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Synthesis of new styrylarenes *via* Suzuki–Miyaura coupling catalysed by highly active, well-defined palladium catalysts†

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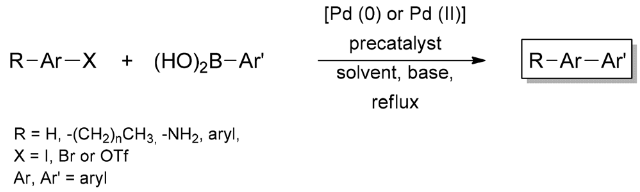
An efficient synthetic route for well-defined palladium(0) complexes [Pd(η^2-dba)(PPh_3)$_2$] (2), [Pd(η^2-dba)(PCy_3)$_2$] (3) and their crystallographic structures is reported. This is the first crystallographic characterization of palladium complexes coordinated with one dibenzylideneacetone and two phosphines. A highly effective, fully controlled method for selective synthesis of mono- (5–9) and distyrylarenes (10–15) *via* Suzuki–Miyaura coupling is described.

The Suzuki–Miyaura cross-coupling reaction appears to be an extremely useful method in the organic synthesis of compounds containing a carbon–carbon bond, *e.g.* biaryl compounds.[1] The formation of a C–C bond is of vital importance in preparative organic processes from molecular, model chemistry to macromolecular and nanomaterial science.

In general, in this kind of reaction, organoboronic acid is coupled with an organic halide or triflate in the presence of a catalyst and a mixture of less polar or polar solvents and base,[2] as shown in Scheme 1.

The reactions of aryl halides or halide equivalents with various nucleophiles have been mainly catalysed by a palladium system. Phosphine and carbenes are well known ligands for this process.[3–8] The character of the active catalytic species when using palladium–phosphine systems is essential.

Two equivalents of phosphine are usually present in the catalyst precursor or just added into the mixture. It appears that they stay on the metal during the reaction. It has been suggested that a monophosphine species could be used as a real catalyst.



Scheme 1 General scheme of Suzuki–Miyaura coupling.

Moreover, bulky and electron-rich phosphines have a tendency to improve the reaction (through chemo- and regioselectivity and yielding).[9–18]

This method turned out to be an effective and really practical way to produce non-natural and natural products, *e.g.* polymers, dendrimers, peptides or amino acids.[19–23]

In this communication we present an efficient, stereoselective method for the preparation of π-conjugated mono- and distyryl-arylene derivatives through the Suzuki–Miyaura coupling (SM) catalyzed by well-defined, highly active, three coordinated palladium(0) complexes.

Commercially available Pd(PPh_3)$_4$, Pd(OAc)$_2$, Pd(dba)$_2$ and Pd_2(dba)$_3$·$CHCl_3$ are generally used as precursors of Pd(0) catalysts with or without the addition of phosphine ligands.

However, it should be mentioned that the catalytic activities of Pd(0) catalysts generated '*in situ*' from these palladium compounds are not always the same, and it is advisable to test all of them in order to achieve efficient catalytic reactions.

These well-defined catalysts are readily obtainable from bis(dibenzylideneacetone) palladium(0) (**1**) on treatment with tricyclohexylphosphine or triphenylphosphine (the best molar ratio is [Pd] : [PR_3] = 1 : 2.02) which results in the formation of mononuclear bis(phosphine)(dibenzylideneacetone) palladium(0) – [Pd(η^2-dba)(PR_3)$_2$] active species with very good yields, *e.g.* for R = Ph_3 – 98% (**2**) and PCy_3 – 95% (**3**), as shown in Scheme 2.

The phosphine was added to a dark purple Pd(dba)$_2$ solid and both substrates were dissolved in toluene to give a yellow-orange solution of the final species. The solid state structures of **2** and **3** were determined by X-ray crystallography. As far as

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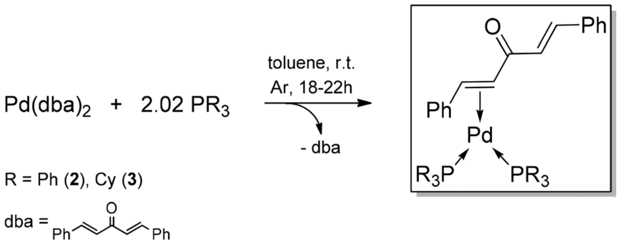
† Electronic supplementary information (ESI) available: Experimental and analytical details, synthesis of **2** and **3**, procedure for catalytic tests, synthesis of mono- (**5–9**) and distyryl arenes (**10–15**), crystal data collection and structure refinement. CCDC 844578 and 844579. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3dt52063c



Scheme 2 Synthesis of well-defined palladium(0) species.

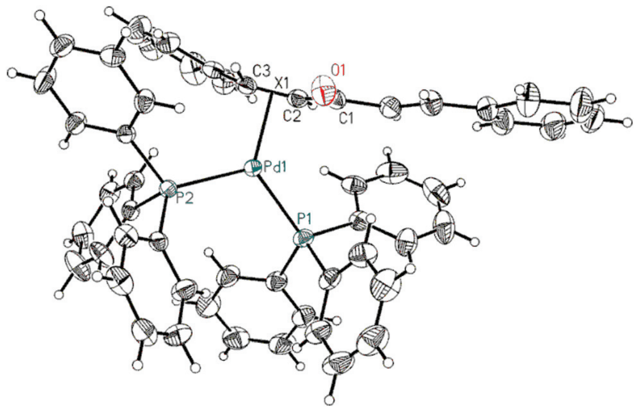


Fig. 1 A perspective view of **2** with labelling scheme. Ellipsoids are drawn at the 50% probability level, hydrogen atoms are shown as spheres of arbitrary radii. Selected geometrical parameters (Å, °): Pd1–X1 2.047(5), Pd1–C2 2.190(5), Pd1–C3 2.160(6), Pd–P1 2.3427(14), Pd–P2 2.3313(14), X1–Pd1–P1 127.00(12), X1–Pd1–P2 118.04(12), P1–Pd1–P2 114.88(5).

we know this is the first crystallographic characterization of palladium complexes coordinated with one dibenzylideneacetone and two phosphines. Fig. 1 and 2 show configurations of two three co-ordinated Pd(0) complexes. Deep yellow (**2**) and orange (**3**) crystals were obtained from a toluene–hexane mixture which was slowly concentrated at room temperature. The relevant geometric parameters for both complexes are presented in Table 3, ESI.†

In both complexes the Pd atoms have a trigonal coordination, taking the middle point of the double C2═C3 bond (X1) as the coordination centre. The Pd atoms are only slightly out of the plane created by the three coordination centres, P1, P2 and X1, the deviations are 0.041(2) Å in **3** and 0.038(2) Å in **2**.

In both complexes only one of the double bonds is involved in the coordination. This difference is reflected in the double bond lengths: those involved in coordination (C2═C3 of 1.425(7) Å in **3** and 1.395(7) Å in **2**) are significantly longer than those which are not taking part in such an interaction (C10═C11 of 1.313(8) Å in 3, 1.292(7) Å in **2**).

The conformations of the organic ligands, defined by the dihedral angles between the terminal phenyl rings, are also similar; the dihedral angles are 33.4(3)° in **3** and 27.1(3)° in **2**. The central conjugated chains are approximately planar (max. deviation is 0.153(4) Å in **3** and 27.1(3) in **2**). In the crystal structure of **3** there are voids which are filled by the disordered solvent (toluene) molecules.

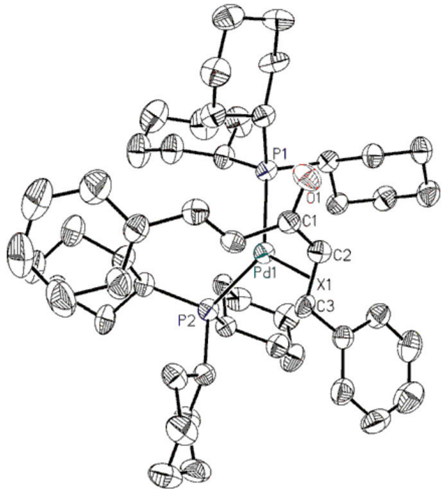
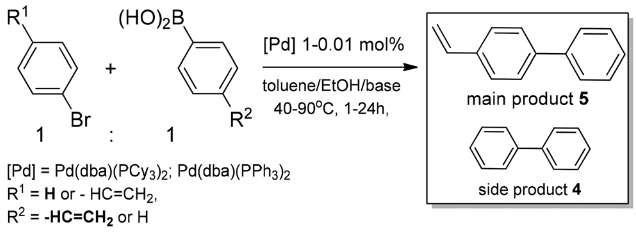


Fig. 2 A perspective view of complex **3** with labelling scheme. Ellipsoids are drawn at the 33% probability level, hydrogen atoms are omitted for clarity. Selected geometrical parameters (Å, °) Pd1–X1 2.052(5), Pd1–C2 2.172(5), Pd1–C3 2.154(5), Pd–P1 2.3832(17), Pd–P2 2.3641(14), X1–Pd1–P1 124.60(17), X1–Pd1–P2 119.68(18), P1–Pd1–P2 115.61(6).



Scheme 3 Pd(0) catalyzed Suzuki–Miyaura coupling of aryl bromines with boronic acids.

The well-known oxidative addition step occurs with coordinatively unsaturated complexes. Our palladium precursors [Pd(dba)(PR$_3$)$_2$] are 16 electron species and they have one free coordination place.

In order to optimize the reaction conditions with respect to activity, selectivity, catalyst loading, time and temperature the model reaction of bromobenzene (or 4-bromostyrene 0.5 mmol, both of them after redistillation) and 4-vinylphenylboronic acid (or phenylboronic acid 0.5 mmol after recrystallization from water) with a molar ratio of 1 : 1, was used according to Scheme 3.

The study of two different substrate combinations allowed us to confirm that the first system was much more effective and efficient than the other. The reason for that is the influence of the different substituent in the 'para' position on the distribution of electron density in the ring and thus on the reactivity of the vinyl group. After many catalytic tests, we know that the boronic acid fragment –B(OH)$_2$ (donating group) increases the reactivity of the group –CH═CH$_2$ in the process. We compared two different well defined catalysts built of

Table 1 Optimizing Suzuki–Miyaura coupling reaction conditions

$Pd(dba)(PPh_3)_2$ – **2**

Entry	Catalyst amount (mol%)	Temp. (°C)	Time (h)	Yield[a] (%)
1	1	40	8	31[b], 33[c]
		60	3	82[b], 84[c]
		90	1.5	88[b], 94[c]
2	0.5	40	12	29[b], 31[c]
		60	5	81[b], 83[c]
		90	2	86[b], 92[c]
3	0.2	40	18	54[b], 56[c]
		60	10	82[b], 84[c]
		90	8	87[b], 90[c]
4	0.1	40	24	16[c]
		60	24	37[c]
		90	24	65[c]
5	0.01	40	24	15[c]
		60	24	22[c]
		90	24	31[c]

$Pd(dba)(PCy_3)_2$ – **3**

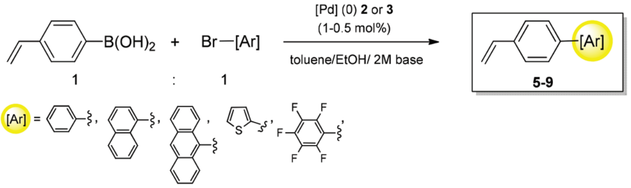
Entry	Catalyst amount (mol%)	Temp. (°C)	Time (h)	Yield[a] (%)
6	1	40	8	54[b], 58[c]
		60	3	89[c]
		80	1	98[c]
7	0.5	40	8	55[c]
		60	6	87[c]
		80	3	97[c]
8	0.2	40	18	79
		60	6	85
		80	3	96[c]
9	0.1	40	24	66[c]
		60	18	79[c]
		80	4	95[c]
10	0.01	40	24	20[c]
		60	24	34[c]
		80	24	46[c]

[a] Determined by GC and GCMS methods. [b] Na_2CO_3. [c] K_2CO_3; open systems under Ar and air were examined.

various types of phosphine characterized by steric effects influencing the stability and reactivity of the catalyst; data are collected in Table 1.

When the catalyst amount was reduced to 0.01 mol% and the temperature was at 40 °C, a longer reaction time was required (24 h). The use of the catalyst in a lower amount (0.01%) gave a low yield of the desired product. On the other hand, the use of a higher amount (1 mol%) of palladium catalyst (**3**) reduced the reaction time to 1 hour (Table 1). The results presented in the table show that it is possible to effectively reduce the temperature to 70 °C. We also used a little more catalyst **3** (1.5 mol%) at 60 °C and achieved a very good yield of 94% after a short time (60 min).

At the same time the first combination of substrates appeared to be much better for obtaining a product with a yield of over 98% for the third complex. An important factor in raising the efficiency of the reaction was the kind of applied base. The most appropriate was potassium carbonate (K_2CO_3), with which it is possible to get nearly 100% conversion of substrates to 4-vinylbiphenyl (**5**).



Scheme 4 Synthesis of styryl-derivative arenes in the presence of **2** or **3**.

In one case, we identified on the basis of MS spectra, trace amounts of the side compound **4**. The reaction is carried out in the presence of complex **2** (1 mol%) at 90 °C (see Table 1, entry 1).

For the full control of the synthesis of the new π-conjugated styrylarene derivatives having an aromatic unit we additionally made several catalytic examinations of the following reaction, see Scheme 4.

In the synthesis of the new olefins we used a biphasic solvent system of toluene (0.25 M solution concentration for halide)–ethanol (2 mL)–base (3 mL, 2 M solution) and the new palladium catalyst (see Fig. 1 and 2). Since the reactive substrate contains the styryl group, the reaction conditions were optimized to eliminate the possible effects of polymerization. All catalytic details are presented in Table 2 below.

Using the new palladium complex significantly reduced the temperature and duration of the reaction. Furthermore, the reaction proceeds efficiently with a lower amount of catalyst, which makes it more economical. Notably, during the course of the reaction the system was homogeneously yellowish in colour and there was 'no reduction' to the black species of the palladium. These reaction parameters have a significant impact on the total control of the process.

The ^1H NMR spectrum of 2-(4-vinylphenyl)thiophene (**8**) (Fig. 3) below shows us a clean, new olefin isolated using a simple, convenient method of flash filtration (glass filter–silica gel–celite).

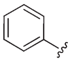
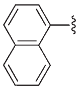
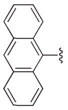
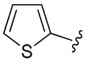
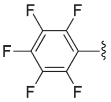
Signals A, B, C and their coupling constants (from 10.9 Hz to 17.6 Hz) come from a typical vinyl group on aromatic compounds. A small amount of anthracene was observed during the catalysis with 9-bromoanthracene. That is why part of the synthesis was performed in the presence of the weaker base Na_2CO_3 and the reaction time was prolonged.

Next, we selected more active catalysts from this palladium system and used them in preliminary catalytic tests in order to choose the best conditions for the selective, controlled synthesis of distyrylarene derivatives from commercially available substrates, Scheme 5.

In order to avoid the formation of by-products, the stoichiometric ratio of 1 : 2 of dibromoaryl to boronic acid derivative was used.

To maintain a homogeneous system an appropriate amount of toluene was used in the synthesis. Typically, the crude mixture was extracted with water and a few crystals of sodium chloride to disperse the slurry. The mixture was left over magnesium sulfate for four to five hours. The final products were purified from the mixture of dichloromethane–hexane by

Table 2 Catalytic test of 4-vinylphenylboronic acid with aryl bromines *via* Suzuki-coupling reaction

Br–[Ar] Ar	Catalysis system [Pd]–base	Temp. (°C)	Time (h)	Molar ratio [Br] : [acid] : [cat.]	Conversion Br–[Ar][a] (%)
	2–K_2CO_3	90	2	$1:1:1\times10^{-2}$	44
			7		97
	3–K_2CO_3	70	2	$1:1:5\times10^{-3}$	67
			4		>99
	2–K_2CO_3	90	2	$1:1:1\times10^{-2}$	21
			18		>99
	3–K_2CO_3	70	2	$1:1:5\times10^{-3}$	65
			4		>99
	2–Na_2CO_3	90	2	$1:1:1\times10^{-2}$	29
			18		82
	2–K_2CO_3	90	2	$1:1:1\times10^{-2}$	64
			7		93
	3–K_2CO_3	70	2	$1:1:5\times10^{-3}$	85
			4		>99
	2–K_2CO_3	90	2	$1:1:1\times10^{-2}$	28
			20		90
	3–K_2CO_3	70	2	$1:1:1\times10^{-2}$	43
			8		>99
	2/K_2CO_3	90	2	$1:1:1\times10^{-2}$	57
			8		92
	3–K_2CO_3	70	2	$1:1:5\times10^{-3}$	89
			3.5		>99

[a] Determined by GC and GCMS methods; open systems under Ar and air were examined.

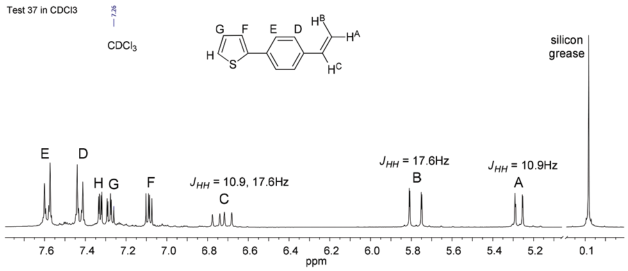


Fig. 3 ^{1}H NMR spectrum of **8** in $CDCl_3$ at 25 °C.

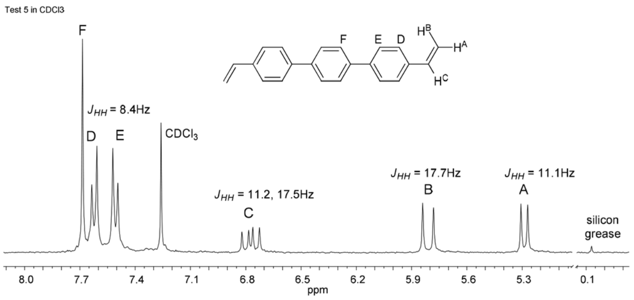
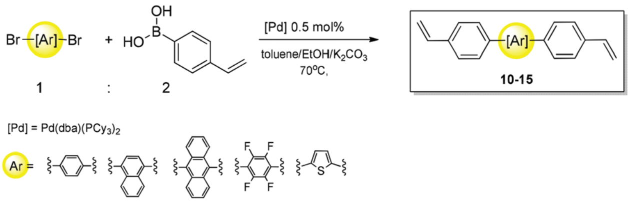


Fig. 4 ^{1}H NMR spectrum of **11** in $CDCl_3$ at 25 °C.



Scheme 5 Synthesis of new distyrylarenes *via* the Suzuki–Miyaura coupling reaction.

precipitation and dried under a high vacuum for 15 minutes at 15–17 °C.

In this way a few new π-conjugated **10–15** organic compounds were synthesized with yields of almost 100%. The clear proton NMR spectrum of the final distyryl-conjugated product is presented above, see Fig. 4. Because of the potential distribution, the olefin should be kept at low temperatures. Compounds **5–15** were isolated and fully characterized spectroscopically.

In conclusion, two very active and selective, mononuclear phosphine palladium(0) complexes (**2**, **3**) were synthesized (with very good yields, *e.g.* for **2** – 98% and for **3** – 95%) and their structures were solved by spectroscopic and X-ray methods. These complexes appeared to be efficient homogenous catalysts in the Suzuki coupling of vinylphenyl boronic acid with mono- and dibromoarenes. A highly selective method for the synthesis of new π-conjugated olefins was presented. The reactivity of the products is now under investigation. All the obtained compounds can be used as starting materials for the synthesis of new symmetrical, molecular-derivatives and stereo-regular-polymeric materials with unique mechanical, thermal and optoelectronic properties. Further results on the use of these compounds for the synthesis of large, high-molecular π-conjugated organic compounds will be reported in due time.

Acknowledgements

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