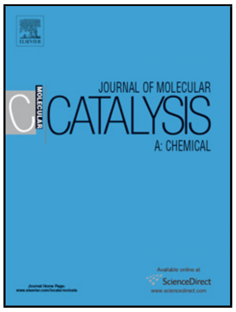

Title: Suzuki-Miyaura Coupling Reactions Using Novel Metal Oxide Supported Ionic Palladium Catalysts

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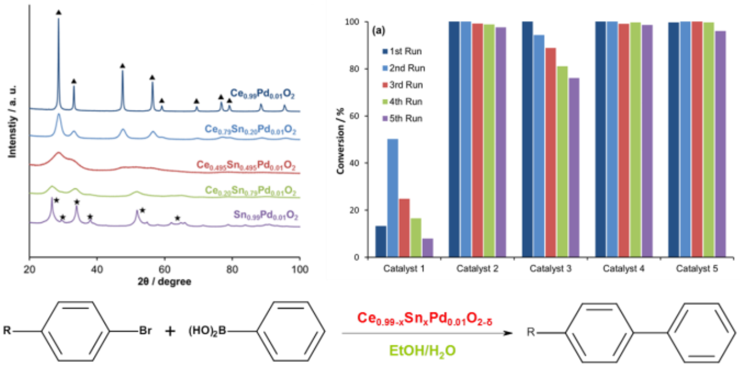
Highlights

- Five novel cerium-tin-palladium-oxides ($Ce_{0.99-x}Sn_xPd_{0.01}O_{2-\delta}$ ($x = 0 – 0.99$)) have been prepared out of non-toxic and inexpensive precursors using a simple and rapid single step solution combustion method
- The catalysts proved to be highly active (TOF > 12,000h^{-1}) for Suzuki-Miyaura cross-couplings of phenylboronic acid with various bromoarenes
- Only minimal amounts of palladium could be detected in the product solution (<0.14 mg/L)
- The catalysts could be reused for at least five times with only minor changes in activity and with no changes concerning the crystal structure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$Ce_{0.99}Pd_{0.01}O_2$
$Ce_{0.79}Sn_{0.20}Pd_{0.01}O_2$
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$Ce_{0.20}Sn_{0.79}Pd_{0.01}O_2$
$Sn_{0.99}Pd_{0.01}O_2$
20
40
60
80
100
2θ / degree
(a)
1st Run
2nd Run
3rd Run
4th Run
5th Run
Conversion / %
0
20
40
60
80
100
Catalyst 1
Catalyst 2
Catalyst 3
Catalyst 4
Catalyst 5
R
Br
+
$(HO)_2B$
$Ce_{0.99-x}Sn_xPd_{0.01}O_{2-\delta}$
$EtOH/H_2O$
R

Suzuki-Miyaura Coupling Reactions Using Novel Metal Oxide Supported Ionic Palladium Catalysts

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Abstract

Palladium substituted CeO_2, SnO_2 and their mixed oxides have been synthesized in quantitative yields out of non-toxic and inexpensive precursors using a simple and rapid single step solution combustion method. The resulting oxides, especially the mixed oxides $Ce_{0.79}Sn_{0.20}Pd_{0.01}O_{2-\delta}$, $Sn_{0.79}Ce_{0.20}Pd_{0.01}O_{2-\delta}$ and $Sn_{0.99}Pd_{0.01}O_{2-\delta}$ proved to be highly active (TOF > 12,000 h^{-1}) for Suzuki-Miyaura cross-couplings of phenylboronic acid with various bromoarenes. The reactions were carried out in ambient air at moderate temperatures using environmentally friendly aqueous ethanol solutions as reaction solvents. Minimal amounts of palladium in the product solution (<0.14 mg/L), the reaction kinetics as well as catalyst poisoning tests support the thesis that the reaction proceeds via dissolved palladium species in a homogeneous reaction mechanism. Nevertheless, the synthesized catalysts could be reused for at least five times with only minor changes in activity and no changes in the crystal structure, indicating the high potential of the investigated catalysts as quasi-heterogeneous C-C coupling catalysts.

Keywords: Ionic catalysts; cross coupling; solid solution; palladium; recyclability; heterogeneous catalysts.

1. Introduction

C-C coupling reactions are an important class of reactions prevalent in synthesis protocols adopted for making active pharmaceutical ingredients, natural products and bioinorganic materials [1] on a lab scale, as well as in industrial settings. The importance of these reactions was further demonstrated by the 2010 Nobel Prize in Chemistry to three eminent chemists (Richard F. Heck, Akira Suzuki and Ei-ichi Negishi) on Pd-catalyzed cross couplings in organic synthesis [2]. Palladium has been extensively used for catalyzing cross-coupling reactions. The catalytic systems are generally organometallic complexes. Several groups have focused their attention towards the development of ligands which effectively catalyze the reaction [3]. If the reaction is carried out with a homogeneous catalyst, complete recovery of the catalyst often becomes a challenge. The catalyst impurities in the product can be harmful when the products are intended as pharmaceuticals owing to the poisonous nature of the metal, as well as of the organic ligands. Therefore, we have focused on ligand free, heterogeneous catalysts for the Suzuki-Miyaura reaction, as these reaction systems have several advantages [1,3]..

The Suzuki-Miyaura reaction in its native form involves the coupling of haloarenes with phenylboronic acids with the major product being the corresponding biphenyls. Functionalized biphenyls are common intermediates of pharmaceutical products. For example, biphenyl tetrazoles show antimicrobial activity [4] and derivatives of biphenyl show anti-tumor effects [5]. Due to the abundance of this compound in a large number of pharmaceutical products, biphenyl can be considered to be a building block of a large variety of pharmaceutical products. Miyaura and Suzuki [6] reported first the use of organoboron compounds for C-C bond formation with the help of $Pd(Ph_3)_4$. A large number of organometallic Pd complexes has been reported since for catalyzing the reaction and the protocol has successfully been applied for large-scale synthesis of pharmaceuticals [3]. Apart from palladium, Suzuki-Miyaura reactions have been also catalyzed by several other transition metal complexes. For example, an iron-MCPA [7] complex and Fe halides have been reported as catalysts for the reaction [8]. Additionally, Cu has also been used for catalyzing the reaction, e.g., Cu nanoclusters were found to be active for catalyzing the reaction [9]. Furthermore, bimetallic catalysts consisting of Cu along with Pd, Pt and Ru also proved activity. Combined Cu/Pd catalysts showed the highest activity among all combinations [9]. Additionally, Ni complexes have also been used for the synthesis of biaryls using Suzuki-Miyaura reactions [10].

We report here palladium substituted CeO_2, SnO_2 and their mixed oxides as catalysts for Suzuki-Miyaura reactions. Palladium-containing metal oxides and mixed metal oxides have already been used successfully for Suzuki-Miyaura cross-coupling reactions. Catalysts of this kind, synthesized by sol-gel methods (e.g., $La_1Fe_{0.95}Pd_{0.05}O_x$) [11] or wet impregnation techniques (Pd/Al_2O_3, Pd/TiO_2, Pd/CeO_2) showed extraordinary high reactivity, good recyclability and minimal metal leaching [12,13].

Pd-doped CeO_2 catalysts developed by Hegde and co-workers were reported as efficient and non-deactivating catalysts for gas-phase oxidation reactions [14]. The solution combustion technique offers a relatively simple, inexpensive and rapid method for the synthesis of noble metal substituted ceria and ceria composites. Furthermore, solution combustion method permits homogeneous mixing of the catalysts precursors on the molecular level (in an aqueous solutions) and ensure high product crystallinity and purity due to the high combustion temperature (>900 °C) [15]. These characteristic features allow the production of oxide-based catalysts with high specific surface and precise phase composition [16]. Preliminary studies on C-C coupling reaction catalyzed by Pd-doped ceria-based catalysts were published by Sanjay Kumar *et al.* [17].

In this study, we have carried out a thorough investigation of Pd-ion substituted CeO_2, SnO_2 and their mixed oxides as catalysts for Suzuki-Miyaura reactions. In particular, a comparison of the activity of the different catalysts depending on their Ce and Sn amount as well as their tolerance to different starting materials were studied. Furthermore, the leaching behaviour and the recyclability of the catalysts were investigated. All in all, the study demonstrates the high potential of the investigated catalysts as heterogeneous C-C coupling catalysts.

2. Experimental details

2.1 Synthesis

General principles and methods for the solution combustion synthesis of nanocrystalline materials have been described and reviewed elsewhere [18,19]. The synthesis of $Ce_{0.99-x}Sn_xPd_{0.01}O_{2-\delta}$ was done analogously to the method reported by Baidya *et al.* [20] using glycine instead of L-tartaric acid as fuel. Glycine as the fuel has been used for combustion synthesis by several investigators and has been reported to impart good nanocrystallinity in the product [14,16,20]. A set of five $Ce_{0.99-x}Sn_xPd_{0.01}O_{2-\delta}$ mixed oxides (with x = 0, 0.2, 0.495, 0.79 and 0.99) was prepared. The appropriate proportions of catalyst precursors and fuel were calculated using the method described by González-Cortés *et al.* [21] considering the oxidizing/reducing valencies (Φ_e) of the redox mixture and assuming an ideal and complete combustion without secondary reactions. In this calculation, oxygen was considered as an oxidizer with the valance -2, whereas carbon (+4), hydrogen (+1) and metals (redox valence corresponding to metal valence) were considered as reducing elements. Nitrogen with the redox valence 0 was not considered. Oxidizing/reducing valencies of the reacting species were ammonium cerium (IV) nitrate =-24, tin (IV) nitrate =-20, palladium (II) nitrate = -10 and glycine = +9 to give the required amount of fuel for the synthesis of 1 mole $Ce_{0.99-x}Sn_xPd_{0.01}O_{2-\delta}$.

For the preparation of 3 g catalyst, appropriate amounts of ammonium cerium(IV) nitrate ($(NH_4)_2Ce(NO_3)_6$, Sigma Aldrich), tin(II) oxalate (SnC_2O_4, Sigma Aldrich), palladium(II) chloride ($PdCl_2$, Aldrich) and glycine ($C_2H_5NO_2$, Sigma Aldrich) were dispersed in 3 ml of water in a borosilicate dish with 600 ml capacity. 2.5 molar equivalent (related to tin (II) oxalate) of nitric acid (HNO_3, 65 %, Merck) were added and the mixture was slightly heated until a viscous, clear solution was obtained. The redox mixture was treated in a muffle furnace at 350 °C. The mixture ignited within 5 minutes, initiating a self-propagating combustion reaction, which yielded a voluminous, porous solid. This solid was ground with mortar and pestle and was heated to 350 °C for another 5 hours. After that procedure, the obtained powders were directly usable as catalyst for the Suzuki-Miyaura cross-coupling reactions.

2.2 Characterization

X-Ray diffraction

The synthesized catalysts were characterized using X-ray diffraction (XRD) with Cukα radiation to analyze the crystal structure. The samples were scanned in a range of 2Θ of 20-100°, a range in which characteristic peaks of CeO_2 and SnO_2 appear.

XPS spectroscopy

XPS analysis was performed with a monochromatic Thermo Fisher K-Alpha spectrometer equipped with an Al X-ray source (1486.6 eV) operating at a base pressure in the range of 10^{-8} to 10^{-10} mbar. High resolution scans were acquired at a pass energy of 50 eV and a step size (resolution) of 0.1 eV. Survey scans were acquired with a pass energy of 200 eV and a step size of 1.0 eV. The instrument work function was calibrated to give a binding energy (BE) of 83.96 eV for the Au 4f7/2 line for metallic gold. The peaks were fitted using a Gaussian/Lorenzian mixed function employing Shirley background correction (Software Thermo Avantage v5.906). All analyses were performed at room temperature.

Specific surface area

Specific surface areas were determined using a Tristar II 3020 (Micromeritics, Norcross, Georgia) with nitrogen as analytical gas. Catalyst samples were degassed under vacuum at ambient temperature for 24 h. The volume of nitrogen adsorption was recorded over a relative pressure range between 0.01 and 0.99. 8 points in the relative pressure range of 0.05 to 0.2 were used for the calculation of the surface area according to the Brunauer-Emmet-Teller (BET) theory.

Particle size distribution

The particle size measurements were conducted with a HELOS/KR Laser diffraction sensor equipped with an OASISDRY/L dry dispersion system by Sympatec GmbH (injector: 4 mm, dispersing pressure: 2.00 bar, optical concentration 1%-20%, measuring range: combined R2+R5 (0.45 µm - 875 µm), evaluation mode: Fraunhofer approximation, software: WINDOX 5.6.0.0). Each analysis was conducted as a 3-fold determination.

2.3 Catalytic activity

The catalytic activities of the prepared catalysts were tested for the Suzuki-Miyuara cross-coupling reaction of phenylboronic acid with various bromoarenes. In a typical experiment, 0.70 mmol of the aryl bromide, 1.5 molar equivalents of phenylboronic acid and 1.5 molar equivalents of base, respectively, and 1.3 mmol of anisole (internal standard) were dissolved in 20 ml of solvent. 5 mg of the catalyst (corresponding to approximately 0.05 mol % palladium) were added. The reaction was carried out under stirring at 75 °C. To monitor the reaction progress, samples from the reaction solution (100 µL) were taken after 15, 30, 60, 90 and 120 minutes. HPLC sample solutions were prepared by dissolving 100 µL of the reaction solution in 1 mL of the initial mobile phase. HPLC analysis was done using an Agilent 1100 series HPLC system (Agilent, Waldbronn, Germany), equipped with an online degasser, quaternary pump, autosampler, thermostatted column compartment and UV-visible diode array detector. An Agilent Poroshell 120 EC-C18 reversed-phase column (50x4.6 mm; 2.7 µm) was used as stationary phase. Analysis was carried out under gradient elution conditions using a mobile phase consisting of methanol and aqueous phosphoric acid (water: phosphoric acid = 300:1 v/v). Column temperature was set to 25 °C. UV-detection was performed at wavelengths of 237 and 270 nm over a run time of 15 minutes.

2.4 Recycling tests

The cross-coupling reaction of phenylboronic acid with 4-bromotoluene using potassium carbonate as base was chosen as model reaction to investigate the recyclability of the different catalysts. The reactions were carried out in 20 ml reaction mixture using the same concentrations of 4-bromotoluene, phenylboronic acid, potassium carbonate and internal standard (anisole) as in the reactivity tests. Five subsequent reactions with each catalyst were carried out. After a reaction time of 120 minutes, the catalyst was filtered off using a filter crucible and was washed with ethanol and water to remove organic and inorganic impurities. The catalyst was dried in a muffle furnace at 350 °C over night. The filtrate was evaporated under reduced pressure. The solid residue was analyzed for its palladium content by ICP-MS. Measurements were performed on an Agilent 7500ce ICP-MS after microwave assisted acidic digestion of the samples. Due to a partial loss of catalyst throughout the recovery procedure, the first experiment was carried out with an initial catalyst loading of 50 mg (corresponding to approximately 0.5 mol % palladium, 10 times more than in the reactivity tests).

2.4. Heterogeneity studies

The reaction of 4-bromotoluene with phenylboronic acid (in EtOH/H_2O = 7/3 v/v) was used for the heterogeneity studies using the same substrate and base concentrations as in the reactivity tests. Based on the results of the reactivity tests, the amounts of the catalysts were chosen so that the obtained conversions of 4-bromotoluene was in the range between 25 and 80 percent at the moment of filtration or catalyst poisoning.

2.4.1 Hot filtration test

Hot filtration experiments were done for each catalyst. The experiments were started in the same manner as the reactivity tests. After a certain reaction time, which ensured conversions of 4-bromotoluene between 25 and 80 % under the chosen reaction conditions, the catalyst was separated from the reaction mixture by filtration through a hot (75 °C) filter crucible. The remaining reaction solution was stirred and heated until a total reaction time of 120 minutes was reached. The reaction progress before and after the filtration was monitored via HPLC-analysis. The used amounts of catalysts and the times of filtration are given in Table 1.

Table 1: Catalyst masses and times of filtration for the hot filtration tests using $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99) as catalysts.

	Catalyst mass (mg)	Reaction time till filtration (min)
$Ce_{0.99}Pd_{0.01}O_{2-\delta}$	25	20
$Ce_{0.79}Sn_{0.20}Pd_{0.01}O_{2-\delta}$	2	15
$Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$	5	20
$Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$	2	10
$Sn_{0.99}Pd_{0.01}O_{2-\delta}$	2	5

2.4.2 Catalyst poisoning

Catalyst poisoning tests were started in the same manner as the hot filtration tests. After a certain reaction time, 100 molecular equivalents (compared to the total molar amount of palladium in the used catalysts) of the catalyst poison 3-mercaptopropyl-functionalized silica gel (MPSG, Sigma-Aldrich, 200-400 mesh, extend of labeling: 1.2 mmol/g) were added to the reaction solution. The reaction progress before and after poisoning was monitored via HPLC-analysis. The used amounts of catalysts, MPSG and the reaction times till the start of the catalyst poisoning are given in Table 2.

Table 2: Employed catalyst masses, masses of the added catalyst poison MPSG (100 molar equivalents) and times of poisoning for the catalyst poisoning tests using $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99) as catalysts.

	Catalyst mass (mg)	MPSG mass (mg)	Reaction time till poisoning (min)
$Ce_{0.99}Pd_{0.01}O_{2-\delta}$	25	120	30
$Ce_{0.79}Sn_{0.20}Pd_{0.01}O_{2-\delta}$	2	15	10
$Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$	5	26	20
$Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$	2	15	10
$Sn_{0.99}Pd_{0.01}O_{2-\delta}$	2	15	5

3. Results

3.1 Catalyst synthesis

The synthesis of the five catalysts via combustion of the prepared redox-mixtures yielded the desired compounds in quantitative amounts (> 99 %) within 1 hour. Redox solutions with high amounts of cerium (Ce ≥ 0.8) underwent a highly violent combustion reaction and produced a powdery solid. With increasing amounts of tin (Sn > 0.2), the combustion reactions became more and more gentle, yielding voluminous spongiform solids. After grinding with mortar and pestle and heating to 350 °C for another 5 hours, the solids could be directly used for characterization or reactivity tests.

3.2 Characterization

3.2.1 XRD

The XRD-profiles of the as-synthesized $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99) compounds are shown in **Figure 1.** The obtained lattice parameters are summarized in **Table 3**. The powder XRD pattern showed broad peaks indicative of nanocrystallinity in the synthesized compounds. Single phase cubic fluorite structures were observed for oxides with tin proportions up to 0.2. The measured cubic lattice constants were in good accordance with the data obtained by Baidya *et al.* [20] for the cerium rich oxides, $Ce_{0.99}Pd_{0.01}O_{2-\delta}$, $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$. Due to the smaller ionic radius of Sn^{4+} (0.81 Å) compared to Ce^{4+}, a decrease of the lattice constant from a = 5.412 Å (for x = 99) to a = 5.400 Å (for x = 0.79) indicated a successful incorporation of tin ions at Ce^{4+} sites in the cubic lattice structure. The XRD patterns in **Figure 1** have been marked with filled triangles (▲) for prominent CeO_2 peaks. $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ shows a good correspondence for these peaks, as can be observed from **Figure 1**. Contrary to the study of Baidya, a single phase cubic structure for the mixed oxides with equimolar amounts of cerium and tin ($Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$) could not be observed in our work. Instead, a more amorphous cubic/tetragonal mixed phase structure was observed when high ratios of tin were used ($Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$). The binary oxide $Sn_{0.99}Pd_{0.01}O_{2-\delta}$ showed a clearly single phase tetragonal structure. The prominent tetragonal peaks of pure SnO_2 have been marked by a filled star (★) in **Figure 1** and crystallization of $Sn_{0.99}Pd_{0.01}O_2$ in tetragonal structure can be clearly observed.

In order to confirm substitution of Pd in the lattice, XRD was recorded in a small range of 35-50° as shown in**Figure 2** . XRD-patterns clearly attributable to PdO or metallic Pd species could not be observed (**Figure 2**). This confirmed the absence of PdO or Pd metal particles and indicated a Pd^{2+} ion substitution in the metal oxide lattice.

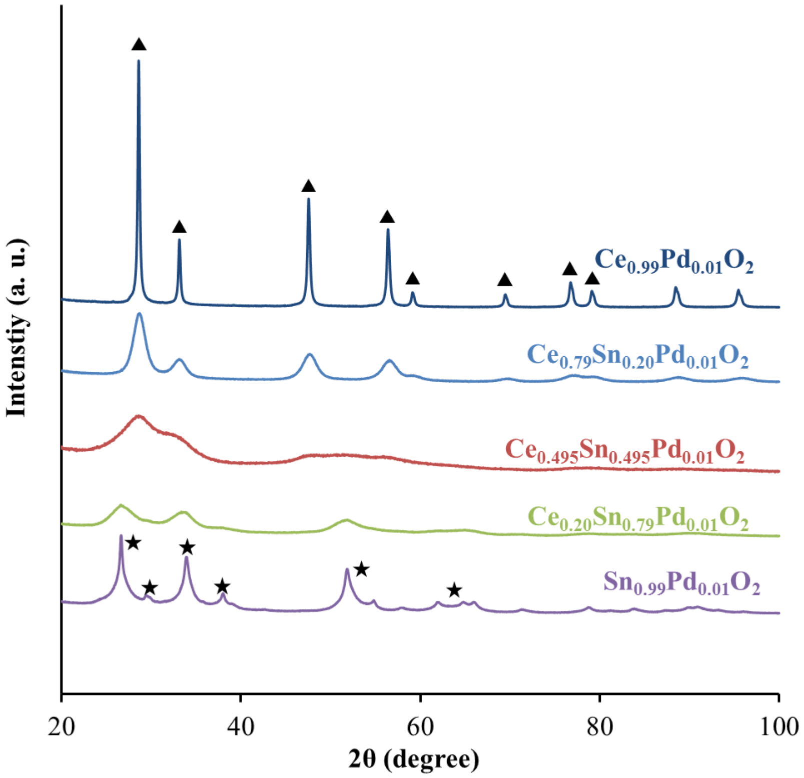


Figure 1: X-Ray diffraction pattern of as-synthesized $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99), ▲ - Cubic fluorite and ★ - Tetragonal

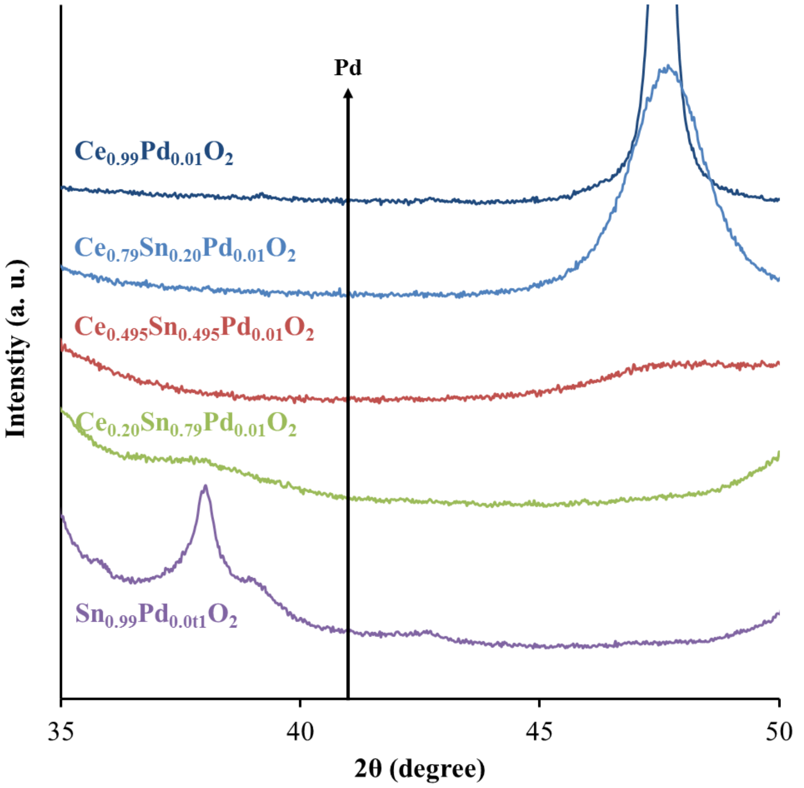


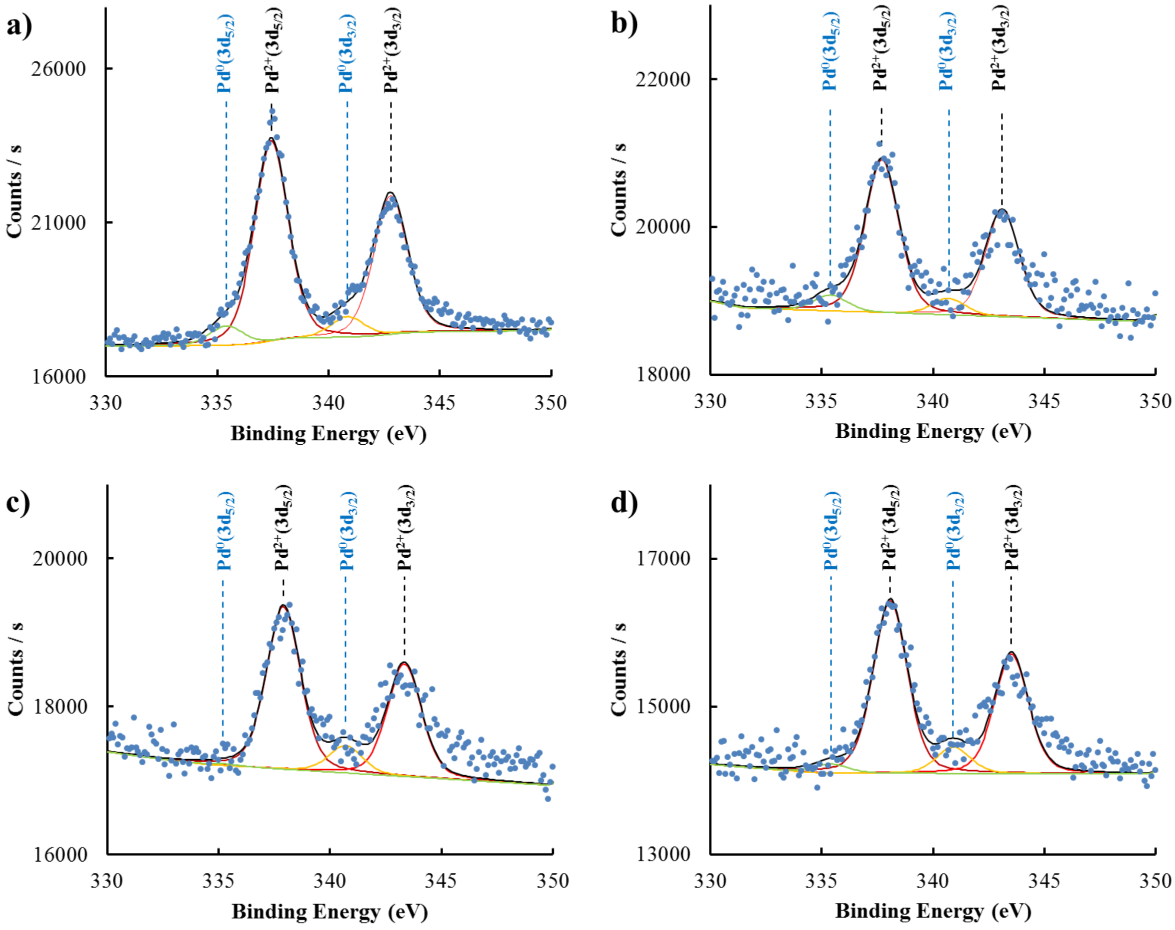
Figure 2: XRD-pattern of $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99). The arrow shows the peak position for Pd.

Table 3: Lattice constants of the as-synthesized mixed oxides

Catalyst	Phase	Lattice constants (Å)		
		Cubic	**Tetragonal**	
		a	**a**	**b**
$\mathbf{Ce_{0.99}Pd_{0.01}O_{2-\delta}}$	cubic	5.412	-	-
$\mathbf{Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}}$	cubic	5.400	-	-
$\mathbf{Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}}$	mixed cubic/tetragonal	5.385	4.562	3.482
$\mathbf{Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}}$	mixed cubic/tetragonal	5.260	4.732	3.234
$\mathbf{Sn_{0.99}Pd_{0.01}O_{2-\delta}}$	tetragonal	-	7.739	3.186

3.2.2 XPS

The predominantly cationic nature of Pd in the Ce/Sn-oxide lattice could also be confirmed by XPS analysis. XPS-scans in the Pd 3d region for all synthesized catalysts are shown in **Figure 3**.



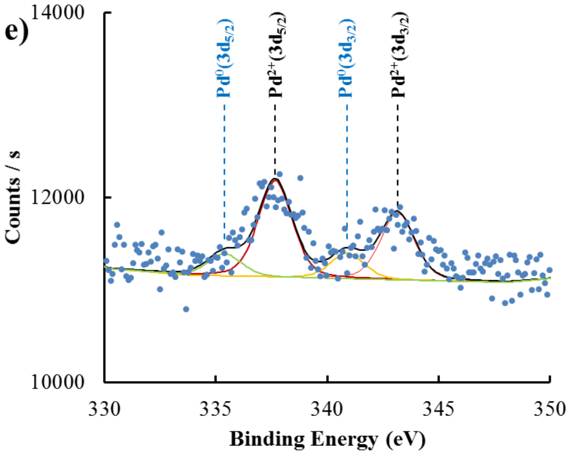


Figure 3: XPS spectra in the Pd 3d region for the novel $Ce_{0.99-x}Sn_xPd_{0.01}O_{2-\delta}$ catalysts: $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ (a), $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ (b), $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$ (c), $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$ (d), $Sn_{0.99}Pd_{0.01}O_{2-\delta}$ (e).

XPS-signals at 337.4 – 338.0 eV for Pd3d5/2 and at 342.8 and 343.5 eV for Pd3d3/2, respectively, are generally attributed to cationic Pd^{2+}. [17,20,22]. Nevertheless, small amounts of metallic palladium (binding energies around 335.3 and 340.8 eV) could also be detected on the surface. Observed binding energies of Pd^{2+} and metallic Pd^0 as well as the relative atomic amounts of both palladium species are summarized in Table 4. As can be seen, the ratio between Pd^{2+} and $Pd^{\ 0}$ is approximately 90/10 for cat 1 – 4. The highest amount for metallic Pd was observed for $Sn_{0.99}Pd_{0.01}O_{2-\delta.}$

Table 4: Ratio between Pd^{2+} and Pd^0 at the catalyst surface and observes binding energies for $Pd3d_{5/2}$ and $Pd3d_{3/2}$.

	Relative Amount (%)		Binding energies (eV)			
			Pd^{2+}		Pd^0	
	Pd^{2+}	Pd^0	$Pd3d_{5/2}$	$Pd3d_{3/2}$	$Pd3d_{5/2}$	$Pd3d_{3/2}$
$Ce_{0.99}Pd_{0.01}O_{2-\delta}$	89.5	10.5	337.4	342.8	340.8	335.4
$Ce_{0.79}Sn_{0.20}Pd_{0.01}O_{2-\delta}$	88.9	11.1	337.7	343.1	340.7	335.4
$Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$	90.4	9.6	337.9	343.3	340.7	335.2
$Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$	89.2	10.8	338.0	343.5	340.9	335.4
$Sn_{0.99}Pd_{0.01}O_{2-\delta}$	77.3	22.7	337.7	343.1	340.9	335.4

3.2.2 Particle size distribution and specific surface area

The particle size distribution and specific surface area are important parameters for catalytic activity, and were therefore included in our studies. The produced oxides appear as fine powders, consisting of agglomerates of the nanocrystalline materials. The analysis of the particle size distribution of these agglomerates revealed particles sizes of ~ 10 – 100 µm with a monomodal size distribution of the cerium-rich catalysts. The catalysts with higher ratios of tin, which originated from more gentle combustion reactions yielding spongiform solids, featured polymodal particle size distributions (**Figure 4**).

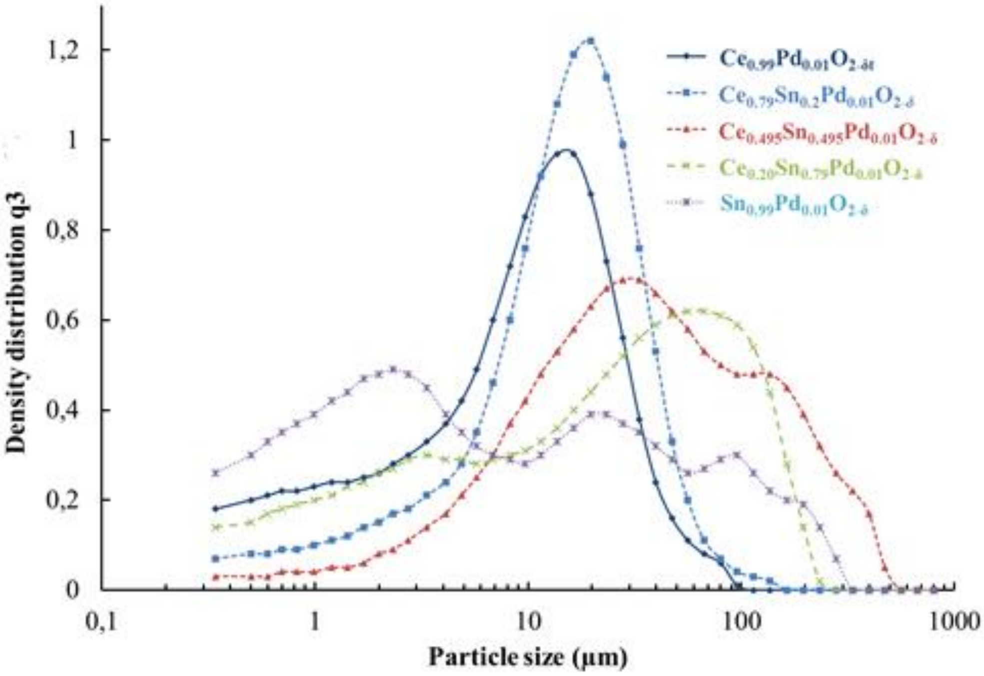


Figure 4: Particle size distributions of as-synthesized $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99).

$Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$, which contained equimolar amounts of cerium and tin, had the highest mass-median-diameter (x_{50}). Minimum x_{50} were observed for the binary oxides $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ and $Sn_{0.99}Pd_{0.01}O_{2-\delta}$. BET measurements showed specific surface areas at the same order of magnitude for all catalysts with $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ having the lowest (26.9 m²/g) and $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$ having the highest surface (97.7 m²/g). The other catalysts had comparable specific surfaces of approximately 50 m²/g (**Table 5**).

Table 5: Characteristic mean diameters x_{10}, x_{50}, x_{90} and specific surface areas of as-synthesized $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99) catalysts

	x_{10} [µm]	x_{50} [µm]	x_{90} [µm]	BET-Surface [m²/g]
$Ce_{0.99}Pd_{0.01}O_{2-\delta}$	0.8	9.6	28.2	26.9
$Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$	2.5	15.3	36.6	41.3
$Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$	5.5	33.8	189.4	48.7
$Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$	1.0	22.4	109.6	97.7
$Sn_{0.99}Pd_{0.01}O_{2-\delta}$	0.6	5.2	92.8	54.8

3.3 Reactivity

The catalytic activity of the as-synthesized catalysts was investigated for the Suzuki-Miyaura cross-coupling reaction of phenylboronic acid with various bromoarenes containing electron donating (methyl-, hydroxyl-), as well as electron withdrawing (acetyl-, trifluoromethyl-) groups in *para* position and the electron withdrawing nitrile group in *ortho* position. The results of the reactivity tests are summarized in **Table 7.** In all experiments, the conversions of the bromoarenes and the yields of the products formed out of the bromoarenes were equal within the error limits of the HPLC measurements. The absence of bromoarene-deriving side products (dehalogenation product Ar' and bromoarene homocoupling product Ar' Ar') indicated that the bromoarene substrates were converted to the desired biphenyl compound to the greatest extent in a highly selective manner. However, side products originating from boronic acid homocoupling (biphenyl, ArAr) and boronic acid oxidation (phenol, ArOH) could be found in quantifiable amounts, whereas the formation of the protodeboronation product (benzene, Ar) could not be observed.

Table 7 shows the reaction progress expressed as relative yield of the desired Suzuki cross-coupling product based on the concentration of the bromoarene (limiting component). The selectivity is defined as the concentration of the desired product divided by the sum of the concentrations of all formed organic products. All the reactions were carried out using 50 % molar excess of phenylboronic acid and potassium carbonate (K_2CO_3, used as base) at 75 °C, either in pure ethanol or in an aqueous ethanolic solutions ($EtOH/H_2O = 7/3$ v/v). Due to the low solubility of potassium carbonate in ethanol, reaction mixtures using pure ethanol appeared as suspensions, whereas the use of aqueous ethanol gave clear and colorless reaction solutions.

In general, $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$, $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$ and $Sn_{0.99}Pd_{0.01}O_{2-\delta}$ (change with tin proportions of 0.2, 0.79 and 0.99, respectively), showed extraordinarily high activities in all investigated Suzuki-Miyaura cross coupling reactions (up to TOF of >12,000 h^{-1} for the coupling of 4-bromoacetophenone with phenylboronic acid). The use of less than 0.05 mol% of active palladium led to a quantitative conversion of all *para*-substituted bromoarenes in less than two hours with aqueous ethanol as reaction solvent. Full conversion within 2 hours could also be reached using 2-bromobenzonitrile as aryl halide, however, 4 times more catalyst had to be used to achieve comparable reaction rates. $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$ also showed catalytic activity in all reactions, however significantly lower reaction rates were observed. The binary oxide $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ proved to be the least active catalyst in all investigated reactions except for the very fast reaction of phenylboronic acid with 4-bromoacetophenon. In this reaction, total conversion of the bromoarene substrate could be achieved within 30 minutes even when the less reactive catalyst 1 and 3 were used (whereby both catalysts showed comparable reaction rates). Suzuki reactions of 4-bromotoluene with phenylboronic acid over pure CeO_2 and pure SnO_2 did not show any progress, indicating that Pd is the active species in the investigated catalysts. All in all, at the current stage, our results do not show any direct context between Ce or Sn loading and catalytic activity. However, there might be a relation between the surface area, as well as the particle size and the catalytic activity: our results show that $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ has the lowest surface area and the lowest catalytic activity. The large particle size of $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$ might be the reason for its low activity. But these are just preliminary conclusions and more investigations are needed prove this theory.

In our studies we also investigated the influence of the solvents, bases and starting bromoarenes. As can be seen in **Table 7,** in all experiments, the use of aqueous ethanolic solvents instead of pure ethanol led to increased reaction rates, which can be attributed to the higher solubility of potassium carbonate in water containing alcoholic solvents. *p*-bromobenzenes containing electron withdrawing substituents showed higher reactivity than bromobenzenes containing electron donating groups. Regardless of the reaction solvent, the reactivity follows the order: 4-bromoacetophenone ≥ 4-bromobenzotrifluoride > 4-bromotoluene > 4-bromophenol.

The influence of different bases and solvent systems were investigated using the moderately fast reaction of 4-bromotoluene with phenylboronic acid catalyzed by $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$. The results of these tests are summarized in **Table 6**.

Table 6: Yields and selectivities after 120 minutes of reaction time observed by HPLC-measurements for the Suzuki cross-coupling reaction of phenylboronic acid with 4-bromotoluene[a]

Entry	Solvent (v/v ratio)	Base	Temperature [K]	Yield [%]	Selectivity [%]
1	$EtOH/H_2O = 7/3$	Na_2CO_3	353	32	97.1
2	$EtOH/H_2O = 7/3$	K_2CO_3	353	92	94.4
3	$EtOH/H_2O = 7/3$	Cs_2CO_3	353	81	96.2
4	$EtOH/H_2O = 7/3$	NaOH	353	88	94.6
5	$EtOH/H_2O = 7/3$	KOH	353	88	95.8
6	$EtOH/H_2O = 7/3$	NaOAc[b]	353	<1	-
7	$EtOH/H_2O = 7/3$	KOAc[b]	353	<1	-
8	$MeOH/H_2O = 7/3$	K_2CO_3	343	96	93.1
9	$i\text{-}PrOH/H_2O = 7/3$	K_2CO_3	353	>99	90.7
10	$n\text{-}PrOH/H_2O = 7/3$	K_2CO_3	353	5	93.5

[a] Reaction conditions: aryl bromide (0.7 mmol), phenylboronic acid (1.5. mol eq.), K_2CO_3 (1.5 mol eq.), 5 mg $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$ (corresponding to 0.05 mol% Pd), 20 ml of solvent.

[b] using 4 mol eq. of base

Although considerable reactivity could be observed using cesium carbonate, potassium hydroxide and sodium hydroxide as base, the often used potassium carbonate proved to be the optimal base when $EtOH/H_2O$ 7/3 (v/v) was used as solvent. The minor activity of the catalyst using sodium carbonate as base may be attributed to the low solubility of Na_2CO_3 in the applied solvent system. Only traces of the product 4-methylbiphenyl could be detected when the weak bases sodium acetate and potassium acetate were used.

A slight increase in catalytic activity with comparable selectivities could be achieved when 2-propanol (at 75 °C) and methanol (at 65°C) were used as alcoholic solvent instead of ethanol. The low product yield when 1-propanol was used can be attributed to the low capability of this system to dissolve highly polar inorganic bases. Taking ecological, toxicological and safety aspects into account 2-propanol/water mixtures may be considered as most practical solvent system for this reaction.

Selectivity

Using HPLC as analytical method, not only the disappearance of the arylbromide and the formation of the biphenyl-product were monitored, also the concentrations of possible side products were determined. Typically observed side products of Suzuki-Miyaura coupling reactions [23,24] are shown in **Figure 5.**

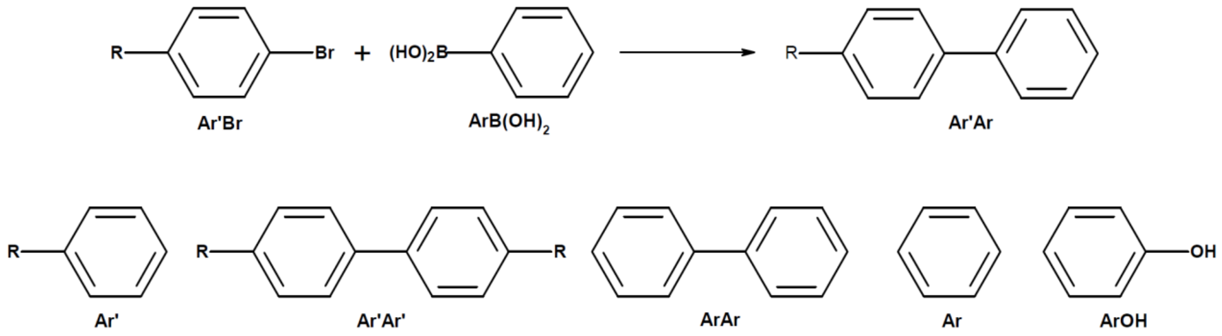


Figure 5: Main product (Ar'Ar) and typically observed side products in Suzuki-Miyaura cross coupling reactions.

Table 7: Yields and selectivities observed by HPLC-measurements for the Suzuki cross-coupling reactions of phenylboronic acid with various bromoarenes, using $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99) as catalyst.[a]

		Pure Ethanol				**EtOH/H_2O = 7/3**			
		15 Minutes		**120 Minutes**		**15 Minutes**		**120 Minutes**	
Product	**Cat[d]**	**Yield**	**Sel.**	**Yield**	**Sel.**	**Yield**	**Sel.**	**Yield**	**Sel.**
4-Methylbiphenyl	**1**	<1	-	<1	-	<1[b]	-	6	98.5
	2	31	92.8	75	90.7	9[b]	98.4	>99	91.4
	3	7	97.9	39	94.9	26	97.3	91	94.4
	4	39	92.7	89	88.0	77[b]	97.3	>99	91.9
	5	48	96.4	85	93.6	82[b]	96.7	98	92.3
4-Phenylphenol	**1**	<1	-	10	96.0	2[b]	-	45	95.3
	2	41	92.2	77	89.1	50[b]	94.0	>99	84.6
	3	7	97.1	34	92.5	23[b]	96.4	80	93.7
	4	44	94.1	93	90.3	30[b]	95.6	97	91.0
	5	31	97.0	70	93.1	69	95.8	>99	91.9
4-Acetylbiphenyl	**1**	7	-	85	99.7	55[b]	99.8	>99	88.4
	2	96	-	>99	96.9	>99[b]	97.7	>99	87.1
	3	53	-	98	98.6	38[b]	99.8	>99	93.3
	4	98	99.6	>99	95.9	98[b]	95.9	>99	85.9
	5	96	99.7	>99	98.2	98[b]	94.7	>99	90.0
4-Trifluoromethylbiphenyl	**1**	<1	-	2	-	<1	-	2	-
	2	20	99.0	88	97.5	95	97.8	>99	87.3
	3	3	-	53	98.3	29	98.8	99	92.7
	4	53	98.2	98	92.1	94	95.3	>99	81.6
	5	61	97.6	97	92.5	>98	92.2	>98	80.3
2-Biphenylcarbonitrile[c]	**1**	<1	-	<1	-	<1	-	2	-

2	78	99.6	>99	89.5	38	98.8	>99	98.4
3	9	-	20	99.6	6	-	29	98.5
4	68	99.7	>99	83.1	74	99.0	>99	83.3
5	64	99.8	>99	83.0	66	98.9	>99	88.7

[a] Reaction conditions: aryl bromide (0.7 mmol), phenylboronic acid (1.5. mol eq.), K_2CO_3 (1.5 mol eq.), 5 mg $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (corresponding to 0.05 mol% Pd), 20 ml of solvent, 75 °C.

[b] After 10 minutes

[c] Using 20 mg of catalyst (0.2 mol% Pd)

[d] **Cat 1:** $Ce_{0.99}Pd_{0.01}O_{2-\delta}$, **Cat 2:** $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$, **Cat 3:** $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$, **Cat 4:** $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$, **Cat 5:** $Sn_{0.99}Pd_{0.01}O_{2-\delta}$.

The obtained selectivities are closely related to the catalyst's activity in our calculations. This can be illustrated comparing the concentration profiles and selectivities during the cross-coupling reactions of phenylboronic acid with 2-biphenylcarbonitrile using $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$, respectively (**Figure 6**).

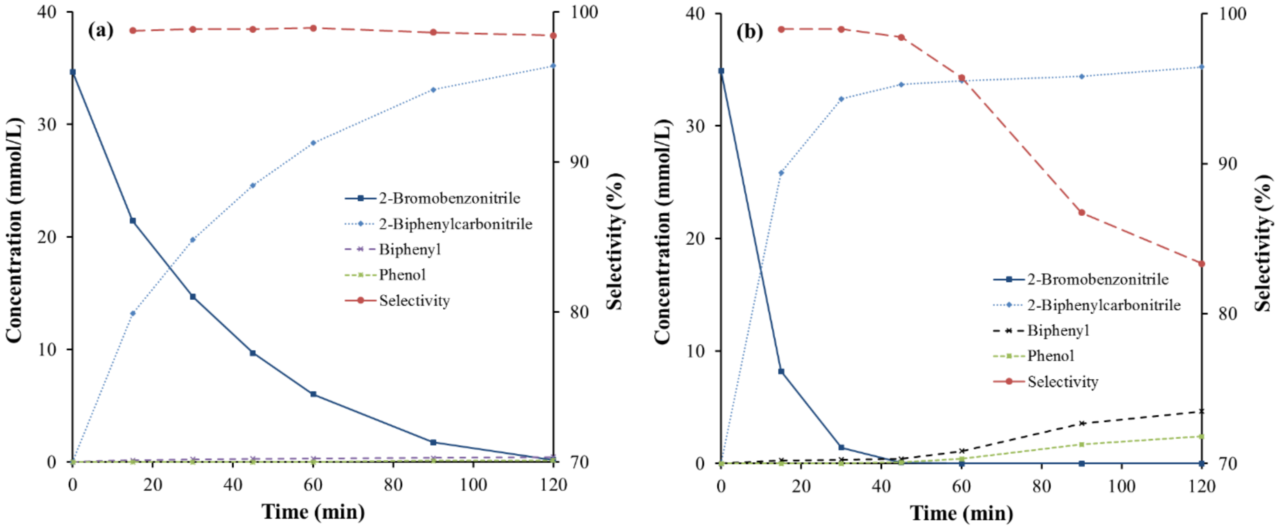


Figure 6: Concentration profiles for the reaction of 2-bromobenzonitrile and phenylboronic acid catalyzed by (a) $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ and (b) $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$.

When full conversion of the starting halide is reached, the values for selectivity are equally high in both reactions (98.4 % after 120 and 45 minutes for $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$ respectively). The side product biphenyl and phenol are formed predominantly at high conversion levels, i.e., in the absence of the already consumed reaction partner 2-bromobenzonitrile. Hence, highly selective reactions can be achieved by termination of the reaction just at the moment of full conversion, even when a high excess of phenylboronic acid is used.

3.3 Recyclability and Pd-leaching

Table 8 and **Figure 7** show the observed relative conversions of 4-bromotoluene after 30 and 120 minutes reaction time, as well as the recoverability of the used solid catalyst in mass percent (**Table 8)**. Detailed diagrams of the obtained conversion vs. time are shown in the supporting information. Using 0.5 mol% Pd, full conversion after 2 hours could be achieved in five subsequent reactions, when the tin-containing catalysts (x = 0 – 0.99) were used, despite a significant loss of catalysts during the whole recycling procedure (filtration and drying). Using $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$, full conversion of 4-bromotoluene within two hours could not be reached in run 4 and 5. However, comparison of the initial reaction rates and the whole reaction progress with the results of the reactivity test shows only minor decrease of the mass specific catalyst activity. A similar recycling behavior could be observed for $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ at a lower activity level.

Table 8: Results of the recycling experiments for the Suzuki-Miyaura reaction of 4-bromotoluene with phenylboronic acid.

			Run 1	Run 2	Run 3	Run 4	Run 5
$Ce_{0.99}Pd_{0.01}O_{2-\delta}$	Conversion [%]	30 min	13	50	25	16	8
		120 min	78	91	81	69	49
	Recoverability [%]		84	70	55	43	33
$Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$	Conversion [%]	30 min	100	100	99	99	98
		120 min	100	100	100	100	100
	Recoverability [%]		88	76	68	68	60
$Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$	Conversion [%]	30 min	100	94	89	81	76
		120 min	100	100	100	98	97
	Recoverability [%]		81	68	58	48	38
$Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$	Conversion [%]	30 min	100	100	99	100	98
		120 min	100	100	100	100	100
	Recoverability [%]		81	66	50	45	32
$Sn_{0.99}Pd_{0.01}O_{2-\delta}$	Conversion [%]	30 min	100	100	100	100	96
		120 min	100	100	100	100	100
	Recoverability [%]		81	68	54	40	32

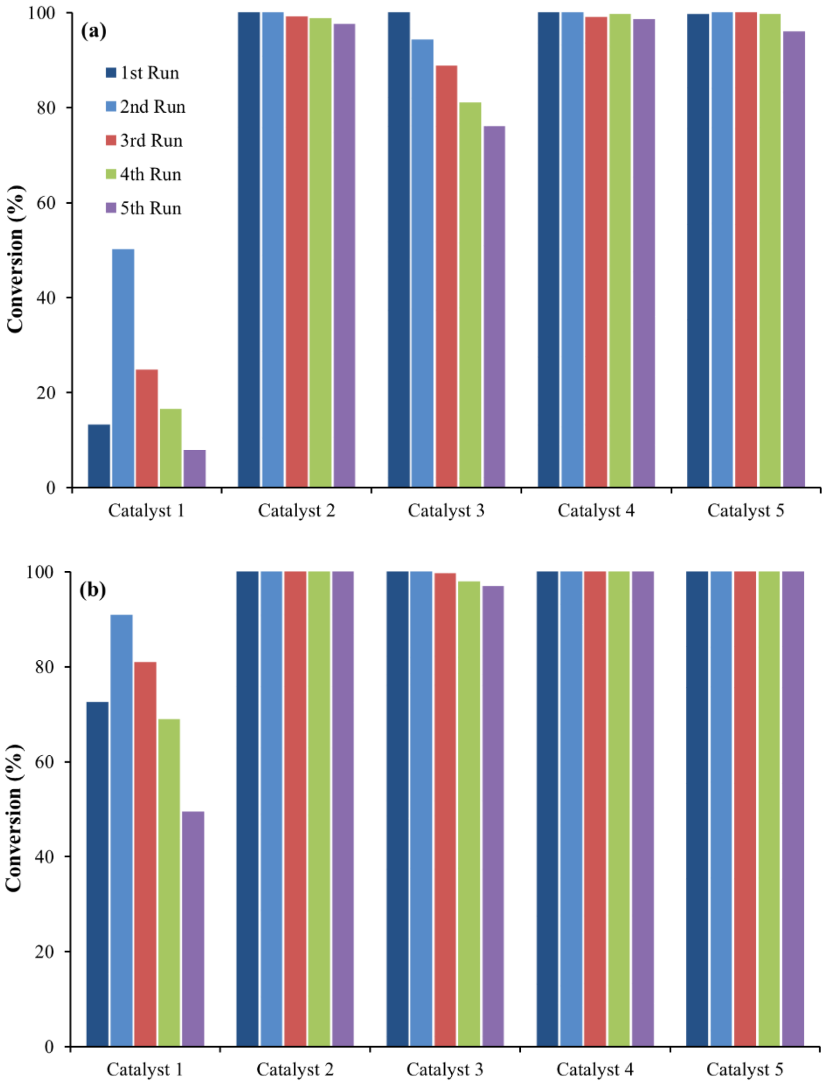


Figure 7: Observed conversions after 30 (a) and 120 minutes (b) for the Suzuki-coupling of 4-bromotoluene with phenylboronic acid in 5 subsequent runs using 0.5 mol% Pd. Cat 1: $Ce_{0.99}Pd_{0.01}O_{2-\delta}$, Cat 2: $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$, Cat 3: $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$, Cat 4: $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$, Cat 5: $Sn_{0.99}Pd_{0.01}O_{2-\delta}$.

To investigate the leaching behaviour of the catalysts, the catalyst was filtered off after each reaction cycle and washed with water and ethanol. The combined reaction and washing solutions were evaporated under reduced pressure and the remaining solids were analyzed for their palladium content by means of ICP-MS. When $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$ were used as catalysts, the palladium contents were determined after each run. Due to the good reproducibility of the results (0.08 ± 0.01 mg/L and 0.15 ± 0.02 mg/L for $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$, respectively) the Pd content in the reaction solutions was determined representatively for run 3 for all other catalysts.

Table 9 shows the obtained Pd-concentrations in the remaining solids as well as the corresponding palladium concentration in solution, represantively for run 3.

Table 9: Pd-contents of the residual solids and corresponding Pd-concentrations in solution for the 3rd reaction

Catalyst	Pd in remaining solids [mg/kg] after 3rd run	Pd in solution [mg/L] after 3rd run
$Ce_{0.99}Pd_{0.01}O_{2-\delta}$	5.0	0.06
$Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$	6.7	0.09
$Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$	5.3	0.07
$Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$	10.0	0.13
$Sn_{0.99}Pd_{0.01}O_{2-\delta}$	11.0	0.14

Figure 8 shows a comparison of the initial reaction rates (expressed as turnover frequencies after 15 minutes reaction time) and the amount of palladium in solution for the third recycling run (catalysts are ordered according to increasing activity). The results demonstrate an apparent correlation between reactivity and amount of leached palladium and support the thesis, that the coupling reaction is actually catalyzed by small amounts of leached palladium via a homogeneous reaction mechanism. Amoroso *et al.* [12] described a sigmoidal shape of the temporal conversion profile for Suzuki-couplings using Pd/CeO_2 catalysts and attributed this finding to an induction time period of the reaction due to the formation of dissolved palladium species, acting as true catalytically active species. Sigmoidal conversion profiles also could be observed in this study in moderately fast reactions, not only for $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ but also for the tin containing catalysts. **Figure 9** illustrates such sigmoidal profiles for the reaction of 4-bromotoluene with phenylboronic acid catalyzed by $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$, respectively.

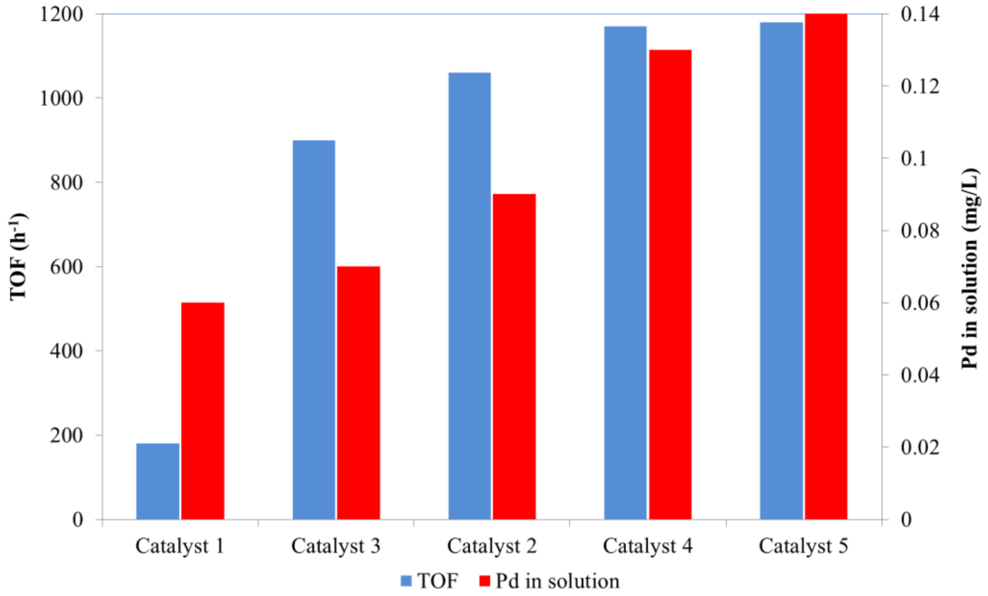


Figure 8: TOF (after 15 minutes) vs. Pd-concentration in solution (mg/L) for the third recycling experiment.

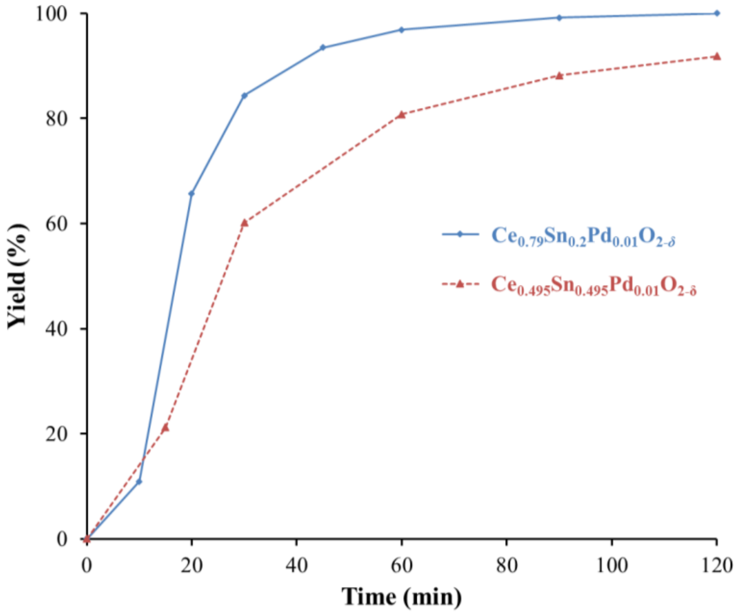


Figure 9: Sigmoidal profile of the reaction progress for the coupling reaction of 4-bromotoluene with phenylboronic acid using $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$.

The results of the recycling tests agree very well with the findings of other studies using Pd-doped metal oxides as precatalysts, and substantiate the hypothesis, that the precatalysts act as palladium reservoir, that slowly releases extremely reactive palladium species [11,12]. The successful recycling of the catalysts might be attributed to a Pd release/capture mechanism, which was not only proposed for Pd on metal oxides [11,12] but also for a wide variety of Pd catalysts on different solid supports [25–28].

In a second recycling series, the catalysts were used for 3 Suzuki reactions in the same manner and afterwards characterized by means of XRD (**Figure 10**). The XRD-patterns of the used catalysts reveal intact fluorite structures of the cerium rich catalysts, $Ce_{0.99}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$ respectively, a crystalline mixed phase structure of the mixed oxides $Ce_{0.495}Sn_{0.495}Pd_{0.01}O_{2-\delta}$ and $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$ and the remaining tetragonal structure of the binary oxide $Sn_{0.99}Pd_{0.01}O_{2-\delta}$. These findings prove the high stability of the produced catalysts at the applied reaction conditions. Also in the used catalysts, patterns attributable to Pd (111) could not be observed, which confirms the absence of PdO or segregated Pd metal species.

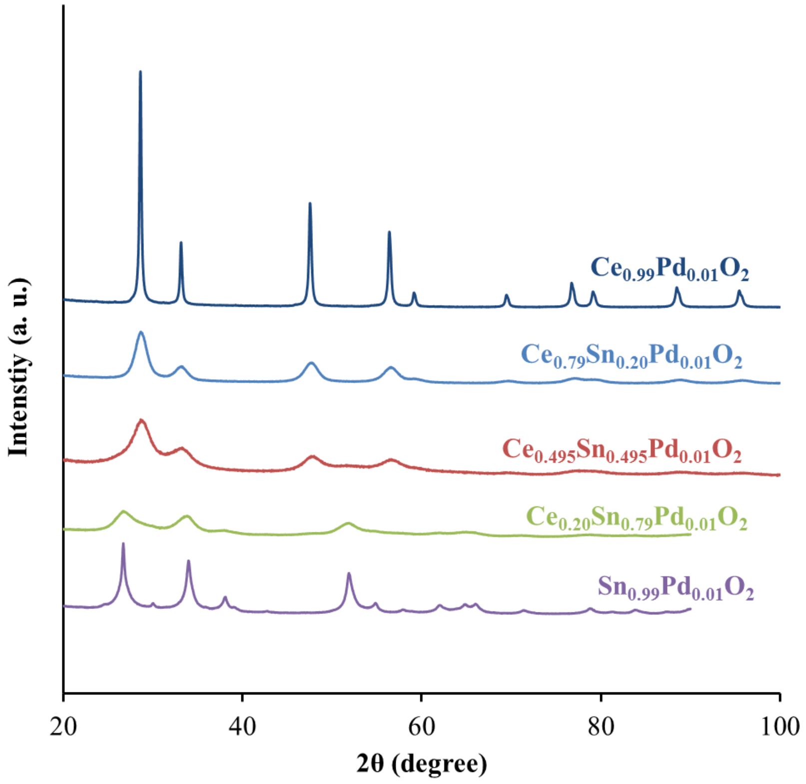


Figure 10: X-Ray diffraction pattern of three times used $Ce_xSn_{1-x}Pd_{0.01}O_{2-\delta}$ (x = 0 – 0.99)

3.4. Heterogeneity studies

In order to get more insight in the homo- or heterogeneous nature of the novel catalysts, we carried out further tests, including the hot filtration test and catalyst poisoning.

3.4.1 Hot filtration test

An often applied test to determine the heterogeneity of a system is the so called hot filtration test. After a certain reaction time, the solid catalyst is removed from the reaction solution by filtration through a hot filter (filter frit or filter crucible). The subsequent reaction progress in the remaining reaction solution without solid catalyst is monitored over time. In our study, this test was performed for all produced catalysts employing the Suzuki cross-coupling reaction of 4-bromotoluene with phenylboronic acid in ethanol/water = 7/3 v/v. Based on the results of the reactivity test, the amount of catalyst and the moment of filtration were chosen in such a way that the obtained conversions of 4-bromotoluene was in the range between 25 and 80 percent. The results of the hot filtration tests are depicted in **Figure 11.**

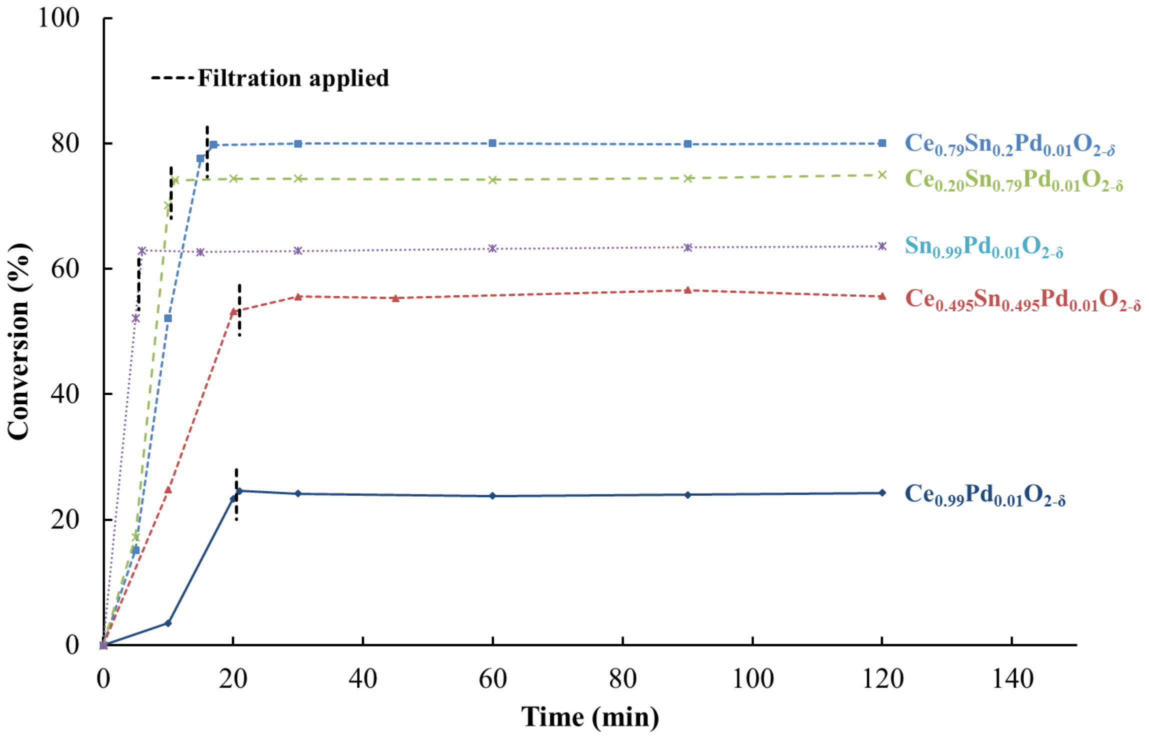


Figure 11: Results of the hot filtration test employing the Suzuki-Miyaura cross-coupling reaction of 4-bromotoluene and phenylboronic acid

In all experiments, the removal of the catalyst by filtration led to a complete stop of the conversion of 4-bromotoluene to 4-methylbiphenyl, although all required reaction participants remained in solution (which was confirmed by HPLC-analysis). This could lead to the assumption, that the reaction is catalyzed by an insoluble catalyst in a heterogeneous manner and there is no catalytic activity of the compounds in the solution after filtration. However, it is known that hot filtration tests are rather problematic for the precise distinction between homogeneous and heterogeneous catalysis [29], since catalytically active leached metal can redeposit on the catalyst very quickly during filtration and may not be detected by a filtration test. Furthermore, massive interruptions in the reaction process (such as filtration) can deactivate dissolved metal species. Thus, more reliable methods for the determination of the homogeneous or heterogeneous nature of metal catalyzed reactions, including three-phase-tests [30] and catalyst poisoning tests [31] have been developed.

3.4.1 Catalyst poisoning

According to Jones *et al.* [31], the catalyst poisoning test represents one of the most potential methods to distinguish between homogeneous and heterogeneous catalytic systems. During this test, materials, which are known to act as selective catalyst poisons for dissolved palladium, are added to the reaction mixtures. Frequently used poisons for palladium catalyzed cross-coupling reactions include Quadrapure TU (polymeric resin), poly(4-vinylpyridine) (PVPy) and 3-mercaptopropyl functionalized silica gel (MPSG) [29]. The addition of such materials leads to the removal of soluble reactive metal from the reaction solution and would lead to a suppression of a further reaction progress in a homogeneously catalyzed reaction.

In this work, we used 3-mercaptopropyl functionalized silica gel (MPSG, 100 molecular equivalents of SH-groups with respect to the employed amount of palladium) as selective catalyst poison for the reaction of 4-bromotoluene with phenylboronic acid in ethanol/water = 7/3 v/v (at the same reaction conditions as in the hot filtration test). The complete suppression of the reaction after addition of the catalyst poison (**Figure 12**) strongly indicates a homogeneous reaction mechanism via dissolved palladium species. Although the good recyclability of the catalysts and the results of the hot filtration test seemingly suggest a heterogeneous reaction mechanism, the findings of the catalyst poisoning experiments, the sigmoidal profile of the reaction progress and the low but detectable amount of palladium in the filtered reaction solution strongly support the above mentioned thesis, that the produced oxides act as precatalysts and release extremely reactive palladium species, which represent the true catalytically active species. Further studies to get more inside in the reaction mechanism will be carried out in the near future.

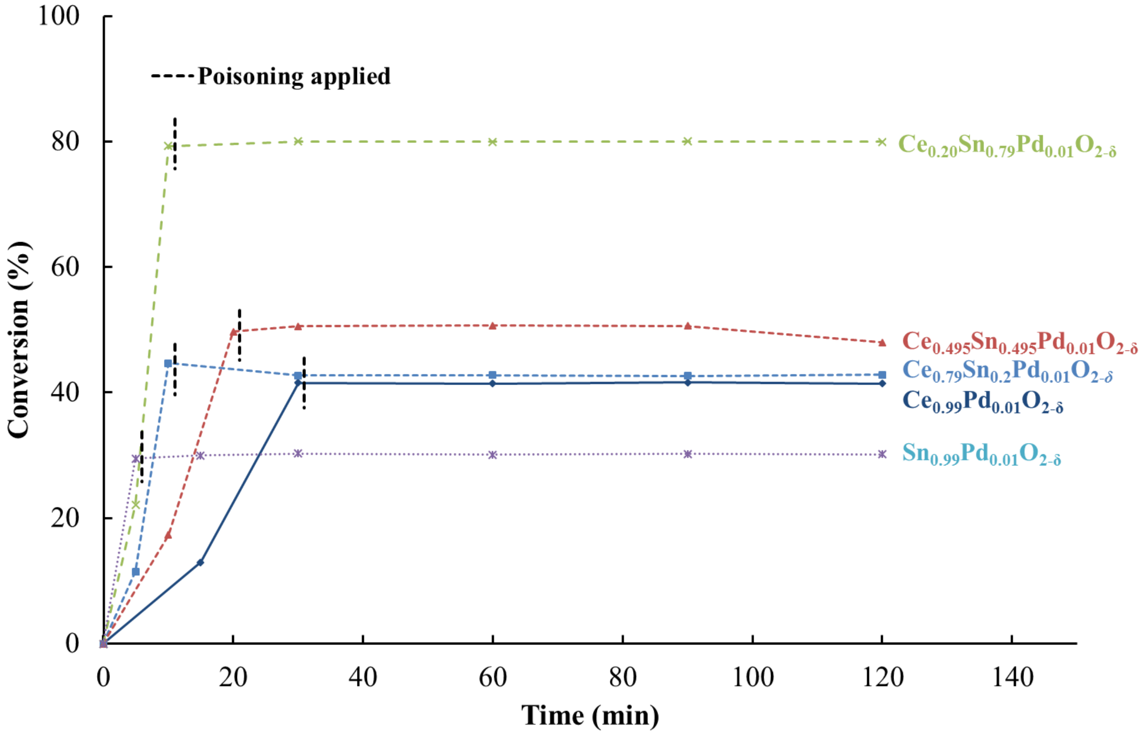


Figure 12: Catalyst poisoning test employing mercaptopropyl functionalized silica gel in the Suzuki-Miyaura cross-coupling reaction of 4-bromotoluene and phenylboronic acid

4. Conclusions

Palladium substituted CeO_2, SnO_2 and their mixed oxides proved to be efficient catalysts for Suzuki-Miyaura cross-coupling reactions. The synthesis of the oxides via a one-step solution combustion method represents a further simplification of rapid and inexpensive preparation strategies, such as sol-gel methods or wet impregnation techniques. In general, tin containing catalysts proved to be clearly more catalytically active than previously reported binary cerium-palladium oxides. Especially, the mixed oxides $Ce_{0.79}Sn_{0.2}Pd_{0.01}O_{2-\delta}$, $Ce_{0.20}Sn_{0.79}Pd_{0.01}O_{2-\delta}$ and $Sn_{0.99}Pd_{0.01}O_{2-\delta}$ showed extraordinarily high activities for the coupling of various bromoarenes with phenylboronic acid, although a direct relation between cerium or tin content and activity could not be found. The best performing catalysts could be reused for at least five subsequent Suzuki-Miyaura reaction, yielding full conversion of the bromoarene-substrate within two hours while releasing only minimal amounts of palladium into the reaction solution. Nevertheless, the presence of low amounts of palladium in solution, as well as sigmoidal profiles of the reaction progress substantiate the thesis, that the as prepared mixed oxides act as precatalysts, which release small amounts of dissolved palladium, the truly catalytically active species. The good recyclability of the catalysts can be explained plausibly by a palladium release/capture mechanism proposed for palladium on metal oxides or other solid supports.

The Suzuki-Miyaura reactions were performed in aqueous alcoholic mixtures. Such solvent systems are capable of dissolving a wide variety of Suzuki-Miyaura cross-coupling educts and products and the obligate inorganic bases. The good recyclability and high leaching resistance in such homogeneous reaction mixtures indicates a high potential of the prepared catalysts for the use in continuous-flow operations, for example in fixed bed reactors.

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