Communication

A comparative study of dibenzylideneacetone palladium complexes in catalysis

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25	^T Fakultat für Chemie und Biochemie, Ruhr Universität Bochum, Universitätsstr. 7
26	
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28	44801 Bochum (Germany), lukas.goossen@rub.de, http://www.ruhr-uni-
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[‡]Max-Planck-Institut für Kohlenforschung, Chemische Kristallographie und Elektronenmikroskopie, Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr (Germany) KEYWORDS: Palladium, Pd₂(dba)₃, Pd(dba)₂, Pd catalysis, Pd nanoparticles, amination,

reproducibility.

ABSTRACT: Commercial $Pd_x(dba)_y$ from various suppliers was found to vary considerably in appearance, homogeneity, purity, and catalytic activity. The Buchwald-Hartwig amination of 4-bromoanisole (5) with aniline (6) was established as a sensitive test reaction to probe the efficiency of $Pd_x(dba)_y$ batches in catalytic transformations. The yields obtained with 17 different $Pd_x(dba)_y$ batches range from 10% to near quantitative yields, and cannot be predicted reliably based on any physical or spectroscopic descriptor alone. The best results in the catalytic test reaction were consistently achieved with a self-made, slowly crystallized Pd_2dba_3 -toluene adduct. A protocol is disclosed that allows converting batches of $Pd_x(dba)_y$ with unsatisfactory or inconsistent performance into this reliable pre-catalyst.

Introduction

Over the past decades, palladium-catalyzed coupling reactions have become established as essential tools for C–C and C–heteroatom bond formation.¹ The pioneering contributions by Heck, Negishi, and Suzuki to this field of research were acknowledged with the Nobel Prize in 2010.² One of the key factors responsible for the tremendous number of synthetic applications achieved with palladium catalysis was the implementation of systematic catalyst screening. The optimal catalyst for a given transformation can be rapidly determined by tuning a common palladium precursor using a range of possible ligands and additives, and by optimizing further reaction parameters such as solvents, bases, and temperatures. In this context, Pd⁰ adducts of dibenzylideneacetone (dba) are among the most widely used Pd⁰ precursors.

 $Pd(dba)_2$ (1) was first synthesized by Takahashi *et al.* in 1970.³ The structural formula suggests a defined stoichiometry, but it has meanwhile become clear that instead, it is a rather complex mixture of species.⁴ Slow crystallization from coordinating solvents results in the formation of defined solvent adducts of $Pd_2(dba)_3$ (2), for example, $Pd_2(dba)_3$ ·CHCl₃

(3), $\cdot CH_2CI_2$ or $\cdot C_6H_6$, in which the solvent molecules are part of elemental crystal cells

(Table 1).⁵

Table 1. Known Pd_x(dba)_y-species

species	appearance	molecular structure of Pd ₂ (dba) ₃ (2)
$Pd(dba)_{a}^{a}(1)$	brown, crystalline ³	
	red-violet, crystalline ^{4a}	
Pd(dba) ₃ •C ₆ H ₆	orange-brown, crystalline4b	
Pd ₂ (dba) ₃ ^a (2)	purple, crystalline ⁶	Pd
Pd ₂ (dba) ₃ •CHCl ₃ ^a (3)	purple needles ⁵	Pd
Pd ₂ (dba) ₃ •CH ₂ Cl ₂	wine-red, crystalline4d	
Pd₂(dba)₃•C ₆ H ₆	purple needles ⁵	
Pd₂(dba)₃•PhMe	purple needles ⁵	

^a commercially available.

It was initially assumed that the reaction of Pd⁰-dba adducts with stronger donor ligands, e.g. phosphines or N-heterocyclic carbenes, would give rise to homoleptic PdL_n complexes in which the number of ligands would depend on the palladium-to-ligand stoichiometry.⁷ However, it has repeatedly been observed that dba coordinates rather

strongly and remains partially bound to the metal, thus influencing the overall catalyst

activity.^{6,8} Fairlamb *et al.* have performed comparative studies with substituted dba derivatives and found a clear influence of the electron-donating nature of the aryl residue on the catalytic activity of palladium-dba-type species.⁹ The more strongly donating the aryl residue, the less stable is the coordination of dba and the easier it is to fully replace it by a phosphine ligand. However, weakening the dba interaction also leads to lower stability of the palladium intermediates and thus, a shorter catalyst lifetimes. The wealth of applications seem to suggest that Pd complexes with dba itself strike the ideal balance between activity and stability that is required for a reliable in situ-conversion to active catalysts bearing customized ligands.

Scheme 1 gives an overview of representative reactions in which dba adducts of palladium are used as catalyst precursors. They include Heck, Suzuki, Negishi, Buchwald-Hartwig, Tsuji-Trost, Sonogashira, Stille, and our own decarboxylative couplings.¹⁰ In some of these cases, dba acts as the stabilizing agent itself, but in most reactions, phosphines or other ligands are added.





Scheme 1. Pd_x(dba)_y-catalyzed reactions.

As reaction developers, we are frequently contacted by synthetic chemists from academia or industry who experience substantial deviations in their experimental outcomes from published reactions when using $Pd_x(dba)_y$ precursors, despite all efforts to avoid known pitfalls, such as varying solvent quality or different handling of reaction substrates.¹¹ In our experience, this is often a consequence of different traditions in the groups of catalyst developers and synthetic chemists: Whereas the former prefer to prepare their own $Pd_x(dba)_y$ complexes using optimized protocols handed down within

their research groups, the latter usually rely on commercially available sources. The

characteristics of the $Pd_x(dba)_y$ precursor employed will substantially affect the yields whenever the reaction under investigation is close to the performance limit of the palladium catalyst and/or the reaction outcome critically depends on the palladium-toligand stoichiometry. In contrast, the quality of the $Pd_x(dba)_y$ complexes will not immediately influence the reaction outcome if catalyst activity is so high that comparable results are achieved even if only a fraction of the palladium precursor is converted to the actual catalyst. The outcome will also be unaffected if the actual catalytic species is colloidal palladium rather than defined PdL_n complexes. Ananikov and Zalesskiy found that commercially available $Pd_x(dba)_v$ samples contain up to 40% Pd nanoparticles and propose that many reactions that are assumed to depend on homogeneous catalysts are in fact catalyzed by such particles.¹² Colacot intensively studied palladium acetate against the two major impurities found in commercial samples: Pd₃(OAc)₅(NO₂) and polymeric [Pd(OAc)₂]_n in a variety of cross-coupling reactions.¹³ Whereas the impurities can be as active as the pure palladium acetate in certain reactions, pure palladium acetate turned out to be superior in precatalyst formation, in this case a cyclopalladation.

The aim of the present study was to correlate the activity of $Pd_x(dba)_y$ samples with their physical and spectroscopic properties and explore whether descriptors exist to predict their catalytic activity.

Results & Discussion

In order to quantify and compare the catalytic activity of a set of commercially available and self-made Pd_x(dba)_y batches, we searched our laboratory database for an easy-toperform reaction that requires a molecularly defined catalyst and that had proven to be particularly sensitive to the choice of the catalyst precursor. We evaluated a series of reactions, including Suzuki couplings, Heck reaction and amination reactions. All these reactions showed varying yields depending on the choice of the palladium precursor, but the Buchwald-Hartwig amination of aryl bromides was most strongly affected. We finally chose the coupling of 4-bromoanisole (**5**) with aniline (**6**, Scheme 2) as a test reaction, because it is easy to conduct and gave yields that varied between 10% all the way up to quantitative yields, depending on the choice of the palladium pre-catalyst.

Using this test reaction, we then investigated the performance of seventeen batches of $Pd(dba)_2$ (1), $Pd_2(dba)_3$ (2) and $Pd_2(dba)_3$ chloroform (3) newly purchased from six



different suppliers A-F (Table 2). The catalytic reaction was performed three times for every batch, using material from different layers of each container. All commercial materials were used as shipped. $MaOBu (1.5 eq.) \\ [Pd] (0.5 mol%) \\ PBu, (0.4 mol%) \\ \end{pmatrix}$

MeC

PhMe. rt. 1h

Scheme 2. Test reaction of 4-bromoanisole (5) with aniline (6).

As a reference material, we used a self-made Pd₂(dba)₃•toluene (4) adduct. In the original synthetic procedure by Ishii, 4 was obtained by reaction of PdCl₂, dba, and sodium acetate followed by crystallization of the resulting dba-palladium adduct from a toluene solution. This way, purple needles with a melting point of 140-141 °C were obtained in 36% yield.⁵ We used an analogous method to convert commercial Pd(dba)₂ (1) into a well-defined toluene adduct by slowly crystallizing it from a toluene solution layered with excess pentane. Only the first crop of crystals, which usually corresponded to no more than 50% of the initial amount, was used. This way, 4 was obtained as dark purple crystals

of cubic or octahedral shape that were around 0.2 mm in size and had a melting point of 185 °C.

The palladium loadings for the reaction were calculated based on the Pd content specified by the supplier¹⁴ or, if not available, based on the molecular formula provided (Table 1). The palladium content of each sample was double-checked by atomic absorption spectroscopy, revealing no major inconsistencies between our own measurements and the data provided by the suppliers. The elemental analyses of all samples of Pd₂(dba)₃ (2), i.e. **3D** and **3E**, showed strong discrepancies between experimentally found and calculated molecular formula, suggesting that some samples contain excess dba (Supporting Information, Table S1). This is not unexpected since Pd dba adducts are often non-stoichiometric in nature, and are known to incorporate solvent molecules during crystallization.

Table 2 lists catalyst specifications for all samples investigated and shows the yields obtained in the test reaction along with visible light microscopy and SEM images. The results were strongly variable, with yields ranging from 10% to nearly 100%. Some catalyst sources consistently gave similar yields, whereas the results obtained with others

varied greatly, which indicates inhomogeneity of the material within the batch. The toluene adduct **4** used as a reference material performed consistently well throughout, confirming that the deviations are mostly caused by factors associated with the catalyst precursors rather than by experimental errors.

We also investigated the palladium precatalysts in the Suzuki-Miyaura coupling of 4-



bromo-6-methyl-2H-pyrone 8 and 4-fluorophenylboronic acid 9 (Scheme 3).

Scheme 3. Test reaction of 4-bromo-6-methyl-2H-pyrone 8 and 4-fluorophenylboronic

acid 9.

Fairlamb *et al.* had established this reaction as a test to investigate the influence of substituents at the dba ligands.^{9a} However, **8** is not commercially available, which complicated the use of this test reaction.¹⁵ Moreover, the yields became too high and too similar to each other already after short reaction time, which precluded a reliable

comparison of pre-catalysts. Less reactive substrate combinations would be required to

test this reaction type. Still, as can be seen from the SI (Table S6), the reactivity trends

found in this alternative test reaction do not contradict those found for the amination.



Fable 2. Analytical data, catalytic performance, microscopy at 200x magnification, and SEM for all samples under investigation.^a

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^aReaction conditions: 5 (1.0 mmol), 6 (1.0 mmol), NaO/Bu (1.5 mmol), Pd_x(dba)_v (0.5 mol% Pd, calculated from the Pd content reported by the supplier) and P/Bu₃ (0.4 mol%) in toluene (2 mL),

¹room temperature, 1h. Yields were determined by GC analysis using *n*-dodecane as internal standard. ^b Theoretical amount of palladium. Pd(supp.) – palladium content reported by the supplier. 2 Pd(AAS) – palladium content determined by atomic absorption spectroscopy. AiC – Amount of insoluble components. AsP – Amount of soluble palladium (equal to Pd(AAS) – AiC). ACS Paragon Plus Environment

Influence of the Pd content. The results summarized in Table 2 reveal no clear correlation between Pd content and catalytic performance. This is an important finding, because we are aware from requests by synthetic chemists that it is often assumed that batches with a high Pd content have a higher purity and will perform better in catalytic reactions than those with a Pd content that is lower than expected from the molecular formula. Besides the normal Pd content, the relative amount of soluble Palladium (AsP in %) versus the amount of insoluble components (AiC in %, consisting mostly of agglomerated Pd black) were also determined.¹⁵

Especially when working with catalyst stock solutions, it is important to know how much of the material actually dissolves in organic solvents, and how much of the bulk material is insoluble metallic palladium. This correlation was verified in a control experiment. The yield obtained in our test reaction dropped from 60% to 28% when the Pd-dba precursor was mixed with Pd black in a 1:1 ratio based on the overall Pd content (Supporting information, Table S7). However, the results listed in Table 2 do not reveal any such correlation between AsP and catalyst activity. Hence, the AsP is no reliable predictor for the performance of a batch of palladium-dba material in sensitive catalytic reactions.

Influence of the molecular formula provided. When comparing the activities of commercial samples of 1, 2, and 3, it seems as though the better control of the stoichiometry in the Pd₂(dba)₃•CHCl₃ adduct (3) causes smaller variations with regard to catalyst performance than the other two compounds. Similar yields were obtained both within each batch and when using materials obtained from different suppliers. However, the overall performance of all Pd₂(dba)₃•CHCl₃ samples (3) is mediocre, which sustains the prejudice catalyst developers have against adducts that contain non-innocent components such as chloroform. The activities of $Pd(dba)_2$ (1) and $Pd_2(dba)_3$ (2) complexes are subject to greater variability both within and between batches of 1 and 2 than for Pd₂(dba)₃•CHCl₃ (3). Thus, at least for this test reaction, the catalyst performance cannot be predicted based on the dba/Pd ratio. For a comparative study of of Pd(dba)₂ vs. $Pd_2(dba)_3$, see also the protocol of Peng.¹⁶

Influence of particle shape and size. Next, all samples were investigated by microscopy

at 200x magnification. Table 2 shows tremendous differences between the samples (see the Supporting Information for more detailed pictures). In the literature, $Pd(dba)_2$ (1) crystals are described as brown to red-violet needles.^{3,4a} Such needles were seen for samples 1A, 1C, 2A, 2C, 2E and 3E. In sample 1A, silver-colored octahedrons, indicative of elemental Pd,¹⁷ are found alongside the needles. Samples **1D**, **2B** and **2D** consist of hexagonal crystals, which has not previously been described for $Pd_x(dba)_y$. In contrast, samples 1B₁ and 1B₂ are black, amorphous powders. 1E and 2F consist of cubic crystals. This crystal shape has been reported for microstructures of Pd₂(dba)₃ (2) crystallized from THF/H₂O mixtures.¹⁸ **3A** and **3D** are violet needles, which is in agreement with literature reports for 3.5 These examples demonstrate how strongly the manufacturing process affects crystal shape and appearance of $Pd_x(dba)_y$ materials.

The only conclusion one might possibly draw from the microscopic investigations in combination with the catalytic test reaction is that amorphous powders should be avoided, because both $Pd(dba)_2$ (1) samples by supplier **B** gave low yields in the test reaction.

Other factors detectable by microscopy, such as crystal shape or color do not lead to reliable predictions with regard to the catalytic performance of the material.

Scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDX).

We next investigated the solid materials by SEM and EDX to obtain further information on the elementary composition and homogeneity of the samples, and to determine the presence, form, and size of palladium nanoparticles (Table 2). All samples were sprinkled on Cu grids and embedded in resin (for more information about methods and sample preparation see the Experimental Section).

The brightness of the material correlates with the Pd content. At the brightest spots in the picture of **1B**, a palladium content of 85% was measured by SEM, the darker areas correspond to a Pd content of around 20%. This is indicative of a mixture of elementary palladium particles with Pd-dba complexes. The palladium particles have sizes of up to 3800 nm, well beyond those of soluble nanoparticles. In contrast, **1C** displays a high level of homogeneity with a Pd content of at most 18.6%. A magnification of 250,000x was necessary to detect bright spots indicative of elemental palladium. Most of these nanoparticles have a size of 2 nm, whereas very few measuring up to 20 nm seem to be

embedded within the crystal matrix and could not be detected on the sample surface, even when incorporating the sample into a resin and preparing resin slices (see Supporting Information and Experimental Section). Since this highly homogeneous material performs comparatively well in the catalytic test reaction, one might conclude that SEM analysis allows to predict catalytic performance based on the homogeneity of the sample and the absence of large, insoluble Pd particles. Indeed, many homogeneous samples including all samples by manufacturer C and 2A and 2E performed well, whereas the catalytic activity was lower for many inhomogeneous samples, e.g. 1E and all samples by supplier B. However, this approach has its limitations, considering that both **1A** and **1D** look similar by SEM but have a very

different catalytic activity.

The chloroform adducts were also investigated by EDX, a technique which allows visualizing the distribution of different atom types. EDX showed that the distribution of chlorine atoms was remarkably inhomogeneous in sample **3A** (Figure 1, EDX 3A CI K). The highest chlorine concentration was found in areas that also have a high palladium

concentration (EDX 3A Pd L). This points towards either chloroform-coated palladium

particles or dissociation of chloroform with formation of palladium chloride particles.



Figure 1. SEM and EDX measurements of sample 3A, 3D and 3E. Visualizing chlorine (yellow) and palladium content (red).

This is interesting, since one would assume from published crystal structures that the chloroform is embedded within the crystal matrix and, thus, homogeneously distributed.⁵ The same observation applies to sample **3D**. However, in this sample, the chloroform is not only adsorbed onto the Pd surface, but is also present inside the crystal matrix (EDX 3D Pd L and EDX 3D Cl K). In our experience, homogeneous solvent adducts of Pd₂(dba)₃ only form if the sample crystallizes very slowly. We thus assume that the

commercial materials were rapidly precipitated from a chloroform-containing solution,

resulting in nonstoichiometric mixtures of Pd_x(dba)_v (CHCl₃)_z with chloroform-coated nanoparticles and/or palladium chloride. This may be a reason why the catalytic activity of the Pd₂(dba)₃•CHCl₃ samples in our test reaction was relatively low. Interestingly, no chlorine was detected in sample **3E** even though ¹H-NMR in solution shows that it is present in the sample (EDX 3E CI). We believe that either the concentration of chloroform is too low for detection, or that chloroform-containing particles have been removed in the separation step that is part of sample preparation (for more information see the Experimental Section). In any case, a prediction of catalytic activity based on EDX is not possible, since despite their differences, all tested samples of 3 have a very similar catalytic activity.

Other spectroscopic studies. Several additional investigations were performed with the goal of establishing a correlation between physical or spectroscopic descriptors and the catalytic activity of dba-palladium adducts.

Any solvation process changes the composition of the dba adducts. This is the main problem when investigating the samples in homogeneous phase, e.g. by ¹H-NMR

spectroscopy. Solution analysis can, thus, be used only to detect organic impurities. In this context, we found peaks in all tested samples that are indicative of traces of water, pentane, acetone, alcohols, or acetic acid (see Supporting Information, Figure S18-S23). However, these small contaminants did not seem to decisively influence the catalytic activity. The samples were also investigated by MAS (magic-angle spinning, Figure S24) ¹³C-NMR, IR (infrared, Table S3) and XRD (X-ray diffraction, Figure S25) spectroscopy. However, none of the observations made in these investigations could be correlated to the performance of the samples in the test reaction (Supporting Information).

We next followed up on the observation that two different batches of Pd₂(dba)₃ (2) obtained from the same supplier had a markedly different catalytic activity (Table 2, sample 2B₁ versus 2B₂). A possible explanation is that the material loses activity during storage, and that newer samples are more active than older ones. A series of control experiments revealed that the sample 2C, which had performed rather well in the first set of experiments (94, 86, and 81% yield), gave only 71, 40, and 68% yield after it had been stored under air for 14 months. In sharp contrast, the crystalline Pd₂(dba)₃•toluene adduct (4) still gave near-quantitative conversion (99, 99, and 99% yield) after this time. We

suspected that the relatively high palladium content of 2C was at the origin of these stability issues, because there may have been insufficient dba to shield the Pd from the environment. We thus purchased a fresh sample of $Pd_2(dba)_3$ (2) from supplier F, which had a Pd content of only 15.31%, and contained excess dba. The new sample had roughly the same initial catalytic performance as 2C (83, 89, and 86% yield). We divided this batch into several samples which we stored under various conditions, and then reinvestigated the catalytic activity after 6 months. These investigations revealed that regardless of whether the material was stored under argon or air, in a glass or airpermeable polyethylene vessel, at room temperature, 40°C or 4°C, the catalytic activity remained almost unchanged (Figure 2). Although additional systematic stability studies are clearly required, this comparative experiments suggest that excess dba leads to enhanced storability of the Pd catalysts.



Figure 2. Reaction of 4-bromoanisole (5) with aniline (6) under standard conditions before and after storing the $Pd_2(dba)_3$ (2) sample under the given conditions for six months.^a

Improving the quality of Pd(dba)₂ batches. The above investigations show how difficult it is for synthetic chemists to be sure that the material they have in stock will perform well in a catalytic transformation. From our experience, it is advisable to convert stock palladium dba into a crystalline adduct with an inert solvent such as toluene.

The efficiency of this strategy was probed for sample **1D**, which had performed particularly poorly in the test reaction (Table 2), and had then been stored under air at room temperature for more than a year. 50 mg (0.09 mmol) of this material were suspended in 15 mL of toluene (p.a. grade, *Acros Organics*) and stirred it for 30 minutes at room temperature. The resulting deep red solution was then separated from the insoluble material by filtration through a pad of Celite. The clear filtrate was frozen by

cooling the Schlenk flask with liquid nitrogen while applying a slight vacuum. The solidified product solution was then carefully layered with 5 mL of diethyl ether and 30 mL of pentane. After warming to room temperature, the slow diffusion of the initially sharply separated solvent layers caused the product to crystallize within a week (Figure 3). This yielded 16.5 mg (18%) large, dark purple crystals of toluene adduct (4) with a melting point of 185 °C. The material thus obtained gave near-quantitative conversion in the test reaction in three independent runs.



Figure 3. Crystallization of the toluene adduct (4) shortly after removing the cold bath.

The fact that this crystallization is time-consuming and low-yielding explains why it is

not a valid large-scale manufacturing process for this material. However, in our hands,

any attempts to obtain the toluene adduct (**4**) faster and in a higher yield led to nonstoichiometric materials with unreliable catalytic activity (See Experimental Section). As can be seen from the crystal structure (Figure 4), even after slow crystallization, the material still has a relatively high level of disorder (50%). However, it is a well-defined adduct of two palladium atoms, three dba molecules and one toluene molecule.



Figure 4. X-ray structure of the Pd₂(dba)₃·toluene adduct (4, 50% disorder).

Conclusion

This systematic evaluation of physical and spectroscopic properties of various commercial dba-Pd adducts has revealed marked differences between the samples with regard to homogeneity, crystal shape and size, color, and palladium content. As to be

expected for a non-stoichiometric adduct, the molecular formula did not always correlate

with the palladium content of the samples. Many of the dba adducts contain impurities and particulate Pd. However, no reliable correlation seems to exist between the spectroscopic or physical data and the catalytic activity. We have found the Buchwald-Hartwig amination of 4-bromoanisole (5) and aniline (6) to be a sensitive and easy-toperform test reaction that allows to rapidly determine the catalytic activity of $Pd_x(dba)_y$ samples. It is recommended to first investigate the catalytic activity of a new batch of $Pd_x(dba)_y$ with this known reaction before using it for new catalytic transformations. The best results in the test reactions were consistently obtained with a self-made Pd₂(dba)₃•toluene adduct (4), which had been slowly crystallized over several days. It can be stored over years under ambient conditions without losing its catalytic performance, which is superior to most newly purchased commercial samples. Even older and partially decomposed dba-Pd batches with unsatisfactory catalytic performance can easily be converted into this reliable pre-catalyst.

Experimental Section

General Information. All solvents were purchased from Acros Organics in p.a. grade

and purified by standard procedures prior to use.¹⁹ 4-Bromoanisole (≥99% purity), Tritert-butylphosphine (98% purity), disodium tetrachloropalladate (99.99% purity) and sodium acetate (≥99% purity) were purchased from Sigma Aldrich and used without further purification. Aniline (≥99% purity) was purchased from Sigma Aldrich and purified by standard procedures prior to use.¹⁹ 4-Bromo-6-methyl-2H-pyrone was synthesized according to literature. Error! Bookmark not defined. 4-Fluorophenylboronic acid (97% purity) and dibenzylideneacetone (≥99% purity) were purchased from TCI and used without further purification. Sodium tert-butoxide (97% purity) and sodium carbonate (99.5% purity) were purchased from Alfa Aesar and used without further purification. All Solvents and liquids were degassed with Argon prior to use. Reactions were performed in oven-dried glassware under a nitrogen atmosphere containing a Teflon-coated stirring bar and dry septum. All reactions were monitored by GC using *n*-Dodecane as an internal standard. Response factors of the products with regard to *n*-Dodecane were obtained experimentally by analyzing known quantities of the substances. GC analyzes were carried out using an HP-5 capillary column (Phenyl methyl siloxane, 30 m x 320 x 0.25, 100/2.3-30-300/3, 2 min at 60 °C, heating rate 30 °C min-1, 3 min at 300 °C). The elementary analyses were measured on a Vario Micro Cube by

Elementar. The melting points were measured on a Digimelt MPA161 of *Stanford Research Systems*. The microscope pictures were taken with the digital microscope VHX-500F of *Keyence*. The sample was placed on a glass slide and illuminated from above (left side) or below (right side). The IR spectra have been measured on a Spectrum 100 ATR-FTIR of *Perkin Elmer*. ¹H-NMR spectra were measured on a FT-NMR spectrometer DPX 400 of *Bruker* and recorded at ambient temperature using CD₂Cl₂ as solvent, with proton resonances at 400 MHz, respectively. All NMR data are reported in ppm relative to the solvent signal. ¹³C-MAS spectra were measured on an AVANCE III 500 Solid State NMR by *Bruker*. The powder diffractograms were measured on a *Siemens* X-Ray powder diffractometer D 5005 using CuK α -radiation (wavelenght 0.15406 nm, acceleration voltage 40 kV, amperage 30 mA), recorded in a measuring range of 1° < 2Θ < 100°. The X-ray analysis of Pd₂(dba)₃·PhMe was done on a diffractometer Oxford Diffraction Gemini S Ultra at 150 K by using MoK α - or CuK α -radiation.

General procedure for the Buchwald-Hartwig amination. An oven-dried 20 mL vessel was charged with $Pd_x(dba)_y$ (0.5 mol% of Palladium), NaO⁴Bu (149 mg, 1.5 mmol) and P⁴Bu₃ (0.4 mol%). Toluene (2 mL), 4-bromoanisole **5** (1 mmol) and *n*-dodecane (50 µL) was added as the standard. The reaction mixture was allowed to stir for 10 minutes before aniline **6** (1 mmol) was added. The resulting mixture was stirred at room temperature under a nitrogen atmosphere. After 60 minutes, the mixture was diluted with ethyl acetate (4 mL), washed with water (2 mL) and extracted with ethyl acetate (3 mL). The organic layer was dried over MgSO₄, filtered and directly analyzed by GC.

General procedure for the Suzuki-Miyaura coupling. An oven-dried 20 mL vessel was charged with $Pd_x(dba)_y$ (0.5 mol% of palladium), 4-bromo-6-methyl-2H-pyrone 8 (0.41 mmol) and 4-fluorophenylboronic acid 9 (0.41 mmol). THF (1.5 mL), 1 M Na₂CO₃ (1 mL) and *n*-dodecane (50 µL) was added as the standard. The resulting mixture was stirred at room temperature under a nitrogen atmosphere. After 60 minutes, the mixture was diluted with ethyl acetate (4 mL), washed with water (2 mL) and extracted with ethyl acetate (3

mL). The organic layer was dried over MgSO₄, filtered and directly analyzed by GC.

Sample preparation for SEM and EDX investigations. All samples were examined for Pdnanoparticles via SEM (scanning electrone microscope, dark and light field pictures). Additionally, the elemental composition of each sample were examined by EDX (energydispersive x-ray spectroscopy). The samples were measured by two different methods. On the one hand, they were sprinkled on Lacey film (200mesh Cu-Grids) to determine form and size of the particles. This allows to determine the Pd-amount of each particle. The second technique allows identifying Pd-nanoparticles inside the crystal matrix. For that, the samples were incorporated into a resin and sliced with a diamond cutter as follows: The samples were fixed in *Beem*-capsule tips for 16h at 60 °C. Then the capsules were filled with the resin mixture *SPURR-Hart* and then hardened for 16h at 60 °C. The hardened sample was trimmed with a *Leica-Trim Em* or by hand. Then, the slices were cutted on a *Reichert-Jung Ultracut* or *OM-U3* with a 35° diamond blade (cutting speed 0.5mm / s, cutting thickness set 28nm). The cuts were transferred to *Lacey-Film* (400mesh Cu-Grid). These slices were tested for the presence, the composition and disposition of

Pd-nanoparticles. The EDX was recorded on a Thermo Scientific [™] NORAN [™] System 7 X-ray Microanalysis System with a Thermo Scientific [™] UltraDry EDS Detector 30mm² SDD (silicon drift detector).

Attempted accelerated synthesis of the toluene adduct. An oven-dried flask was charged with Na₂PdCl₄ (294 mg, 1.00 mmol) and dibenzylidenacetone (710 mg, 3.00 mmol). Under nitrogen atmosphere, degassed methanol (8.33 ml) and toluene (41.67 ml) were added. The reaction mixture was heated to 60 °C, under inert gas atmosphere, transfered to a flask with sodium acetate (331 mg, 4.0 mmol) and stirred for one hour. After cooling down to room temperature, the solution was washed with water (3x 30 ml) and dried , -20 °C overnight. The resulting dark purple crystals were washed with cold acetone (187 mg, 0.19 mmol, 19 %). In three parallel runs of the Buchwald-Hartwig-Amination of 4-Bromoanisole (5) with Aniline (6, see Scheme 2) yields of 80, 25 and 59% were achieved.

ASSOCIATED CONTENT

Supporting Information

The following Supporting Information is available free of charge on the ACS Publications website at DOI: Elementary analyses, melting points, microscope pictures, spectral data (IR, ¹HNMR, ¹³CMAS, XRD), properties of crystals and Pd nanoparticles, catalytic test reactions, SEM and EDX Data of the tested commercial samples and X-ray analysis of the toluene adduct **4** (PDF) AUTHOR INFORMATION

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Corresponding Author

*E-mail: lukas.goossen@rub.de

ORCID

Lukas J. Goossen: 0000-0002-2547-3037

Author Contributions

All authors contributed to writing the manuscript. HJB performed and evaluated the SEM and EDX measurements. HK was responsible for the crystal structure. All authors have given approval to the final version of the manuscript. [+] These authors contributed equally.

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(14) The palladium-loadings for the reaction were calculated according to the given Pdcontent by the supplier. In some cases, suppliers **A** and **D** gave a range for the Palladium-

> content. In this case, we performed the reaction with the minimum, medium and maximum possible amount of Palladium in order to display any discrepancies resulting from this number. If no Palladium-content was given, the corresponding palladium-loading for the reaction was calculated according to the theoretical amount of metal from the molecular formula.

> (15) A Pd_x(dba)_y sample was weighed and dissolved in an excess of chloroform. The undissolved solid was separated from the solution by filtration and weighed. By dividing its weight through the weight of the complete sample (from the beginning), the AiC in % is determined. By subtracting the AiC from the measured Pd content in % (determined by AAS) we calculate the AsP, from which we expect to display the amount of actually solvable Pd in a sample.

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