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Synthesis of stilbenoids via the Suzuki–Miyaura reaction catalysed by palladium *N*-heterocyclic carbene complexes

Adriana Tudose, Anna Maj, Xavier Sauvage, Lionel Delaude, Albert Demonceau *, Alfred F. Noels

Laboratory of Macromolecular Chemistry and Organic Catalysis, University of Liège, Sart-Tilman (B.6a), B-4000 Liège, Belgium

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Dedicated to Prof. Bogdan Marciniec on the occasion of his 65th birthday.

Abstract

The Suzuki–Miyaura reaction of aryl halides with *trans*-2-phenylvinylboronic acid using a series of related in situ generated *N*-heterocyclic carbene palladium(II) complexes was studied in order to evaluate the effect of ligand structure and electronics on the catalytic activity and to investigate the nature of the catalyst species. The nature of the substituents of the carbene ligand was found to be critical. Specifically, the presence of alkyl groups on the *ortho* positions of the phenyl substituents was a requisite for obtaining the most efficient catalyst systems.

Keywords: Aryl halides; Boronic acids; Homogeneous catalysis; *N*-Heterocyclic carbene ligands; Palladium and compounds; Stilbenes; Suzuki–Miyaura coupling reactions

1. Introduction

Coupling reactions leading to the formation of new C–C bonds, typically catalysed by ubiquitous palladium complexes, form the bedrock of many contemporary syntheses [1,2]. Among them, the Suzuki–Miyaura reaction [3–9] of organic electrophiles, such as aryl or alkenyl halides and triflates, with organoboron compounds in the presence of a base is nowadays one of the most reliable and widely applied cross-coupling reactions in total synthesis. Among its numerous applications, the Suzuki–Miyaura reaction is particularly useful as a method for the construction of conjugated dienes and higher polyene systems of high stereoisomeric purity, as well as of biaryl and related systems [3–16].

Various forms of Pd compounds have been explored as catalysts for the Suzuki–Miyaura coupling reaction. Generally, the precise architecture of the Pd species plays a crucial role in designing highly efficient Pd catalyst systems. In particular, palladium complexes in which both steric and electronic properties can be tuned by varying the organic ligands have been developed. Thus, Pd complexes based on electron-rich and sterically hindered tertiary phosphines have been demonstrated to enable the smooth reaction of traditionally sluggish aryl chlorides [17–19]. New classes of Pd(II) complexes having Pd–carbon σ-bonds, e.g., palladacycle complexes and PCP pincer-type complexes [20], have also led to significant breakthroughs in this area. On the other hand, the past few years have seen significant advances in palladium *N*-heterocyclic carbene complexes [21–25]. The best of these show excellent activity in Suzuki–Miyaura reactions [26,65], as do catalysts formed in situ upon treatment of palladium complexes, such as $Pd(OAc)_2$ or $Pd_2(dba)_3$ (dba = dibenzylideneacetone), with free *N*-heterocyclic carbenes (NHCs) or imidazol(in)ium salts as carbene precursors [27–32].

For the initial screening of catalyst performance, arylboronic acids are (almost) always used as model reagents. Even though a multitude of arylboronic acids have already been employed, some of which have been successfully used in the commercial production of pharmaceuticals [33–35], 1-alkenylboronic acids have been much less investigated [18,36,37]. As part of our research programme directed to the synthesis of stilbene derivatives [38–40], we have focused our attention onto the Suzuki–Miyaura coupling reaction of *trans*-2-phenylvinylboronic acid with aryl halides. On the other hand,

* Corresponding author. Tel.: +32 4 366 3495; fax: +32 4 366 3497.
E-mail address: A.Demonceau@ulg.ac.be (A. Demonceau).

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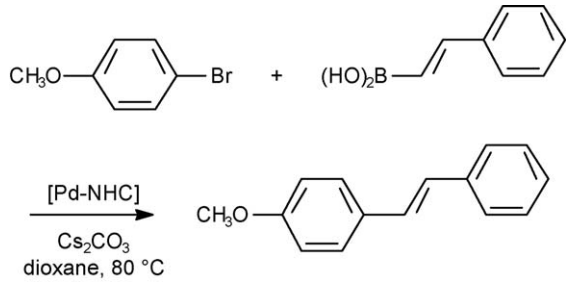
we are also particularly interested in *N*-heterocyclic carbenes and in their use as ancillary ligands in catalysts for olefin metathesis and atom transfer radical reactions [41–48]. Thus, having in hand a library of imidazol(in)ium salts as carbene precursors, we undertook an investigation of the synthesis of stilbenoids via the Suzuki–Miyaura coupling reaction catalysed by in situ generated palladium *N*-heterocyclic carbene complexes.

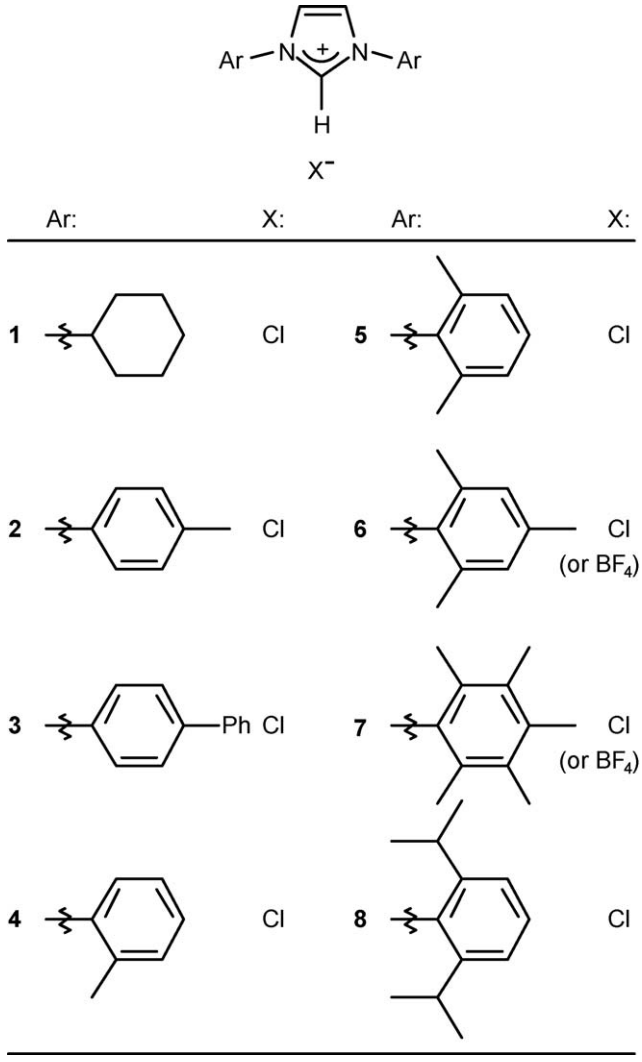
2. Results and discussion

2.1. Influence of the NHC ligand

We first initiated a catalyst screening for the Suzuki–Miyaura coupling between *p*-bromoanisole and *trans*-2-phenylvinylboronic acid as the model reaction (Scheme 1). The reactions were performed in dioxane at 80 °C, using catalytic systems consisting of a combination of one equivalent of $Pd(OAc)_2$ (0.5 mol.% with respect to *p*-bromoanisole) and four equivalents of imidazolium salt (**1**–**8**) (Scheme 2), in the presence of caesium carbonate as the base. Table 1 shows the effects of various imidazolium salts on the coupling reaction. As can be seen in Table 1, 4-methoxystilbene was produced in high yields irrespective of the carbene precursor as a mixture of *cis*- and *trans*-isomers, the latter isomer being predominant. We noted however a significant rate enhancement with the use of catalyst systems **5**–**7** possessing methyl groups on the *ortho* positions of the phenyl substituents in comparison to systems **1**–**3** devoid of any substituent at positions 2 and 6. For example, under the unoptimised reaction conditions summarised under Table 1, about 90–95% of *p*-bromoanisole were consumed after 8 h reaction in the presence of palladium catalysts **5**–**7**, contrary to 63, 72, and 75% with systems **1**, **2**, and **3**, respectively. In addition, the reaction rate decreased with the number of methyl groups on the phenyl substituents: **5** > **6** (X = Cl) > **7** (X = Cl) (Fig. 1), supporting the importance of the electronic effects within the carbene ligand on the catalytic activity. On the other hand, comparing catalytic systems **5** (Ar = 2,6-dimethylphenyl) and **8** (Ar = 2,6-diisopropylphenyl), it can be seen that increasing the steric bulk was deleterious to the reaction (Table 1; Scheme 2).



Scheme 1. The Suzuki–Miyaura coupling reaction under investigation.



Scheme 2. Imidazolium salts under investigation.

Table 1
Experimental data for the Suzuki–Miyaura reaction between *p*-bromoanisole and *trans*-2-phenylvinylboronic acid, catalysed by palladium-based systems **1**–**8**[a]

Imidazolium salt	Conversion (%)[b]		Isolated yield (%)[c]
	8 h	24 h	24 h
1	63	88	85
2	72	82	83
3	75	97	95
4	76	97	93
5	97	100	98
6 (X = Cl)	95	100	97
6 (X = BF_4)	97	100	98
7 (X = Cl)	79	97	96
7 (X = BF_4)	88	100	98
8	77	96	92

[a] *Experimental conditions*: $Pd(OAc)_2$, 0.01 mmol; imidazolium salt **1**–**8**, 0.04 mmol; Cs_2CO_3, 4 mmol; *trans*-2-phenylvinylboronic acid, 2.4 mmol; 1,4-dioxane, 2 mL; 1 mL of a solution containing 2 mmol of *p*-bromoanisole and *n*-decane in dioxane; 80 °C, under an inert atmosphere of nitrogen.

[b] Based on *p*-bromoanisole and determined by GC using decane as internal standard.

[c] Yields are of isolated, analytically pure material.

2.2. Influence of the aryl halide

Having established that catalyst systems **5**–**8** bearing methyl or isopropyl groups on the *ortho* positions of the phenyl sub-

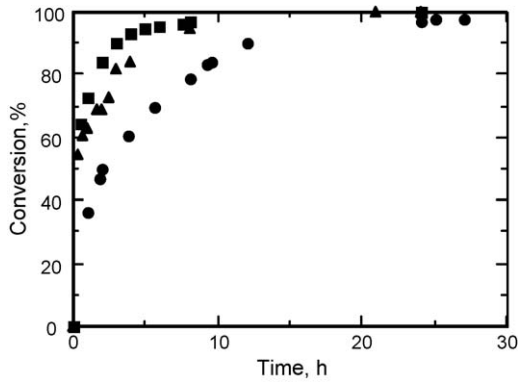


Fig. 1. Influence of the catalyst system on the reaction rate of *p*-bromoanisole with *trans*-2-phenylvinylboronic acid. Pd–NHC catalyst systems: **5** (■), **6** (X = Cl, ▲), and **7** (X = Cl, ●). The reaction conditions are the same as in Table 1.

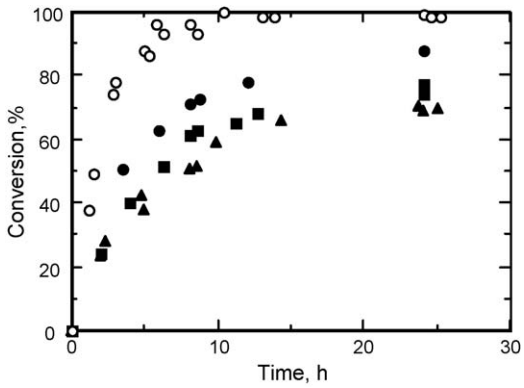


Fig. 2. Influence of the catalyst system on the reaction rate of chlorobenzene with *trans*-2-phenylvinylboronic acid. Pd–NHC catalyst systems: **5** (■), **6** (X = Cl, ▲), **7** (X = Cl, ●), and **8** (○). The reaction conditions are the same as in Table 2.

stituents show essentially the best activity in the test reaction, we next examined their performance in the coupling of *trans*-2-phenylvinylboronic acid with aryl chlorides, which are challenging substrates for both academic and industrial applications. The results from this study are summarised in Table 2. Interestingly, contrary to *p*-bromoanisole, with chlorobenzene and *p*-chloroanisole system **8** (Ar = 2,6-diisopropylphenyl) performed better than systems **5**–**7** (X = Cl) bearing methyl groups on the *ortho* positions of the phenyl rings (Table 2 and Fig. 2). Thus, 96% conversion of chlorobenzene was obtained with the former catalyst system versus 50–70% with the latter. As expected, with **6** (Ar = mesityl, X = Cl), better conversions to the desired product were obtained with aryl bromides than with their chloride counterparts, the general trend being Ar–Br > Ar–Cl and C_6H_5–X > *p*-$CH_3OC_6H_4$–X (Fig. 3a) according, respectively, to the higher bond dissociation energy of C–Cl versus C–Br and to the deactivating effect of the methoxy substituent of the substrate. By contrast, there does not appear to be such a trend with system **8** bearing 2,6-diisopropylphenyl substituents (Fig. 3b). System **8** performs indeed well with aryl chlorides and poorly discriminates between the aryl halides under investigation. These tendencies were confirmed by intermolecular

Table 2
Experimental data for the Suzuki–Miyaura reaction between *p*-chloroanisole or chlorobenzene, and *trans*-2-phenylvinylboronic acid, catalysed by representative palladium-based systems[a]

Imidazolium salt	Conversion (%)[b]			Isolated yield (%)[c]
	8 h	24 h	48 h	48 h
p-Chloroanisole				
2	28	34	36	–
4	30	37	42	–
5	29	37	43	–
6 (X = Cl)	27	32	36	–
6 (X = BF_4)	32	38	42	–
7 (X = Cl)	23	30	36	–
7 (X = BF_4)	51	58	62	60
8	76	89	94	90
Chlorobenzene				
2	2	2	2	–
4	3	3	3	–
5	61	76	77	75
6 (X = Cl)	51	69	73	69
6 (X = BF_4)	62	78	82	81
7 (X = Cl)	71	88	94	92
7 (X = BF_4)	80	92	96	95
8	96	99	100	95

[a] *Experimental conditions*: $Pd(OAc)_2$, 0.01 mmol; imidazolium salt, 0.04 mmol; Cs_2CO_3, 4 mmol; *trans*-2-phenylvinylboronic acid, 2.4 mmol; 1,4-dioxane, 2 mL; 1 mL of a solution containing 2 mmol of *p*-chloroanisole or chlorobenzene, and *n*-decane in dioxane; 80 °C under nitrogen.

[b] Based on the chloroarene and determined by GC using decane as internal standard.

[c] Yields are of isolated, analytically pure material.

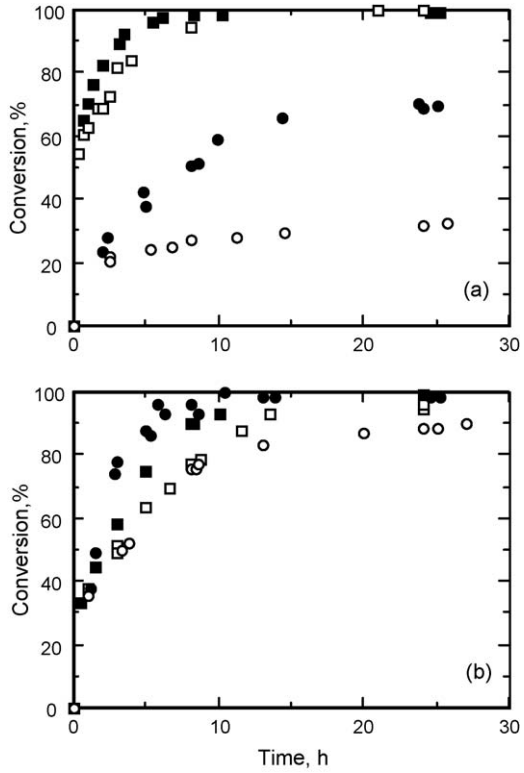


Fig. 3. Influence of the substrate on its reaction rate with *trans*-2-phenylvinylboronic acid catalysed by Pd–NHC systems **6** (X = Cl) (a) and **8** (b). Substrates: bromobenzene (■), *p*-bromoanisole (□), chlorobenzene (●), and *p*-chloroanisole (○). The reaction conditions are the same as in Table 2.

competitions: with catalyst system **8** *p*-bromoanisole was 1.28 times more reactive than *p*-chloroanisole, whereas with **6** (X = Cl) the reactivity ratio reached 2.4. On the other hand, bromobenzene was 3.8 and 7.7 times more reactive than chlorobenzene in the presence of catalyst systems **8** and **6** (X = Cl), respectively, demonstrating that the catalyst has to be fine-tuned to each haloarene. This has already been exemplified for palladium(0) complexes with hindered phosphines, and the recent finding that oxidative addition of chloro-, bromo-, and iodoarenes to sterically hindered Pd(0) complexes occurs through three different mechanisms [49] should be of utmost importance for understanding the effect of other hindered ligands, such as NHCs, on the relative reactivities of haloarenes.

2.3. Influence of the counter-ion

Our attention next shifted to the effect of the counter-ion of the imidazolium salt (Tables 1 and 2, and Fig. 4). Interestingly, with systems **6** and **7** (all other variables being constant) imidazolium tetrafluoroborates gave slightly higher conversions to the coupled product than the parent imidazolium chlorides. The origin of this counter-ion effect is not yet understood. Although overlooked for the palladium-catalysed coupling reactions at purine [50], the counter-ion effect has been assigned to either ion pairing effects in imidazolium salts ([51], see also [52–54,66]), or increasing Lewis acidity of the metal centre with the weaker coordinating BF_4^- anion [55]. Although plausible in the very early stages of the coupling reaction, the latter explanation is however highly questionable as the reaction proceeds, i.e., when an increasing amount of halide is formed as a side-product from the coupling of the haloarene with *trans*-2-phenylvinylboronic acid. Finally, despite the enhanced usefulness of imidazolium tetrafluoroborates, the rest of the studies with in situ formed catalysts were performed using chloride salts because of their ready availability.

2.4. Influence of the base

The Suzuki–Miyaura coupling reaction was also greatly affected by the base employed. As shown in Fig. 5 and

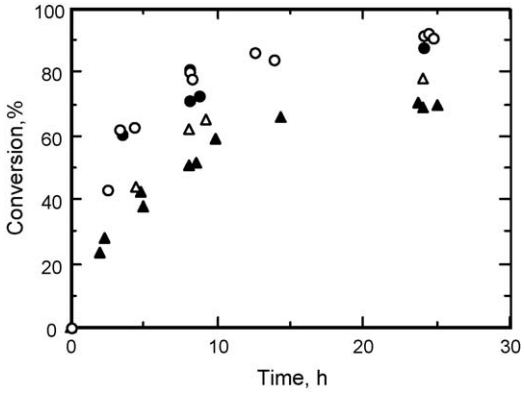


Fig. 4. Influence of the counter-ion of the imidazolium salt on the reaction rate of *trans*-2-phenylvinylboronic acid with chlorobenzene catalysed by Pd–NHC systems **6** (X = Cl (▲) or BF_4 (△)) and **7** (X = Cl (●) or BF_4 (○)). The reaction conditions are the same as in Table 2.

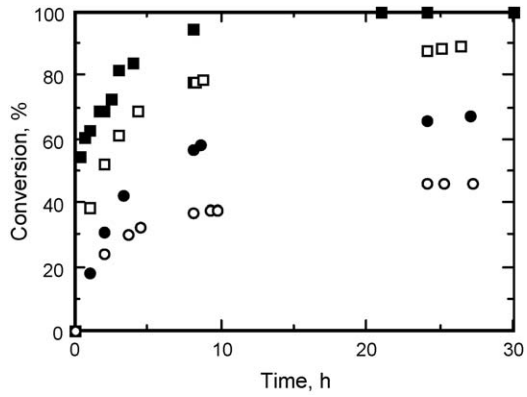


Fig. 5. Influence of the base on the reaction rate of *p*-bromoanisole with *trans*-2-phenylvinylboronic acid catalysed by Pd–NHC system **6** (X = Cl). Base: Cs_2CO_3 (■), K_2CO_3 (□), Na_2CO_3 (●), and Li_2CO_3 (○). The reaction conditions are the same as in Table 3.

Table 3, the activity of the alkali metal carbonate increased with the increasing size of the alkali metal: $Cs_2CO_3 > K_2CO_3 > Na_2CO_3 > Li_2CO_3$. Caesium carbonate produced indeed 4-methoxystilbene almost quantitatively in less than 10 h, whereas with Li_2CO_3 the yield culminated at 54% after 2 days. It seems that the formation of the active species and hence of the coupling product are more facilitated in the presence of a carbonate of larger-sized alkali metal, plausibly because the solubility increases and the dissociation energy of alkali metal carbonate decreases with the increasing size of alkali metal. On the other hand, KF worked even better. The conversion obtained here was higher than that obtained using Cs_2CO_3 and completion of the reaction was attained in around 3 h. KF was then singled out for further brief testing with selected catalyst systems. Again KF proved to be more effective in combination with systems **7** (X = Cl) and **8** for the coupling of *trans*-2-phenylvinylboronic acid with bromobenzene or *p*-bromoanisole (Table 3). However, when aryl chlorides were employed as the substrates, the activities dropped drastically compared to those shown by Cs_2CO_3,

Table 3
Experimental data for the Suzuki–Miyaura reaction between *p*-bromoanisole and *trans*-2-phenylvinylboronic acid, catalysed by representative palladium-based systems in the presence of various bases[a]

Imidazolium salt	Base	Conversion (%)[b]			
		2 h	8 h	24 h	48 h
6 (X = Cl)	Li_2CO_3	24	37	46	54
	Na_2CO_3	31	57	66	70
	K_2CO_3	52	78	88	91
	Cs_2CO_3	69	95	100	
	K_3PO_4	32	68	92	99
	KF	88	100		
7 (X = Cl)	KF	87	100		
8	KF	85	99		

[a] *Experimental conditions*: $Pd(OAc)_2$, 0.01 mmol; imidazolium salt, 0.04 mmol; base, 4 mmol; *trans*-2-phenylvinylboronic acid, 2.4 mmol; 1,4-dioxane, 2 mL; 1 mL of a solution containing 2 mmol of *p*-bromoanisole and *n*-decane in dioxane; 80 °C under nitrogen.

[b] Based on *p*-bromoanisole and determined by GC using decane as internal standard.

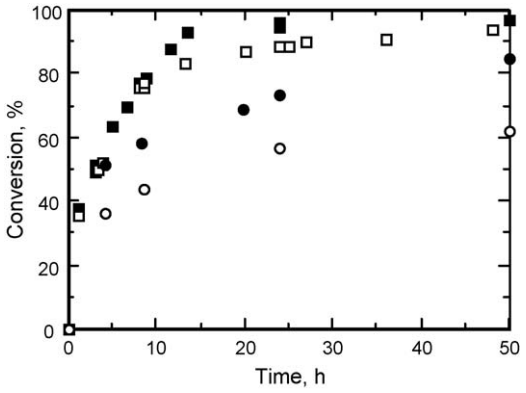


Fig. 6. Influence of the substrate/Pd ratio on the reaction rate of *p*-bromoanisole (■, ●) or *p*-chloroanisole (□, ○) with *trans*-2-phenylvinylboronic acid catalysed by the Pd–NHC system **8**. The reaction conditions are the same as in Table 1 (substrate:$Pd(OAc)_2$:imidazolium salt **8** = 200:1:4 (■, □) or 1000:1:4 (●, ○)).

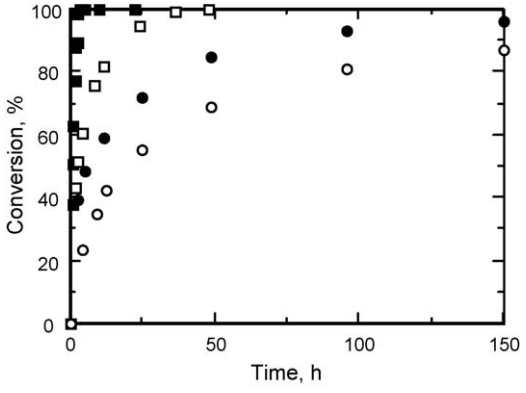


Fig. 7. Influence of the substrate/Pd ratio on the reaction rate of *p*-bromoanisole with *trans*-2-phenylvinylboronic acid catalysed by Pd–NHC system **6** (X = Cl) in the presence of KF as the base. The reaction conditions are the same as in Table 3 (*p*-bromoanisole:$Pd(OAc)_2$:imidazolium salt **6** = 200:1:4 (■), 1000:1:4 (□), 2000:1:4 (●), and 5000:1:4 (○)).

indicating that the catalyst system ($Pd(OAc)_2$ + imidazolium salt + base) has to be fine-tuned to each aryl halide.

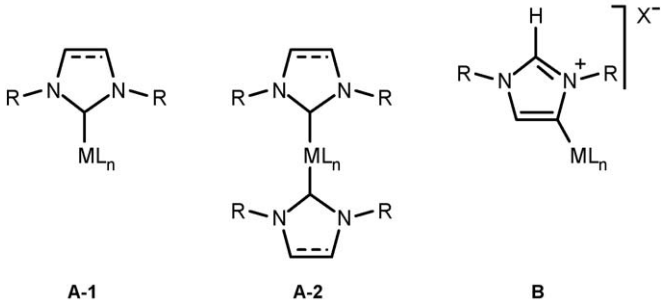
Given the success enjoyed with systems **6**–**8** in combination with either caesium carbonate or potassium fluoride, we were keen to see whether catalytic activity could be maintained for lower catalyst loadings. Thus, coupling reactions were performed using a molar ratio of aryl halide/$Pd(OAc)_2$ = 1000 instead of 200 in the standard conditions outlined under Tables 1–3. As can be seen in Fig. 6, turnover numbers reached 850 and 620 when using *p*-bromoanisole and *p*-chloroanisole, respectively, in combination with catalyst system **8** and Cs_2CO_3. Interestingly, a turnover number as high as 4350 was obtained for the reaction of *p*-bromoanisole and *trans*-2-phenylvinylboronic acid catalysed by **6** (X = Cl) in the presence of KF (initial ratio *p*-bromoanisole/$Pd(OAc)_2$ = 5000) (Fig. 7).

2.5. Stereochemistry of stilbene and 4-methoxystilbene

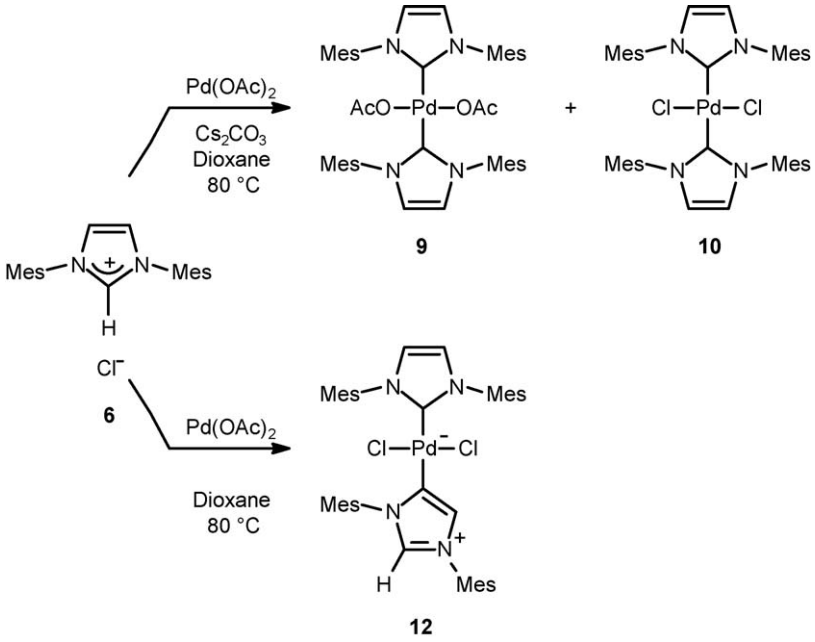
The reaction temperature that we used (80 °C) produced a mixture of *trans*- and *cis*-isomers, and the *trans*/*cis* selectivity depended on all the reaction partners, e.g., the haloarene, the imidazolium salt, the base, and the temperature, and sometimes changed with the reaction time. We found however that a reaction temperature lower than 40 °C was optimal for obtaining selectively the *trans*-isomer, but at the expense of reaction rates. A similar trend was observed for the coupling of *trans*-octenylboronic acid and *trans*-2-phenylvinylboronic acid with aryl halides catalysed by a palladium complex bearing the hindered 2-(2′,6′-dimethoxybiphenyl)dicyclohexylphosphine ligand [18]. In addition, Jacobsen recently described an elegant asymmetric synthesis of quinine [37], where the same catalytic system was utilised in the coupling at room temperature of a *trans*-alkenyl pinacol boronate ester with a 4-bromoquinoline derivative in both excellent yield and high *trans* selectivity (*trans*/*cis* > 20:1). However, when potassium *trans*-styryl trifluoroborate was used instead of *trans*-2-phenylvinylboronic acid for Suzuki–Miyaura couplings performed in a mixture of *i*-PrOH–H_2O (2:1) at reflux [36], the *trans*-compound was formed with no detectable *cis*-isomer, illustrating therefore that the effect of the temperature on the stereochemistry of the coupling product [56] is so far unpredictable in Suzuki–Miyaura reactions involving alkenyl–boron reagents. Work is currently ongoing to gain a better understanding as to the factors affecting the *trans*/*cis* selectivity and the alkene isomerisation process.

2.6. The catalytic species

It has been reported that palladium(II)–NHC complexes bearing either one (**A-1**) or two carbene ligands (**A-2**, Scheme 3) could be easily prepared from palladium(II) compounds and the corresponding imidazol(in)ium salts [57]. Metal binding at the C-2 position is usually observed, and complexes bearing two NHCs can potentially exist as *cis* or *trans* (**A-2**, Scheme 3) isomers, depending on the steric hindrance of the nitrogen substituent R. As illustrated in Scheme 4, when a mixture of palladium(II) acetate, 2 equiv. of *N*,*N*′-bis(mesityl)imidazolium chloride (**6**), and caesium carbonate was stirred under conditions similar to those used for Suzuki–Miyaura coupling reactions (80 °C in dioxane), the expected $Pd(OAc)_2(NHC)_2$ complex (**9**) was formed together with $PdCl_2(NHC)_2$ (**10**) as an inseparable mixture [58]. Surprisingly, a similar reaction between $Pd(OAc)_2$ and imidazolium salt **6** (2.1 equiv.) but in the absence of Cs_2CO_3 did not afford the expected C-2 ligated complexes **9** and **10**. Instead, complex **11** containing both a C-2 NHC ligand and a



Scheme 3. "Normal" C-2 (**A-1** and **A-2**) and "abnormal" C-4(5) (**B**) coordination modes of *N*-heterocyclic carbene ligands.



Scheme 4. Reactivity of palladium acetate with imidazolium chloride **6**.

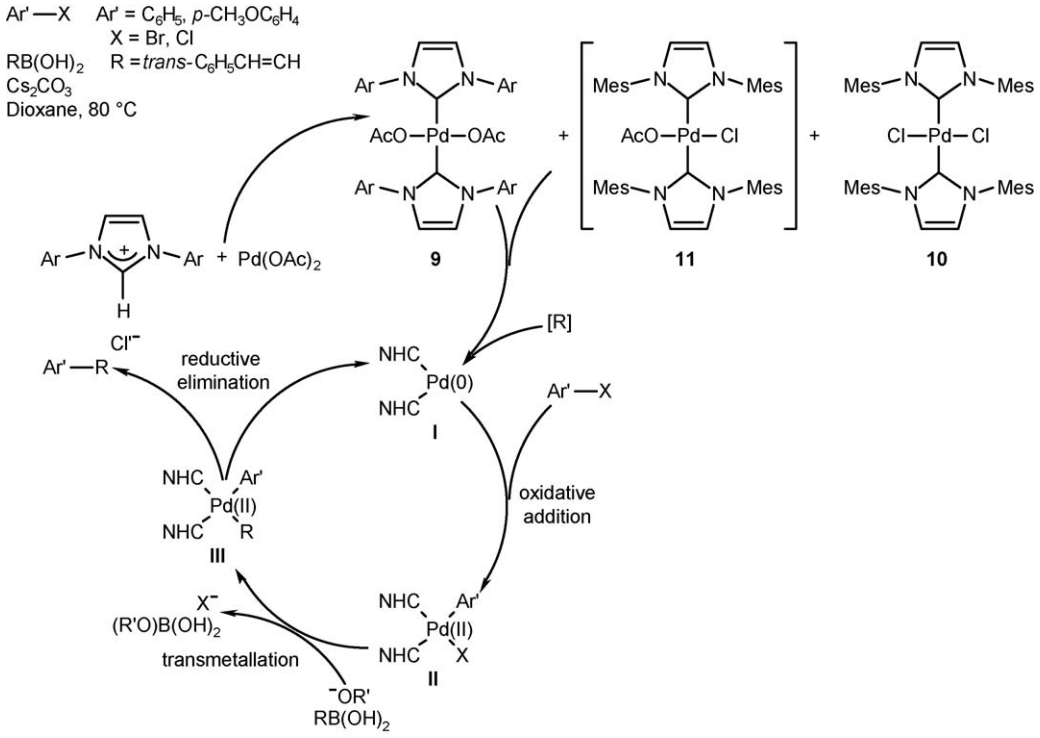
C-4(5) NHC ligand was isolated in high yield, revealing therefore an unusual coordination mode (**B**, Scheme 3) for the NHC ligand. In addition, attempts to convert complex **11** into the C-2 isomer **10** in the presence of a base were unsuccessful [58,59].

In light of these results, we therefore suggest that under the conditions used for the Suzuki–Miyaura coupling reactions, the normal C-2 NHC–Pd complexes should have been produced upon treatment of palladium acetate with the imidazolium chlorides **1**–**8**, at least with chloride **6**. In addition, since 4 equiv. of imidazolium chlorides were employed instead of 2 equiv. in the afore-mentioned reactions, formation of $Pd(NHC)_2$ species should be favoured. On the other hand, as under our reaction conditions generation of the palladium active species occurs in the presence of the reagents (boronic acid and aryl halide), it is likely that in the early stages of the reaction both $Pd(OAc)_2(NHC)_2$ (**9**) and $PdCl_2(NHC)_2$ (**10**) complexes are formed in situ. Interestingly, it has been proved that the well-defined complex **10** is an inactive catalyst for the Suzuki–Miyaura reactions [58], inferring that only complex **9** ($Pd(OAc)_2(NHC)_2$) and/or – eventually – a mixed acetate–chloride complex $PdCl(OAc)(NHC)_2$ (**11**) are responsible for the catalytic activity.

Classical C-2 and non-classical C-4(5) bindings of NHCs have also been reported in iridium chemistry [60]. Interestingly, the nature of the counter-ion of the imidazolium salt has a pronounced effect on the binding mode [51]. Thus, the use of imidazolium bromides afforded almost quantitative yields of C-2-bound iridium NHC products, while the use of tetrafluoroborates resulted in the formation of the abnormal C-4(5)-bound complex as the major product. To the best of our knowledge, such counter-ion effect has never been reported in palladium chemistry, and the higher activity in Suzuki–Miyaura reactions of imidazolium tetrafluoroborates **6** and **7** compared to their chloride counterparts (Tables 1 and 2, and Fig. 4) is not yet understood but work is currently in hand. In this context, it is worth noting that the binding mode of the NHC to Pd was shown to substantially affect the catalytic behaviour of the palladium complexes. The well-defined palladium bis(C-2-NHC) complex **10** (Scheme 4) was indeed inactive in Suzuki–Miyaura coupling reactions, while the mixed (C-2-NHC)(C-4(5)-NHC) complex **12** led to the desired products in high yields, suggesting that the C-4(5) binding mode results in complexes with enhanced reactivity. In this line, it is also noteworthy that complex **12** was not as efficient as the in situ formed catalyst [58].

It is generally agreed that the Suzuki–Miyaura coupling reactions involve three steps (oxidative addition of the organic halide, followed by transmetallation and reductive elimination (Scheme 5)), and proceed through Pd(0) species resulting from the reduction of the in situ generated $PdX_2(NHC)_2$ complexes, such as **9** and/or **11**. The exact nature of the catalytically active Pd(0) species is still in question. However, recent work on reactions involving Ar–X with the pre-catalyst $[Pd^0(NHC)_2]$ suggested dissociation of one NHC to generate a $[Pd^0(NHC)]$ fragment, which then undergoes oxidative addition of aryl halide. In particular, detailed kinetic studies by Cloke suggested that oxidative addition reactions occurred via a two-coordinate 14-electron $[Pd^0(NHC)]$ complex [61]. Furthermore, the ability of the oxidative addition product $[Pd(NHC)_2(Ar)Cl]$ to reversibly dissociate free carbene was also demonstrated. Studies by Herrmann on the Heck reaction with $[Pd^0(NHC)_2]$ also suggested the intermediacy of the same $[Pd^0(NHC)]$ complex [62].

Several factors are thought to be responsible for the success of *N*-heterocyclic carbene ligands in Suzuki–Miyaura couplings: (1) their electron-rich nature enhances the rate of oxidative addition, (2) these ligands coordinate tightly to palladium, thus disfavouring the formation of Pd black, and (3) their steric bulk favours a monocarbene–Pd species and increases the rate of reductive elimination, although it impedes oxidative addition and transmetallation of sterically hindered substrates. The donor



Scheme 5. Proposed mechanism for the Suzuki–Miyaura coupling reaction.

properties of aryl substituted *N*-heterocyclic carbenes have been so far assigned to the lone pair donation from the carbene carbon. Recently, however, Plenio ([63], see also [64]) provided strong evidence of the additional donation of electron density of the aromatic π-face of the NHC aryl groups towards the metal. In light of these results, the different reactivity patterns exhibited by the different Pd–NHC systems, in particular 2,6-dimethylphenyl (**5**–**7**) and 2,6-diisopropylphenyl (**8**) substituted systems, with respect to the aryl halides could be due to a through-space interaction between the aryl substituents of the NHCs and the catalytically active palladium species. Work is ongoing to probe whether this explanation is valid.

In conclusion, the nature of the catalytically active species is not certain under the conditions used to generate them in situ. Furthermore, the number of active species is also unknown so that comparing the activity of the different NHC precursors might be questionable. In particular, the concentration of active species might be rather low, which translates into catalytic activity in the Suzuki–Miyaura reaction lower than those displayed by the most efficient well-defined precatalysts reported to date [26,65].

3. Conclusions

We have shown that simple catalysts formed in situ from palladium acetate and a wide range of imidazolium salts are active for the Suzuki–Miyaura coupling of *trans*-2-phenylvinylboronic acid with aryl halides. Generally speaking, aryl bromides are more reactive than aryl chlorides, and Cs_2CO_3 and KF are the most suited bases. However, rationalising the influence of the carbene structure on the catalytic activity is somewhat more difficult. A plausible explanation relies on the stabilisation of the catalytically active palladium(0) species not only by the strong σ-donation of the carbene carbon, but also by the π-donation of the NHC aryl groups towards the metal.

4. Experimental

4.1. General

Aryl halides, *trans*-2-phenylvinylboronic acid, palladium acetate, and the inorganic bases were obtained from commercial sources. *trans*-2-Phenylvinylboronic acid, palladium acetate, and the inorganic bases were used as received. 1,4-Dioxane, *n*-decane, as well as the aryl halides were distilled under vacuum from calcium hydride, and stored under nitrogen. Imidazolium salts **1**–**8** were synthesised according to the literature [43] and their purity was checked by ^{1}H and ^{13}C NMR. All of the experiments were carried out under a nitrogen atmosphere. Conversions were determined by gas chromatography using a Varian 3900 apparatus (column type, WCOT Fused Silica; stationary phase, VF-1 ms; column length, 15 m; inside diameter, 0.25 mm; outside diameter, 0.39 mm; film thickness, 0.25 μm). The coupled products were isolated by column chromatography (silica) and their spectroscopic data were compared with those of authentic samples [40]. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX 400 spectrometer operating at 400.13 and 100.62 MHz, respectively.

4.2. General procedure for Suzuki–Miyaura couplings

Palladium acetate (2.25 mg, 0.01 mmol), the imidazolium salt (0.04 mmol), the base (4 mmol), and *trans*-2-phenylvinyl-

boronic acid (355 mg, 2.4 mmol) were successively placed in a glass tube containing a bar magnet and capped by a three-way stopcock. The reactor was purged of air (three vacuum–nitrogen cycles) before dioxane (2 mL) was added. The mixture was stirred before adding 1 mL of a solution containing 2 mmol of aryl halide and *n*-decane (internal standard) in dioxane. All liquids were handled with dried syringes under nitrogen. The reaction mixture was heated in a thermostated oil bath at 80 °C. Gas chromatography was used to monitor the reaction progress. To this aim, aliquots were withdrawn from the reaction mixture at regular time intervals and then workup with a 5% Na_2CO_3 aqueous solution and ether was followed by drying the organic phase over $MgSO_4$ overnight and filtration through a plug of cotton-wool.

4.3. General procedure for concurrent Suzuki–Miyaura couplings

The general procedure was similar to that described above, except that the amounts of *trans*-2-phenylvinylboronic acid and caesium carbonate were reduced. Experimental conditions were as follows: $Pd(OAc)_2$, 0.01 mmol; imidazolium salt, 0.04 mmol; Cs_2CO_3, 1 mmol; *trans*-2-phenylvinylboronic acid, 0.4 mmol; 1,4-dioxane, 2 mL; 1 mL of a solution containing 1 mmol of aryl bromide, 1 mmol of aryl chloride and *n*-decane in dioxane. Reaction time, 10 h at 80 °C, under an inert atmosphere of nitrogen.

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