A Highly Active and Reusable Catalyst for Suzuki Coupling: $BaCe_{1-x}Pd_xO_{3-x}$ ($0 < x \leq 0.1$)

Xiaoying Ouyang[1], Jun Li[2,3], Ram Seshadri[1,2,3], Susannah L. Scott[1,4]

[1]Department of Chemistry and Biochemistry, [2]Materials Department, [3]Materials Research Laboratory, and [4]Department of Chemical Engineering
University of California, Santa Barbara, CA, 93106

sscott@engineering.ucsb.edu

Abstract

A catalyst consisting of $BaCeO_3$ perovskite with low levels of substitution of Pd(II) on the *B* (i.e., Ce) site and a corresponding number of oxygen vacancies was prepared by a high-temperature synthesis method. The $BaCe_{1-x}Pd_xO_{3-x}$ phase extrudes nanoparticles of *fcc*-Pd when heated in a reducing atmosphere. The oxidized form of the Pd-doped perovskite is highly active for the Suzuki coupling of aryl bromides and iodides with 4-phenylboronic acid (TOF ca. 50,000 at 80 °C), provided the solvent system contains 2-propanol. The alcohol is suggested to be a reducing agent for Pd(II), extracting ligand-free Pd(0) from the perovskite into solution. The fully reduced form of the perovskite is a poor catalyst, because of the inaccessibility of the Pd(0). A lower level of cationic Pd substitution in the oxidized phase is associated with a shorter induction period, corresponding to less required reorganization of the remaining perovskite upon extraction of Pd. The catalyst showed little decline in activity after being recycled seven times, suggesting that the perovskite may recapture Pd(II) from the reaction medium. The concentrations of soluble Pd before and after the reaction are also consistent with its dissolution/re-absorption: the Pd level decreased over the course of the reaction, and was undetectable (< 0.1 ppm) at the end.

Introduction

Supported versions of homogeneous catalysts have been studied intensively over the last two decades. In practical terms, solid catalysts facilitate separation from the reaction medium, enabling their recovery and reuse. Consequently, less precious metal is consumed, which is advantageous both economically and environmentally. The search for “green” palladium catalysts for C-C bond-forming processes, such as the Suzuki, Heck and Sonogashira reactions, is motivated by these reasons, as well by the need to minimize residual Pd in the product. A large number of “heterogeneous” catalysts for Suzuki coupling reactions have been reported, including Pd supported on carbon (1), silica (2), polymers (3) and dendrimers (4). A family of unsupported heterogeneous Pd-containing perovskite catalysts has also been reported (5, 6). Most Pd-containing heterogeneous catalysts show much lower catalytic activities than homogeneous C-C couping catalysts, and many (perhaps all) involve the formation of soluble Pd during the catalytic cycle (7). Thus removal residual Pd at the end of the reaction remains a problem.

In this contribution, we describe a novel, low surface area (ca. 1 m^2/g) $BaCe_{1-x}Pd_xO_{3-x}$ perovskite catalyst for Suzuki coupling reactions. Recently, we showed that $BaCeO_3$ can incorporate low levels of Pd(II) on the *B* (Ce) sites, and that this Pd moves out of and back into the perovskite lattice in response to heating under reducing (5 % H_2/95 % N_2) or oxidizing (pure O_2) conditions, respectively, based on the reversible change in cell volume observed by XRD during redox cycling, and the appearance and disappearance of reflections due to *fcc*-Pd (8, 9). The XPS spectrum of oxidized $BaCe_{1-x}Pd_xO_{3-x}$ ($x = 0.05, 0.10$) shows that essentially all of the near-surface Pd is present in cationic form. When reduced, the XPS signals due to cationic Pd are completely suppressed, but the signals due to Pd(0) do not become appreciably more intense. This surprising observation was interpreted as overgrowth of the metal nanoparticles by $BaCeO_3$. Reoxidation of *fcc*-Pd/$BaCeO_3$ resulted in the reappearance of XPS signals corresponding to cationic Pd, confirming that the metal is reabsorbed as Pd(II) into the perovskite lattice (8, 9).

Experimental Section

Synthesis of $BaCe_{1-x}Pd_xO_{3-x}$. $BaCe_{1-x}Pd_xO_{3-x}$ was prepared by grinding together BaO_2 (99 %, Cerac), CeO_2 (99.9 %, Cerac), and PdO (99.95 %, Cerac) in their stoichiometric ratios (1 : 1-*x* : *x*), pelletizing the ground powders, and heating them in flowing O_2 at 1000 °C for 10 h. BaO_2 was chosen as the Ba source because it is less hygroscopic than BaO, and more easily decomposed than $BaCO_3$. The pellet was then reground, pelletized, and heated for another 10 h at 1000 °C in flowing O_2. This fresh sample is called "as-prepared", and has a BET surface area of ca. 1 m^2/g. Reduction of as-prepared $BaCe_{1-x}Pd_xO_{3-x}$ was carried out in flowing 5 % H_2/95 % N_2 at 1000 °C for 1 h, as previously described (8). This treatment causes complete reduction of Pd(II) to Pd(0). Reoxidized $BaCe_{0.95}Pd_{0.05}O_{2.95}$ was prepared by reoxidation of the reduced material in flowing O_2 at 1000 °C for 10 h. None of these treatments affect the BET surface area appreciably.

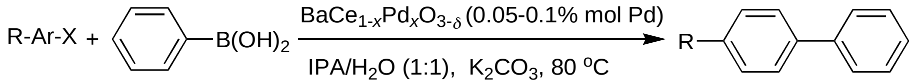
General procedure for Suzuki coupling. 4-Bromoanisole (125 µL, 1 mmol), phenylboronic acid (186 mg, 1.5 mmol), K_2CO_3 (0.55 g, 4 mmol) and the $BaCe_{1-x}Pd_xO_{3-x}$ catalyst were mixed in a 20 mL scintillation vial. A preheated 2-propanol/water solution (IPA/H_2O, 1:1 v/v, 12 mL, 80 °C) was added, the vial was immediately placed on a hot plate stirrer and its temperature was maintained at (80 ± 1) °C. The reaction mixture was stirred at 1000 rpm for 3 min, then cooled to room temperature. The 4-methoxybiphenyl product was extracted with diethyl ether (3 × 15 mL). The organic fractions were washed with deionized water and dried with $MgSO_4$. After filtration, volatiles were removed under reduced pressure to yield the isolated product.

To promote phase transfer in the toluene/H_2O solvent system, 1 drop of Aliquat® 336 (tricaprylmethylammonium chloride, Aldrich) was added. For kinetic studies, aliquots (0.1 mL) were withdrawn by syringe at timed intervals (20 – 360 s) and immediately diluted with 0.2 mL aqueous HCl to quench the reaction. The acid-quenched mixtures were extracted with C_6D_6, and the organic phase was subjected to analysis by ^{1}H NMR. For the recycling study, the reaction mixture was prepared according to the method described above. At the end of the reaction, it was cooled to room temperature and diluted with 10 mL acetone to dissolve the solid, organic product. The liquid phase was removed carefully by syringe. Solid $BaCe_{1-x}Pd_xO_{3-x}$ remaining in the scintillation vial was washed with diethyl ether, dried and reused in subsequent reactions.

Analysis of soluble Pd by ICP. A series of reactions was initiated according to the procedure described above. After 20 s, 1 min, 3 min or 1 h, the hot reaction mixture was passed quickly through a 0.45 μm syringe filter to remove solid $BaCe_{1-x}Pd_xO_{3-x}$, then the solvent was removed under reduced pressure. A mixture of $BaCe_{1-x}Pd_xO_{3-x}$ and K_2CO_3 in IPA/H_2O, heated at 80 °C for 1 h, was subjected to the same workup procedure. Each of the solid residues was suspended in 12 mL 10 M aqueous HCl. The mixtures were filtered to produce clear solutions for subsequent analysis on a Thermo Jarrell Ash (TJA) High Resolution ICP spectrometer. A ICP standard solution of Pd (Aldrich) was diluted to 10 ppm for use as the high standard.

Results

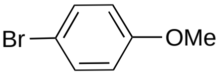
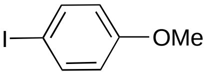
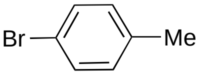
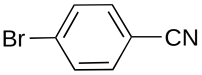
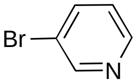
Suzuki coupling reactions with aryl halides. Two as-prepared $BaCe_{1-x}Pd_xO_{3-x}$ materials ($x = 0.05$ and 0.10) were successfully utilized in several Suzuki coupling reactions. Both aryl iodides and aryl bromides react smoothly with 4-phenylboronic acid, eq 1, to yield the corresponding biaryls in high yields (≥ 95%). For both 4-bromoanisole and 4-iodoanisole, the biaryl yields reached nearly 100 % in 3 min with $BaCe_{0.95}Pd_{0.05}O_{3-\delta}$ as the catalyst, corresponding to an effective TON of ca. 2,000 and an effective TOF of nearly 50,000 h^{-1}. Results are summarized in Table 1.



(1)

Kinetic analysis. The kinetics of Suzuki coupling were investigated and compared for $BaCe_{0.95}Pd_{0.05}O_{2.95}$ and $BaCe_{0.90}Pd_{0.10}O_{2.90}$. The results are shown in Figure 1a. The reaction between 4-bromoanisole and 4-phenylboronic acid catalyzed by $BaCe_{0.95}Pd_{0.05}O_{2.95}$ shows no induction period. However, a short but measurable induction period (< 1 min) was observed with $BaCe_{0.90}Pd_{0.10}O_{2.90}$. The biaryl yield reached 100 % after 160 s for $BaCe_{0.95}Pd_{0.05}O_{2.95}$, and after 240 s for $BaCe_{0.90}Pd_{0.10}O_{2.90}$.

Table 1 Suzuki couplings catalyzed by $BaCe_{1-x}Pd_xO_{3-x}$ (x = 0.05, 0.10) [a]

entry	substrate	x	reaction time min	isolated yield (%)	TON [c]	TOF [c] h^{-1}
1		0.05	2.7	95 (100) [b]	2,045	45,400
		0.10	4.0	95 (100) [b]	1,015	15,225
2		0.05	2.5	96 (100) [b]	2,070	49,680
3		0.05	3.0	98	2,110	42,200
4		0.05	3.0	96	2,070	41,400
5		0.05	3.0	95	2,045	40,910

[a] Reagents and conditions: 3.0 mg $BaCe_{1-x}Pd_xO_{3-\delta}$ (0.05 mol % Pd, x = 0.05; 0.10 mol % Pd, x = 0.10), 1.0 mmol aryl halide, 1.5 mmol $PhB(OH)_2$, 4.0 mmol K_2CO_3, 12 mL IPA-H_2O (1:1, v/v), 80 °C. [b] Estimated by ^1H NMR. [c] The TON and TOF effective values, based on the total Pd introduced with the perovskite catalyst.

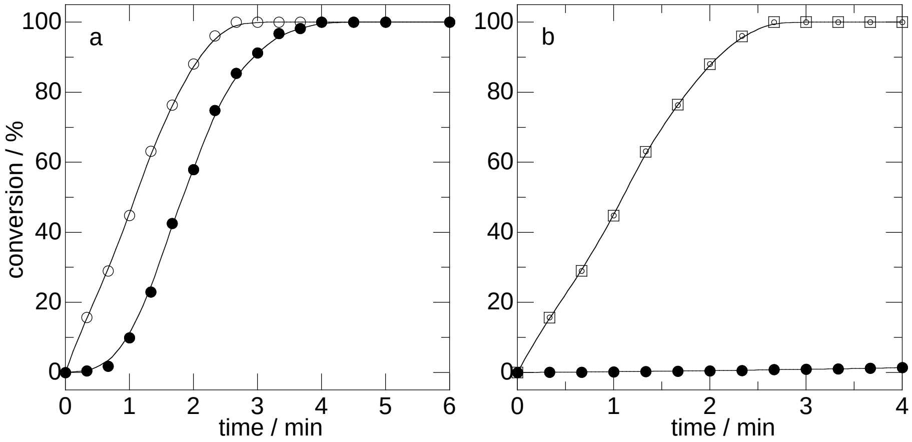


Figure 1 Kinetic profiles for the coupling of 4-bromoanisole with phenylboronic acid to yield 4-bromonaphthalene, (a) using as-prepared $BaCe_{0.95}Pd_{0.05}O_{2.95}$ (open circles) or $BaCe_{0.90}Pd_{0.10}O_{2.90}$ (filled circles) as the catalyst; and (b) using $BaCe_{0.95}Pd_{0.05}O_{2.95}$ as-prepared (small open circles); reduced (filled circles); and reoxidized (open squares) as the catalyst. Reagents and conditions: 3.0 mg catalyst (0.05 mol % Pd, x = 0.05; 0.10 mol % Pd, x = 0.10), 1.0 mmol 4-bromoanisole, 1.5 mmol $PhB(OH)_2$, 4.0 mmol K_2CO_3, 12 mL IPA-H_2O (1:1, v/v), 80 °C. Lines are drawn only to guide the eye.

Similar kinetic experiments were carried out to compare the activities of the fully oxidized and fully reduced forms of $BaCe_{0.95}Pd_{0.05}O_{2.95}$, Figure 1b. The activity of the reduced catalyst is much lower than that of the as-prepared (i.e., oxidized) catalyst, resulting in only 2 % yield after 4 min. However, high activity is completely restored upon reoxidation of the reduced catalyst.

Analysis of soluble Pd. To assess the amount of "ligand-free" soluble Pd present in the reaction mixture, the solution containing 4-bromoanisole/4-phenylboronic acid reaction and $BaCe_{0.95}Pd_{0.05}O_{2.95}$ was filtered after 20 s, 1 min, 3 min and 1 h, and the filtrate subjected to ICP analysis. In addition, ICP analysis of Pd was performed on a mixture of $BaCe_{0.95}Pd_{0.05}O_{2.95}$ and K_2CO_3 in IPA/H_2O, in order to verify whether Pd dissolution occurs only in the presence of the aryl halide. Interestingly, although the Pd levels before, during and after the reaction were all rather low (< 0.2 ppm), the Pd content was highest in the absence of substrate. It decreased progressively during the reaction until it eventually became undetectable (< 0.05 ppm), Figure 2.

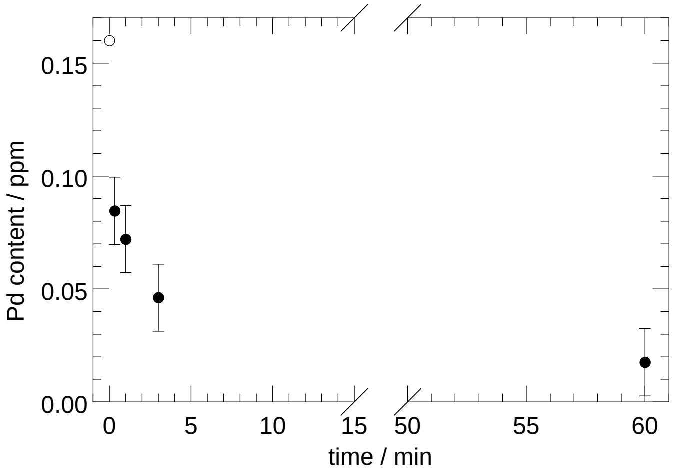


Figure 2 Analysis of soluble Pd from $BaCe_{0.95}Pd_{0.05}O_{2.95}$ by ICP, as a function of reaction time (reagents and conditions: 3.0 mg $BaCe_{0.95}Pd_{0.05}O_{2.95}$ (0.05 mmol Pd), 4 mmol K_2CO_3, 1.0 mmol 4-bromoanisole, 1.5 mmol $PhB(OH)_2$, 12 mL IPA-H_2O (1:1, v/v), 80 °C). The measurement for t = 0 min corresponds to the catalyst stirred with K_2CO_3 in IPA/H_2O (i.e., in the absence of the aryl halide) at 80 °C for 1 h.

Maitlis' filtration test. To investigate whether the Pd-doped perovskite is the actual catalyst, or a reservoir of soluble Pd, a Maitlis' filtration test (10) was performed. The reaction of 4-bromoanisole with 4-phenylboronic acid, catalyzed by $BaCe_{0.95}Pd_{0.05}O_{2.95}$, was interrupted at 20 s and 1 min, corresponding to conversions of 16 and 45 %, respectively, by filtering the hot reaction mixture to remove the solid perovskite. The filtrates were allowed to cool to room temperature without stirring. After 3 h, the biaryl yields in both samples were estimated to be 100 % by ^1H NMR.

Solvent effect. Several different solvent systems were investigated for the coupling of 4-bromoanisole with 4-phenylboronic acid catalyzed by $BaCe_{0.95}Pd_{0.05}O_{2.95}$. The results are summarized in Table 2. A phase-transfer catalyst (Aliquat® 336) was added in the experiment involving toluene/H_2O. However, only the IPA/H_2O solvent system was effective, resulting in a biaryl yield of 100 %; all other solvents gave rather low yields.

Table 2 Effect of solvent system on Suzuki coupling[a] catalyzed by $BaCe_{0.95}Pd_{0.05}O_{3-\delta}$

solvent	additive	time (h)	yield (%)
IPA/H_2O (1:1, v/v)	-	30	100 [b]
THF/H_2O (1:1, v/v)	-	30	20 [c]
$^tBuOH/H_2O$ (1:1, v/v)	-	30	5 [b]
toluene/H_2O (1:1, v/v)	Aliquat® 336 [d]	30	5 [b]
toluene	-	30	trace [b]

[a] Reagents and conditions: 3.0 mg $BaCe_{0.95}Pd_{0.05}O_{3-\delta}$ (0.05 mol % Pd), 1.0 mmol 4-bromoanisole, 1.5 mmol $PhB(OH)_2$, 4.0 mmol K_2CO_3, 12 mL solvent, 80 °C. [b]Estimated by ^1H NMR. [c] Estimated by GC-MS. [d]One drop of the neat liquid.

Catalyst recycling. The solid Pd-doped perovskite catalysts are easily filtered from the reaction mixture for reuse. The activity of the recycled $BaCe_{0.95}Pd_{0.05}O_{2.95}$ catalyst was investigated in the coupling of 4-bromoanisole with 4-phenylboronic acid. The results in Table 3 show that high activity was retained even after seven cycles of catalyst use.

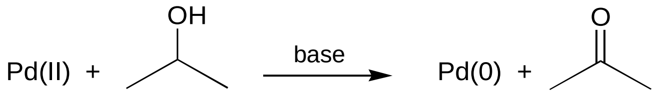
Table 3 Effect of recycling the $BaCe_{0.95}Pd_{0.05}O_{3-\delta}$ catalyst, on yields in Suzuki coupling [a]

cycle	time (min)	yield (%) [b]
1	5	100
2	5	100
3	5	100
4	5	98
5	5	100
6	5	98
7	5	99

[a] Reagents and conditions: 3.0 mg $BaCe_{0.95}Pd_{0.05}O_{2.95}$ (0.05 mol % Pd), 1.0 mmol 4-bromoanisole, 1.5 mmol $PhB(OH)_2$, 4 mmol K_2CO_3, 12 mL IPA-H_2O (1:1, v/v), 80 °C. [b] Estimated by ^1H NMR.

Discussion

Formation of the active sites. The results of the Maitlis' filtration test suggest that the active sites for the Suzuki coupling reaction are soluble, "ligand-free" Pd species, rather than Pd present on the solid surface of the perovskite. This is consistent with many previous studies of "heterogeneous" Pd catalysts which act by leaching Pd into solution (7). Furthermore, the requirement for IPA in the solvent system and the observation by ICP of soluble Pd in the absence of the aryl halide substrate suggest that the active site is extracted from the solid reservoir via a reaction with the solvent. According to XPS, only Pd(II) is present on the surface of $BaCe_{0.95}Pd_{0.05}O_{2.95}$ (8, 9). However, Pd(0) is considered essential for entry into the catalytic cycle via its oxidative addition of the aryl halide. Therefore, we propose that reduction of Pd(II) to Pd(0) by basic, aqueous IPA is involved in the extraction of Pd, eq 2. This is analogous to the extrusion of Pd(0) caused by reduction with H_2 (8), although the reaction conditions are different (80 °C for IPA vs. 1000 °C for H_2).



(2)

The level of Pd loading in the perovskite plays a role in the length of the induction period, during which the Pd is extracted from its reservoir. Removal of Pd(II) requires an accompanying rearrangement of the perovskite structure, with formation of a corresponding amount of $Ba(OH)_2$, eq 3.

$$BaCe_{1-x}Pd_xO_{3-x} + 2x\,H^+ + 2x\,e^- \rightarrow x\,Pd(0) + (1-x)\,BaCeO_3 + x\,Ba(OH)_2 \qquad (3)$$

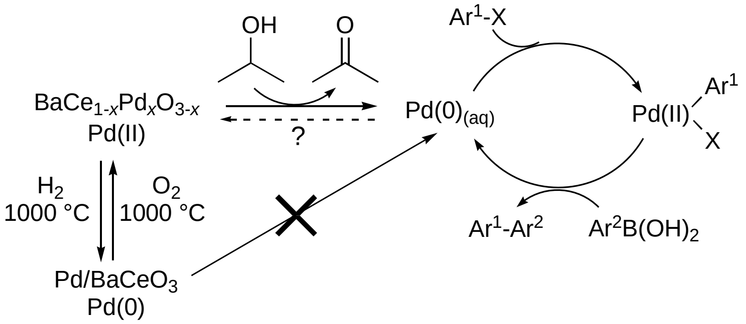
The greater rearrangement of the perovskite structure in the catalyst associated with the higher level of Pd-doping may be responsible for the longer induction period. After the onset of catalytic activity, the slopes of the two conversion vs. time curves for $x = 0.05$ and $x = 0.10$ in Figure 1a are very similar, demonstrating that the two catalysts produce the same soluble active site in similar amounts.

The dramatic suppression of catalytic activity upon H_2 reduction of the catalyst is curious, considering the requirement noted above for formation of Pd(0) in order to enter the catalytic cycle. It is attributed to the unavailability of Pd(0) at the liquid/solid interface. The strong Pd 3*d* signals representing near-surface Pd(II) in the XPS spectra of the as-prepared and reoxidized forms of $BaCe_{1-x}Pd_xO_{3-x}$ disappear completely upon treatment of the catalyst in H_2 at 1000 °C (8, 9). Although powder XRD confirmed that *fcc*-Pd(0) is formed (average particle size, 80 nm by line-broadening), it is not present at the perovskite surface. Instead, the metal nanoparticles are overgrown by $BaCeO_3$ and/or by the $Ba(OH)_2$ formed concurrently with Pd(0). This likely prevents the release of soluble Pd(0) into the reaction medium, since the metal is not exposed to the reaction medium. A similar effect of suppressed activity in the reduced form of $LaFe_{0.57}Co_{0.35}Pd_{0.05}O_3$, although no explanation was proposed (6).

Proposed mechanism. Based on the evidence described above, we propose that $BaCe_{1-x}Pd_xO_{3-x}$ acts as a reservoir of "ligand-free" soluble Pd for the Suzuki coupling reaction. Due to the large ionic radii of Ba^{2+} and Ce^{4+}, Pd(II) is very stable at the *B*-site of the host lattice. Reductive extraction under mild conditions (basic, aqueous

IPA, 80 °C) results in formation of the active, ligand-free Pd(0) species, but at very low levels which do not tend to form inactive Pd colloids by aggregation. Indeed, the effective turnover frequencies reported here are among the highest reported in the literature to date. The soluble, "ligand-free" Pd(0) presumably undergoes oxidative addition of the aryl halide, followed by reductive coupling with the phenylboronic acid.

Although recapture of soluble Pd by the perovskite has not been demonstrated conclusively, the ability to reuse the catalyst several times without significant loss of activity suggests that reabsorption of Pd may occur. If this were not the case, rapid depletion of near-surface Pd in the low surface area (1 m^2/g) catalyst would be expected to cause a precipitous loss of activity upon catalyst recycling. The dissolution/re-absorption of Pd may also contribute to the stabilization of soluble Pd(0) by preventing the formation of inactive Pd black. The residual Pd in solution at the end of the reaction is significantly lower than that reported for either homogeneous catalysts (e.g., $Pd(PPh_3)_4$, residual [Pd] = 40 – 80 ppm (11)) or heterogeneous catalysts (e.g., Pd/C, residual [Pd] < 6 ppm (12); $LaFe_{0.57}Co_{0.35}Pd_{0.05}O_3$, residual [Pd] = 2 ppm (5, 6)). The proposed reaction mechanism is summarized in Scheme 1.



Scheme 1 Proposed mechanism for Suzuki coupling by Pd-doped perovskite catalysts

Conclusions

$BaCe_{1-x}Pd_xO_{3-x}$ catalysts (x = 0.05 and 0.10), synthesized by a high temperature solid-state method, are very active in Suzuki coupling (TOF ca. 50,000) and produce very low levels of residual Pd (< 0.05 ppm) in the reaction medium. The as-prepared and reoxidized forms of the catalyst have very similar catalytic activities, while the H_2-reduced catalyst in which metallic Pd has been extruded from the perovskite lattice shows much lower activity. Reductive extraction of Pd(II) by basic, aqueous 2-propanol in the reaction medium occurs in the absence of the aryl halide substrate. The low levels of residual Pd at the end of the reaction and the ability to recycle the catalyst without loss of activity suggest that recapture of soluble Pd may also be occurring. The longer induction period exhibited by $BaCe_{0.90}Pd_{0.10}O_{2.90}$ relative to $BaCe_{0.90}Pd_{0.10}O_{2.95}$ is attributed to the greater reorganization requirement of the remaining perovskite host.

Acknowledgements

The authors are grateful to Catalytic Solutions, Inc., and the U.S. Department of Energy, Basic Energy Sciences, Grant No. DE-FG02-05ER15725, for funding. This work made use of MRL Central Facilities supported by the MRSEC Program of the National Science Foundation under award DMR05-20020.

References

1. R. G. Heidenreich, K. Kohler, J. G. E. Krauter, and J. Pietsch, *Synlett*, 1118-1122 (2002).
2. K. Shimizu, R. Maruyama, S. Komai, T. Kodama, and Y. Kitayama, *J. Catal.*, **227**, 202-209 (2004).
3. B. J. Gallon, R. W. Kojima, R. B. Kaner, and P. L. Diaconescu, *Angew. Chem. Int. Ed.*, **46**, 7251-7254 (2007).
4. A. K. Diallo, C. Ornelas, L. Salmon, J. R. Aranzaes, and D. Astruc, *Angew. Chem. Int. Ed.*, **46**, 8644-8648 (2007).
5. M. D. Smith, A. F. Stepan, C. Ramaro, P. E. Brenan and S. V. Ley, *Chem. Commun.*, 2652-2653 (2003).
6. S. P. Andrews, A. F. Stepan, H. Tanaka, S. V. Ley, and M. D. Smith, *Adv. Synth. Catal.*, **347**, 647-654 (2005).
7. N. T. S. Phan, M. Van Der Sluys, and C. W. Jones, *Adv. Synth. Catal.*, **348**, 609-679 (2006).
8. J. Li, U. G. Singh, J. W. Bennett, K. Page, J. C. Weaver, J. P. Zhang, T. Proffen, A. M. Rappe, S. L. Scott, and R. Seshadri, *Chem. Mater.*, **19**, 1418-1426 (2007).
9. U. G. Singh, J. Li, J. W. Bennett, A. M. Rappe, R. Seshadri, S. L. Scott, *J. Catal.*, **249**, 347-356 (2007).
10. J. E. Hamlin, K. Hirai, A. Millan, and P. M. Maitlis, *J. Mol. Catal.* **7**, 543-544 (1980).
11. D. Ennis, J. McManus, W. Wood-Kaczmar, J. Richardson, G. E. Smith, and A. Carstairs, *Org. Proc. Res. Dev.* **3**, 248-252 (1999).
12. D. A. Conlon, B. Pipik, S. Ferdinand, C. R. LeBlond, J. R. Sowa, Jr. B. Izzo, P. Collins, G. J. Ho, J. M. Williams, Y. J. Shi, Y. Sun. *Adv. Synth. Catal.* **345**, 931-935 (2003).

$BaCe_{1-x}Pd_xO_{3-\delta}$ ($0 \leq x \leq 0.1$): A Highly Active and Reusable Catalytic System for Suzuki Coupling

X. Ouyang, J. Li, R. Seshadri and S. L. Scott

Keyword Index

Perovskite catalyst
Palladium
Heterogeneous catalysis
Suzuki coupling
Aryl halides