaction mixtures were then stirred at 40 °C for 20 h. A summary of the outcomes of these reactions are presented in Table 2. **1** and **2** both converted *p*-iodobenzaldehyde into the desired *hetero*-coupled product with greater than 91% selectivity (determined by GC analysis; Table 2). The observed catalytic activities revealed a significant dependence on the nature of the solvent: the catalysts exhibited extremely low activities in CH₂Cl₂ (Table 2; entries 1b & 2b), but achieved 77–81% conversions in toluene (Table 2; entries 1a & 2a) and complete conversion in H₂O (Table 2; entries 1c & 2c).

Suzuki-Miyaura cross-coupling reactions were expanded to the use of aryl bromides under otherwise identical reaction conditions; the results of these reactions are summarized in Table 3. **1** and **2** exhibited comparable percentage conversions and selectivities of *p*-bromobenzaldehyde (Table 3; entries 3-8) to those of analogous reaction conditions with the iodo- precursor. Again, the highest conversion was obtained for H₂O. Interestingly, the catalytic activities appeared to be unaffected by the functional group position on the bromobenzaldehydes. The bromoanisoles revealed a substantial dependence on the nature of the solvent as well as on the location of the methoxy functional group. In aqueous solution, the bromoanisoles yielded slightly lower conversions and selectivities than those of the analogous bromobenzaldehydes (Table 3; entries 9c, 10c, 13c, & 14c). Selectivity for the desired *hetero*-coupled products was generally high (70–100%) for aldehyde-substituted precursors, regardless of the substitution pattern, solvent or catalyst employed (Table 3; entries 3–8). However, much greater variation in selectivity was observed for methoxy-substituted precursors (0–99%). Most notably, catalyst

1 did not yield any of the *hetero*-coupled biphenyl product from *m*-bromoanisole in H₂O, yet catalyst **2** was highly selective under the same conditions (Table 3; entries 11c & 12c). It is difficult to identify clear trends in the observed reactivity; the variation in selectivities is likely due to inter-play of steric, electronic and solvation effects. In general, both catalysts were significantly less active when tested in both polar and apolar organic solvents. Less than 50% conversion to the *hetero*-coupled product was obtained when the bromoanisoles were used (Table 3; entries 9-

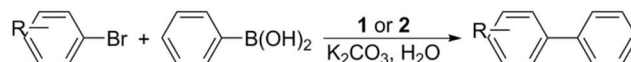
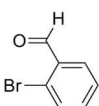
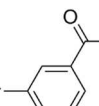
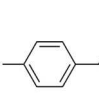
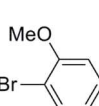
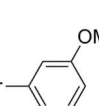
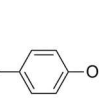
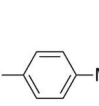
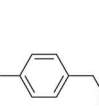


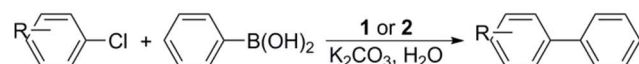
Table 3 Suzuki-Miyaura reactions of aryl bromides by **1** and **2**

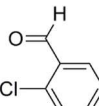
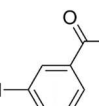
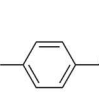
Substrate	Catalyst	Entry	Conversion (%)	S ^{hetero} (%)
	1	3a	92.3	84.4
		3b	17.4	95.9
		3c ^b	96.1	100
	2	4a	84.3	79.8
		4b	59.0	90.4
		4c ^b	92.3	100
	1	5a	77.8	83.4
		5b	60.4	97.6
		5c ^b	98.1	95.7
	2	6a	72.5	69.3
		6b	79.9	88.3
		6c ^b	92.9	97.1
	1	7a	87.5	92.1
		7b	82.2	99.8
		7c ^b	100	100
	2	8a	86.6	86.6
		8b	81.4	98.5
		8c ^b	99.3	96.1
	1	9a	31.7	13.4
		9b	46.4	91.5
		9c	93.6	84.6
	2	10a	37.3	14.3
		10b	43.1	67.9
		10c	91.3	95.5
	1	11a	44.9	31.0
		11b	2.8	76.3
		11c	33.1	0
	2	12a	39.8	22.5
		12b	52.9	77.3
		12c	62.9	99.1
	1	13a	47.9	24.4
		13b	60.9	95.9
		13c	100	99.5
	2	14a	46.1	22.1
		14b	34.3	78.9
		14c	90.8	89.0
	1	15a	43.9	58.5
		15b	93.0	92.4
		15c	100	100
	2	16a	50.5	54.5
		16b	100	88.5
		16c	96.6	89.1
	1	17a	44.3	39.7
		17b	68.9	90.2
		17c	100	100
	2	18a	41.2	25.5
		18b	60.1	81.6
		18c	98.6	76.7

^a Reaction conditions: aryl bromide (0.270 mmol), phenylboronic acid (0.324 mmol), K₂CO₃ (0.811 mmol), **1** or **2** (1.0 mol% Pd), solvent (a-toluene, b-CH₂Cl₂, c-H₂O; 3.0 mL), 40 °C, 20 h; all reactions were monitored for conversion by GC. ^b 0.1 mol% Pd

14a,b) with the exception of **1** in CH₂Cl₂ (Table 3; entry 13b). It is of particular note that the catalysts were considerably more selective in CH₂Cl₂ than in toluene.

Interestingly, the catalysts were not only more active in

Table 4 Suzuki-Miyaura coupling of aryl chlorides by **1** and **2**

Substrate	Catalyst	Entry	Conversion (%)	S ^{hetero} (%)
	1	19a	42.1	7.2
		19b	18.0	15.8
		19c	87.8	27.0
	2	20a	44.6	23.4
		20b	59.7	100
		20c	100	92.3
	1	21a	40.6	1.4
		21b	15.5	4.7
		21c ^b	76.6	20.6 ^c
	2	22a	42.0	8.9
		22b	39.6	28.4
		22c	96.9	78.8
	1	23a	29.7	11.4
		23b	13.2	12.1
		23c	83.9	89.1
	2	24a	45.2	26.0
		24b	64.7	79.8
		24c	96.1	86.5

^a Reaction conditions: aryl chloride (0.357 mmol), phenylboronic acid (0.429 mmol), K₂CO₃ (1.07 mmol), **1** or **2** (1.0 mol% Pd), solvent (a-toluene, b-CH₂Cl₂, c-H₂O; 3.0 mL), 40 °C, 48h; all reactions were monitored by GC. ^b 2.0 mol% Pd ^c 79.3% selectivity for bifunctionalized *homo*-coupled biaryl product.

reactions employing *p*-functionalized aryl halides, but they were also significantly more selective. *p*-Bromotoluene and *p*-bromoethylbenzene were selected to assist in the examination of the apparent regioselectivity (Table 3; entries 15c & 16c). In contrast to the bromobenzaldehydes and the bromoanisoles, high conversion completeness of the substrate to the desired *hetero*-coupled product were evident for reactions performed in both H₂O and CH₂Cl₂ (Table 3; entries 15-18b,c). However, these catalysts were found to be significantly less active in toluene, since **1** and **2** not only exhibited less than 50% conversion, but were also selective for the undesired *homo*-coupled product (Table 3; entries 15-18a). Both **1** and **2** could activate C–Br bonds in all three solvents with similar conversions and selectivities at lower catalyst loadings (0.1–1.0 mol%). The catalysts appeared to be more active in aqueous media than in either organic medium, for which the catalytic activities were only moderate. The activities in apolar toluene were generally high when halogenated benzaldehydes were employed, but the overall conversion values decreased dramatically for coupling reactions performed using methoxy- and aliphatic-substituted reagents, under otherwise identical conditions. Interestingly, the reactivity pattern observed in more polar CH₂Cl₂ was generally reversed; the highest conversions were measured for methyl- and methox-substituted reagents. Hence, there is a clear solvent dependence upon reactivity (Tables 2 & 3; entries a&b). However, both catalysts were highly selective for the *homo*-coupled products. **1** and **2** activated C–I or C–Br bonds most readily for *para*-substituted reagents, presumably due to a combination of preferential steric and electronic effects of the incoming precursors. The steric demands of the bulky aldehyde and methoxy- functional groups may also protect the C–Br bond from engaging in competing oxidative addition reactions.

Following the optimization of **1** and **2** for the Suzuki coupling of aryl bromides, it was decided to explore the use of aryl chlorides. Aryl chlorides are the most important industrial target,

since they are both cost effective and generate significantly less harmful/corrosive by-products than the analogous aryl bromide and iodides. In our studies, the higher bond dissociation energy of the C–Cl bond resulted in the need for significantly longer

Table 5 Recyclability of **1** and **2** in Suzuki-Miyaura biaryl coupling of the *p*-bromobenzaldehyde supernatant (*sup*) and precipitate (*ppt*)

Catalyst	Entry	% Pd		Conversion %	
		<i>sup</i> ^b	<i>ppt</i> ^b	<i>sup</i>	<i>ppt</i>
1	25a	15	85	87.8	92.5
	25b	97	3	50.4	12.5
	25c	23	77	55.4	98.6
2	26a	52	48	81.0	78.3
	26b	73	27	54.5	4.1
	26c	26	74	0.2	100
Pd-PVP	27 ^c	-	-	0.06	51.5

^a Reaction conditions: *p*-bromobenzaldehyde (0.270 mmol), phenylboronic acid (0.324 mmol), K₂CO₃ (0.811 mmol), Pd (1 mol%), solvent (a-toluene, b-CH₂Cl₂, c-H₂O; 3.0 mL), 40 °C, 20 h; all reactions were monitored by GC. ^b % Pd of supernatant and precipitate determined by ICP-MS. ^c *p*-bromobenzaldehyde (0.270 mmol), phenylboronic acid (0.324 mmol), K₂CO₃ (0.811 mmol), H₂O (3.0 mL), Pd-PVP (0.537 mmol), 40 °C, 20 h

reaction times than those for C–Br to achieve comparable overall conversions at the same reaction temperature (Table 4). Catalyst **1** activated the carbon-chloride bonds with ranges of 13–42% and 76–88% conversion for organic and aqueous solvents, respectively (Table 4; entries 19, 21 & 23). In contrast, **2** resulted in conversion ranges of 40–65% and 96–100%, respectively (Table 4; entries 20, 22 & 24).

As was observed for the use of brominated reagents (*vide supra*), a broad range of selectivity values were measured using *ortho*-, *meta*- and *para*-substituted chlorobenzaldehydes. However, catalyst **2** was consistently more selective than **1** in all solvents. In fact, catalyst **1** only gave appreciable yields of the *hetero*-coupled product when operated in H₂O. In contrast, **2** was moderately, or highly selective in CH₂Cl₂ or H₂O. Interestingly, the rarely-observed bifunctionalized *homo*-coupled product (4,4'-biphenyldicarboxaldehyde) was obtained from a 2.0 mol% loading of **1** with 79.3% selectivity from *m*-chlorobenzaldehyde (Table 4; entry 21c). In the *para*-position, **1** was 89.1% selective for the desired product (Table 4; entry 23c). Conversely, **2** always created the *hetero*-coupled product as the major product in greater than 96% conversion with selectivities of 92, 79, and 87% for the *ortho* (Table 4; entry 20c), *meta*- (Table 4; entry 22c), and *para*- (Table 4; entry 24c) positions, respectively. From this data, there is no obvious trend that relates total conversion (reaction rate) to the corresponding degree of product selectivity. This infers that catalyst structure and/or solvation effects play important roles in the reaction.

3. A quantitative assessment of the effect of solvent system upon Suzuki coupling by catalysts **1** and **2**. the

The above studies proved that catalysts **1** and **2** were able to convert a broad range of aryl iodides, bromides and chlorides into the desired functionalized biphenyl products with varying degrees of proficiency in the three contrasting solvent systems. As might be expected, the trends in activity appeared to depend in part on the electronic influence of R group on the aryl halide precursors.

For example, whereas OMe substituents greatly deactivated the C–X bond activation, aldehyde functionalized aryl halides were much more easily converted to the corresponding biphenyl aldehydes in high yields by **1** and **2**, especially for *para*-substituted precursors. However, the polarity of the solvent was clearly most highly influential in terms of both reaction selectivity and reactivity. In general, selectivity toward *hetero*-coupled biaryl products in the Suzuki reaction was significantly enhanced for both **1** and **2** in solvents with larger dielectric constants (H₂O = 80.4; CH₂Cl₂ = 9.1; toluene = 2.4). It became evident that **1** and **2** were more selective for the *hetero*-coupled product in solvents with higher polarity; therefore, further studies were made to gain a better understanding of the possible mechanistic pathways responsible for catalytic enhancement effects in certain solvent systems. In particular, a more thorough characterization of the active catalysts and *post*-catalytic species was carried out.

The stabilities of **1** and **2** were first assessed in toluene, CH₂Cl₂ and H₂O in Suzuki reactions with *p*-bromobenzaldehyde and phenylboronic acid. Immediately after cessation of the Suzuki reaction, the hot reaction mixtures were centrifuged (15 min, 8.5 krpm) to isolate any solid residues, which were then separated from the organic supernatant. After cooling, the solid and liquid phases were then analysed by ICP-MS to determine the %Pd content of each (Table 5). For both **1** and **2**, the Pd elemental analysis indicated that only a minority of metal had precipitated from reactions performed in CH₂Cl₂, suggesting that the molecular catalysts retained their original structures when employed in CH₂Cl₂ (Table 5; entries 25b & 26b). However, both catalysts appeared to undergo significant precipitation when operated in H₂O or toluene, which is indicative of either oligomerization or decomposition due to detachment of Pd from the carbene ligands.

Subsequently, the isolated solid and liquid phases were employed in repeat catalytic runs under the original reaction conditions, but using newly added organic reagents. This was achieved by direct re-use of the supernatant, or by the addition of fresh solvent to dissolve/suspend the residual solids. The products of the repeat reactions were monitored by GC (Table 5). Interestingly, conversion was observed for both the recycled supernatant and solids in all cases. The solid residues obtained from initial reaction in H₂O or toluene each showed high catalytic activity upon re-use (Table 5; entries 25a,c & 26a,c), presumably due to the poorly-defined, yet catalytically-active heterogeneous (colloidal or nanoparticulate) species that had been generated. This type of complex catalysis has been documented in several previous instances;^{36–40} a recent review by Ananikov specifically describes the inter-play of well-defined homogeneous and less defined heterogeneous catalysts in C–C coupling reactions.⁴¹ Both the supernatant and the solid residues obtained from the initial reactions in toluene converted *p*-bromobenzaldehyde to *p*-biphenylaldehyde with high selectivity upon re-use (Table 5; entries 25a & 26a). This indicates that the molecular species was only partially decomposed to give heterogeneous species along with molecular species. Repeat reactions in CH₂Cl₂ only showed appreciable conversion for the supernatant, suggesting that **1** and **2** remained mostly solubilized (Table 5; entries 25b & 26b). The reverse outcome was observed for reactions in H₂O, suggesting that the catalysts were almost completely decomposed (Table 5; entries 25c & 26c). For example, the relative palladium content

detected by ICP-MS after catalysis by **1** in CH₂Cl₂ was 97% in the supernatant and only 3% in the precipitate. This result is in stark contrast to 23% versus 77% (supernatant versus precipitate) that was observed after catalysis had been conducted in H₂O (Table 5; entry 25c).

The fact that similar overall conversions and coupling selectivities were observed in the Suzuki reaction using **1** or **2** in three highly contrasting solvents is an example of how particular attention must be paid to identify the composition of the ‘real’ active species.^{28–28,42–46} In the present study, it could easily be incorrectly assumed from the raw conversion data that **1** and **2** were proficient in all solvent systems. However, it is very apparent from the above hot isolation tests that the predominant catalytic species are different when operated in H₂O or CH₂Cl₂. Meanwhile, an ill-defined mixture of homogeneous and heterogeneous species appeared to co-exist in toluene. In an attempt to further probe the identity of the catalytically-active heterogeneous species, pre-formed 4.5 nm Pd nanoparticles (Fig. S3) capped with poly(vinylpyrrolidone) as a stabilizer were employed in the Suzuki reaction under otherwise identical reaction conditions to those used in the previous reactions. The Pd-PVP nanoparticles were employed in H₂O-based Suzuki reactions as an alternative source of pre-formed heterogeneous Pd catalysts. These results showed coupling catalysis in the presence of the Pd-PVP nanoparticles without the requirement for either **1** or **2**; the associated reactivity and product selectivity was also very similar to that observed when the molecular catalyst, **2** was employed exclusively (Table 5; entry 27). This is convincing additional evidence for the hypothesis that heterogeneous Pd(0) species in H₂O are indeed catalytically active for the Suzuki reaction.²⁸

The activation energies for **1** and **2** in H₂O, CH₂Cl₂ and toluene were also measured in order to provide kinetic insight into the nature of the different active species in each solvent. This was

achieved by measuring the rate of coupling for *p*-bromobenzaldehyde as a function of catalyst loading (Fig. 2 & Table 6). Complete conversion of *p*-bromobenzaldehyde with phenylboronic acid to yield the desired *hetero*-coupled product was achieved in H₂O for all catalyst loadings in the range 0.1–0.5 mol% in less than 5 h. Catalyst loading lower than 0.1 mol% usually resulted in incomplete conversion (Fig. S4). As expected for truly catalytic systems, higher catalyst loadings required proportionately less time to reach complete conversion. Above 0.25 mol% the effect of higher loading was minimal since all reactions reached completion in less than 3 h for both **1** and **2** (Table 6; entries 28 & 29). The data summarized in Table 6 imply a

Table 6. Rate constants for **1** and **2** for *p*-bromobenzaldehyde in H₂O

Catalyst	Entry	0.10 mol %	0.25 mol %	0.50 mol %
1	28	0.3046	0.4407	0.5462
2	29	0.8979	0.9601	0.9667

^a Reaction conditions: *p*-bromobenzaldehyde (3.24 mmol), phenylboronic acid (3.89), K₂CO₃ (9.73 mmol), H₂O (15.0 mL), 40 °C; all reactions were monitored by GC.

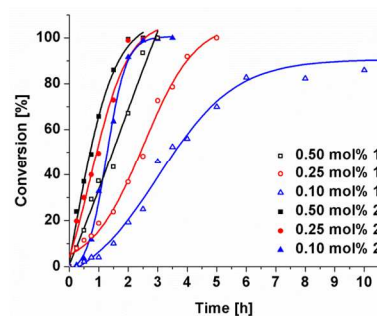


Figure 2. Conversion of *p*-bromobenzaldehyde with phenylboronic acid as a function of time in Suzuki-Miyaura coupling by **1** and **2** at 40 °C with 0.10, 0.25, and 0.50 mol% catalyst loading in H₂O

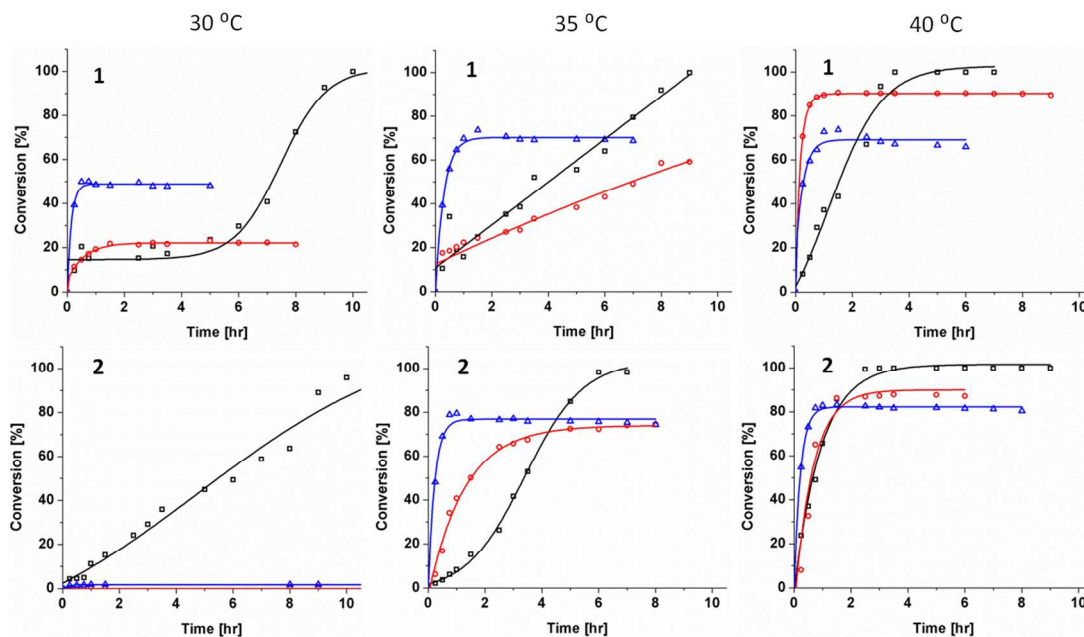


Figure 3. Reaction of *p*-bromobenzaldehyde with phenylboronic acid as a function of time in Suzuki-Miyaura coupling by 0.5 mol% of **1** (top row) and **2** (bottom row) at 30, 35, and 40 °C in toluene (red), CH₂Cl₂ (blue), and H₂O (black).

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pseudo-first order reaction with respect to the *p*-bromobenzaldehyde concentration. Also, catalyst **2** was significantly more effective than **1** in H₂O for all catalyst loadings studied.

Examination of the temperature dependences for **1** and **2** at 24, 30, 35, and 40 °C were also made by means of kinetic experiments in toluene, CH₂Cl₂, and H₂O. The results are summarized in Fig. 3 and the corresponding rate constants are presented in Table 7. This study provided some further interesting insights into the comparative identities and reactivities of the dominant active Pd species in each solvent system. Reactions performed at low temperature were most sensitive to the nature of the solvent. Specifically, both **1** and **2** affected the coupling of *p*-bromobenzaldehyde with phenylboronic acid in H₂O at 30 °C, with high coupling selectivity (Fig. 3; left column). In contrast, reactions in toluene and CH₂Cl₂ at the same temperature gave low yields for **1**, while **2** was found to be inactive. The reaction temperature was then increased in 5 °C steps to 40 °C, which resulted in increased activity for all three solvent systems, albeit with a modest reduction in coupling selectivity (Fig. 3; centre and right columns).

The fact that no turnover was observed at 30 °C in the organic solvents, while appreciable reactivity was observed above 35 °C, suggested that a kinetic activation barrier had been overcome between 30 and 35 °C. This type of temperature-dependent behaviour is commonplace for molecular species. Meanwhile, since appreciable turnover was observed in H₂O at temperatures as low as 24 °C (Fig. S4), it is clear that a different, more easily activated catalytic species was responsible for the observed reactivity.

It is also noteworthy that distinct induction periods of *ca.* 1–5 h were observed for reactions involving **1** and **2** in H₂O at lower temperatures, resulting in s-shaped reactivity profiles (Fig. 3; black data). This is presumably because at lower temperatures, the generation of the active heterogeneous Pd species occurred more slowly. Meanwhile, reactions performed at 35 or 40 °C with **1** and 40 °C with **2** did not show any appreciable induction period. These observations are also consistent with the supposition that molecular catalysis dominated in organic solvents while newly-generated heterogeneous catalysts were dominant in H₂O: single-site homogeneous species should be immediately highly active above a minimum temperature threshold, but could also become rapidly poisoned. In contrast, decomposition of the molecular species in H₂O to generate the active heterogeneous Pd species appeared to require a significant amount of time as reflected in the induction phase.

Table 7. Rate constants of **1** and **2** for *p*-bromobenzaldehyde

Catalyst	Entry	24 °C	30 °C	35 °C	40 °C	45 °C
1	30a	-	0.2393	0.4091	1.8077	-
	30b	-	0.3492	1.3739	2.8619	-
	30c	0.0610	0.2144	0.2656	0.5206	-
2	31a	-	-	0.3678	1.3877	2.9481
	31b	-	0.0037	0.5999	1.7767	4.8967
	31c	0.1442	0.2183	0.2614	1.5986	-

^a Reaction conditions: *p*-bromobenzaldehyde (3.24 mmol), phenylboronic acid (3.89), K₂CO₃ (9.73 mmol), solvent (a-toluene, b-CH₂Cl₂, c-H₂O; 15.0 mL); all reactions were monitored by GC.

Activation energy data for the Suzuki coupling reaction was obtained in the three solvent systems with the slope-ratio method. Arrhenius plots created using the temperature-dependent activity data for **1** and **2** (Fig. 4 & Table 8) show that the Suzuki reaction rates were faster in organic solution than in H₂O. However, the corresponding activation energies in organic solvents (159–171 kJ mol⁻¹) were significantly larger than the comparable activation energies in H₂O (111–116 kJ mol⁻¹). This substantial difference in energy could be attributed to the different physical nature of the active catalysts, in which the homogenous molecular catalysts **1** and **2** experienced a larger energy barrier for the oxidative addition of the aryl halide precursors.

Comparative activation energies for the Suzuki coupling of *p*-chlorobenzaldehyde in toluene, CH₂Cl₂, and H₂O solutions could not be obtained because the reactivities were minimal at lower temperatures. The C–Cl bond was most effectively activated by the supposed heterogeneous Pd(0) species in H₂O. Kinetic trials were performed in aqueous solution using *p*-chlorobenzaldehyde, in which both the catalyst mol% and the temperature were varied (Fig. 5). While the reactions of both **1** and **2** resulted in complete conversion of the chlorinated precursors in H₂O, **2** was the most proficient. Accordingly, the rate constants for **2** increased drastically as the catalyst loadings increased (Table 9).

In contrast to *p*-bromobenzaldehyde, **1** and **2** were found to be initially selective for the *homo*-coupled product, but as the reaction proceeded, both catalysts became more selective for production of the desired *hetero*-coupled product. After approximately 30 h, the reaction selectivity had reached a steady-state, favouring approximately 80% of the *hetero*-coupled product. The origin of this selectivity evolution over such a significant period of time is most likely due to the evolving nature of the active catalyst species, as molecular **1** or **2** are converted to eventually stable heterogeneous catalysts. It is somewhat more difficult to determine the identity of transient intermediate Pd catalysts (such as small Pd clusters) that may exist in solution prior to steady-state selectivity being reached. A so-called ‘cocktail-type’ mixture of active Pd-based species could dominate during the first 25–30 h of reaction (Fig. 6).^{41,47} A representative example of a typical reaction pro-

gression is depicted in Fig. 6 (see ESI for all other selectivity curves).

Table 8. Activation energies for **1** and **2** for *p*-bromobenzaldehyde

Catalyst	Entry	Activation Energy (kJ mol ⁻¹)
1	32a	159.2
	32b	166.3
	32c	111.3
2	33a	169.8
	33b	171.2
	33c	115.9

^a Calculated from the slope of the Arrhenius plots in Figure 4.

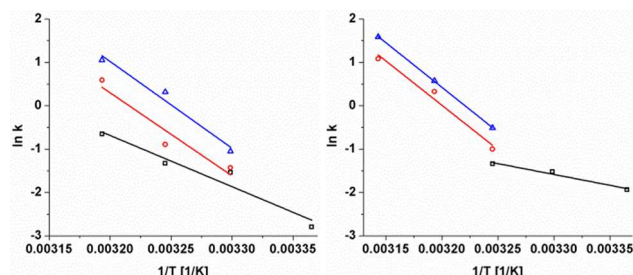


Figure 4. Arrhenius plots for the activation of *p*-bromobenzaldehyde by **1** and **2** in toluene (red), CH₂Cl₂ (blue), and H₂O (black)

Table 9. Rate constants of **1** and **2** of *p*-chlorobenzaldehyde in H₂O

Catalyst	Entry	0.05 ^b	0.10 ^b	0.25 ^b	0.50 ^b	1.0 ^b	1.5 ^b
1	34	-	-	-	0.0141	0.0193	0.0206
2	35	0.0598	0.0919	2.2459	0.0270	0.0547	-

^a Reaction conditions: *p*-chlorobenzaldehyde (4.28 mmol), phenylboronic acid (5.14), K₂CO₃ (12.86 mmol), H₂O (15.0 mL); all reactions were monitored by GC. ^b mol%

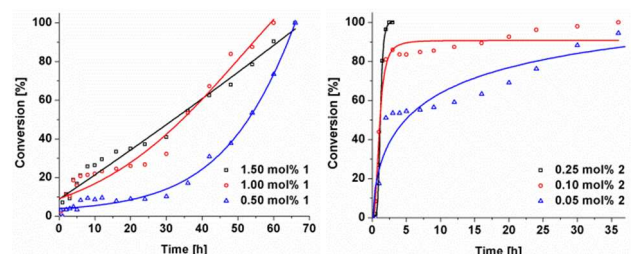


Figure 5. Conversion of *p*-chlorobenzaldehyde with phenylboronic acid as a function of time in Suzuki-Miyaura coupling by catalysts **1** (left) and **2** (right) at 40 °C in H₂O

Based on the rate constant obtained from 0.25 mol% of catalyst **2**, it was decided to double and quadruple the catalyst loading to 0.5 and 1.0 mol% of **1** and **2**, respectively (Figs. S5 & S6). As expected, the rate of **2** was significantly faster and more selective in the activation of aryl chlorides, which was consistent with the data gathered for the corresponding aryl bromides. Although these observations follow classical kinetic control, it was somewhat surprising that higher catalyst loadings resulted in lower rate constants (Table 9). In an attempt to understand this trend, the reaction mechanism was further investigated by varying the number of stoichiometric equivalents of phenylboronic acid and potassium carbonate, (Fig. S7). These data suggested that the phenylboronic acid and the potassium carbonate did not affect the rate determining step of this mechanism. The temperature de-

pendence of this system was also examined at 24, 30, 35, and 40 °C using 0.25 mol% of catalyst **2** (Fig. 7 & Table 10). The *hetero*-coupled aryl product was only produced in complete conversion at 35 and 40 °C and the corresponding rate constants were found to increase with increasing temperature (Table 10).

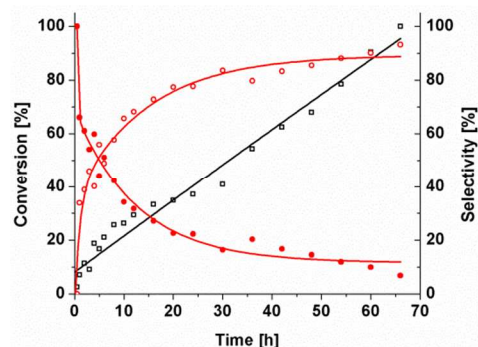


Figure 6. Conversion (black) and selectivity (red) of *p*-chlorobenzaldehyde with phenylboronic acid as a function of time in Suzuki-Miyaura coupling at 40 °C with 1.5 mol% of **1** in H₂O. Open and closed circles denote selectivities of the *hetero*- and *homo*-coupled products, respectively.

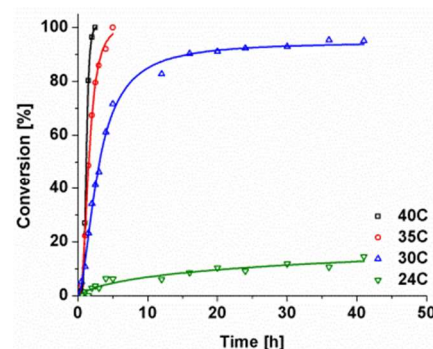


Figure 7. Suzuki-Miyaura coupling of *p*-chlorobenzaldehyde with phenylboronic acid as a function of time using 0.25 mol% of **2** at 24, 30, 35, and 40 °C in H₂O

Table 10. Rate constants for **2** using *p*-chlorobenzaldehyde in H₂O

Catalyst	Entry	24 °C	30 °C	35 °C	40 °C
2	36	0.0031	0.1476	1.0439	2.2459

^a Reaction conditions: *p*-chlorobenzaldehyde (4.28 mmol), phenylboronic acid (5.14), K₂CO₃ (12.86 mmol), H₂O (15.0 mL), 40 °C; all reactions were monitored by GC.

The activation energy for *p*-chlorobenzaldehyde in H₂O was determined on the basis of the slope of the Arrhenius plot (Fig. S14). The activation energy was determined to be 321.8 kJ mol⁻¹, which is in accord with the current literature values for similar systems.

Conclusions

In conclusion, two new palladium(II) carbene complexes were synthesized and studied for their catalytic activities in the Suzuki reaction. Their comparative behaviour in toluene, CH₂Cl₂ and H₂O were assessed. Both **1** and **2** were able to activate C–I, C–Br, and C–Cl bonds in polar and nonpolar aprotic solvents, as well as in H₂O. However, it was shown that catalyst decomposition was prevalent in toluene and H₂O, yielding new, presumably heterogeneous, yet equally active catalyst species. In CH₂Cl₂, the mo-

lecular catalysts were largely stable and recyclable. In toluene solution, both forms of the catalyst were found to co-exist. Kinetic studies revealed that the average activation energy for dissociation of the C–Br bond in organic solvents was 166 kJ mol⁻¹ compared to only 113 kJ mol⁻¹ for H₂O. The latter result infers that the heterogeneous species generated from the original Pd(II) carbene complexes were more reactive for the Suzuki coupling reaction, and that catalyst decomposition was not actually detrimental in the Suzuki-Miyaura cross-coupling reaction. The results of this study exemplify how well-defined molecular and less well-defined heterogeneous Pd species can provide misleadingly similar results in solution-phase catalysis.

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Notes and references

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† Electronic Supplementary Information (ESI) available: [synthetic procedures, UV-Vis for catalysts **1** & **2**; TEM images of palladium nanoparticles; additional catalytic activity data under alternative reaction conditions; additional selectivity data for **1** & **2**; Arrhenius plot of the arylchloride.] See DOI: 10.1039/b000000x/

‡ CCDC 976184 contains the CIF data for catalyst **2**. This data is available free-of-charge from www.ccdc.cam.ac.uk.

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Two new 1,2-acenaphthenyl *N*-heterocyclic carbene-supported palladium(II) Suzuki-Miyaura catalysts behave homogeneously in toluene and dichloromethane solutions, but generate highly active heterogeneous catalysts in aqueous media that activate C–Cl bonds at 40 °C.

