Heterogeneous or Homogeneous? A Case Study Involving Palladium-Containing Perovskites in the Suzuki Reaction

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Abstract: The utility of a series of palladium-containing perovskite catalysts in the Suzuki reaction is described; turnover numbers of up to 400,000 are reported. A detailed investigation into the mode of action of these catalysts encompassing kinetic studies, catalyst poisoning, microscopy and three-phase tests demonstrate that these *heterogeneous* materials are pre-catalysts that operate by a solution-phase mechanism

Keywords: cross-coupling; heterogeneous catalysis; homogeneous catalysis; palladium; perovskite; Suzuki reaction

Introduction

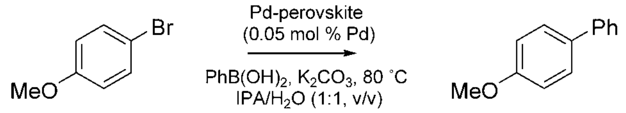
'Homogeneous'[1] palladium catalysts are widely used in many cross-coupling reactions, and systems capable of demonstrating astonishingly high turnover numbers for deactivated substrates at room temperature have been disclosed.[2–7] Whilst these techniques are certainly state-of-the-art in terms of their substrate tolerance, catalyst loading and reactivity, their complexity may preclude application on a large scale. Additionally, the removal of residual palladium and associated ligands from these reactions is often difficult, and as such, effective and economical catalysts free from these constraints are essential for the translation of laboratory methods to larger scale operations in industry.[8] 'Heterogeneous' catalysts can be removed from reaction media by a simple filtration, but relatively few examples of successful and highly active 'heterogeneous' catalysts for use in cross-coupling reactions have been reported. A range of approaches has been adopted in an attempt to solve this problem including encapsulation[9–11] or incarceration,[12,13] the use of polymeric supports,[14–16] other insoluble palladium sources such as Pd/C[17–20] and transition metal-free cross-coupling reactions.[21,22]As such, the search for an efficient, cheap and practical 'heterogeneous' catalytic system is a major challenge. However, desorption of the transition metal from the 'heterogeneous' support can occur, resulting in its entry into a conventional solution-phase catalytic cycle.[23–25] This has prompted investigations into the nature of the catalytically active species in these and other systems.[26–28]

The utility of a palladium-containing perovskite $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ (LaPd*, a catalyst originally developed for automotive emission control)[29] in the Suzuki cross-coupling,[30] has been disclosed earlier.[31] In this paper, investigations into the reactivity of a series of Pd-containing perovskites in the Suzuki reaction are outlined, and a range of experiments designed to ascertain whether this process proceeds by way of a 'homogeneous' or a 'heterogeneous' mechanism are delineated.

Results and Discussion

It was considered important to investigate whether the identity of the metals other than palladium in the perovskite structure was an important influence on reactivity and turnover number in cross-coupling reactions. With this in mind, seven palladium-containing perovskites were screened for their activity in the Suzuki reaction of 4-bromoanisole with phenylboronic acid under our previously reported conditions (Scheme 1).

The kinetic profiles of all seven catalysts are pictured in Figure 1.



Scheme 1. Suzuki reaction.

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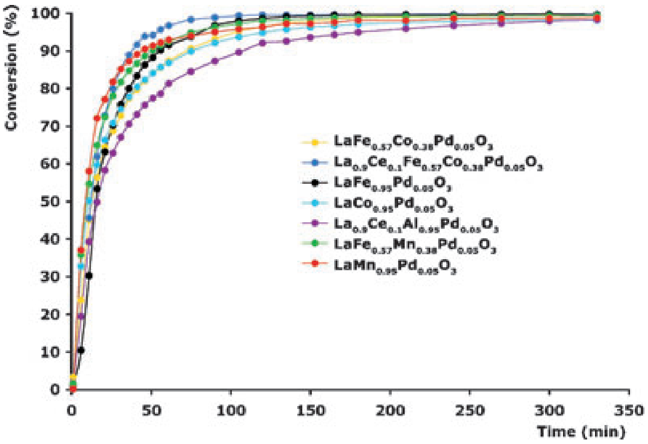


Figure 1. Kinetic profiles of palladium-containing perovskite catalysts in the Suzuki reaction of phenylboronic acid with 4-bromoanisole.

All seven chosen catalysts are effective in this Suzuki reaction, with relatively little difference between them, although the $La_{0.9}Ce_{0.1}Fe_{0.57}Co_{0.38}Pd_{0.05}O_3$-catalysed reaction went to completion in the shortest period of time. Attempts to perform the reaction with perovskites deficient in palladium (such as $LaCe_{0.1}Fe_{0.6}Co_{0.4}O_3$, $LaFeO_3$, $LaCoO_3$, or $LaFe_{0.6}Co_{0.4}O_3$) were unsuccessful. It was also important to establish the lifetimes of the catalysts, and so turnover numbers were measured for all seven catalysts for the same reaction, Table 1.

This demonstrated that turnover numbers varied from 151,000 (for $La_{0.9}Ce_{0.1}Al_{0.95}Pd_{0.05}O_3$) to almost 400,000 for $LaFe_{0.95}Pd_{0.05}O_3$. At this stage it was decided to concentrate our studies on a single catalyst – $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ – as this is prepared on an industrial scale, and is also the catalyst for which our generic Suzuki conditions have been developed. In our previous paper a three-phase test[33,34] indicated that the reaction was proceeding *via* the intermediacy of a soluble catalyst, generated in the presence of a solution-phase aryl bromide.[25,31] In an attempt to clarify, and further investigate, this phenomenon a series of mechanistic investigations was undertaken. Distinguishing whether a catalyst operates by a homogeneous or a heterogeneous mechanism is non-trivial, and it has been demonstrated in a series of elegant studies [35–37] that a combination of kinetics, poisoning studies, microscopy and other methods offer the best prospect of making a definitive judgment. Taking this into account, it was decided to initiate these studies with an examination of the kinetics of the coupling of 4-bromoanisole and phenylboronic acid.

Table 1. Turnover numbers for palladium-containing perovskites.

Catalyst	TON (Pd^{-1})
$LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$	243,000[32]
$La_{0.9}Ce_{0.1}Fe_{0.57}Co_{0.38}Pd_{0.05}O_3$	351,000
$LaFe_{0.95}Pd_{0.05}O_3$	399,000
$LaCo_{0.95}Pd_{0.05}O_3$	213,000
$La_{0.9}Ce_{0.1}Al_{0.95}Pd_{0.05}O_3$	151,000
$LaFe_{0.57}Mn_{0.38}Pd_{0.05}O_3$	177,000
$LaMn_{0.95}Pd_{0.05}O_3$	190,000

Substrate/catalyst ratio = 27000 : 1 (bromoanisole:perovskite) = 0.00019 mol% Pd. The reactions were run until LCMS conversion did not increase by more than 1% over 24 h (typically approx. 2 weeks). At this point conversions were estimated based on ^1H NMR analysis and TON calculated accordingly.

Kinetic Experiments

Kinetic studies are one of the most effective methods of investigating whether a catalyst is actually a *precatalyst* as such systems often display sigmoidal kinetics with an identifiable induction period. Monitoring the coupling of 4-bromoanisole and phenylboronic acid under the standard Suzuki conditions (sampling every 20 seconds for the first four minutes) demonstrated that there was a short, but measurable induction period of approximately four minutes, Figure 2.

During this period the reaction rate was considerably lower than it was in the following time of approximately one hour. This induction period probably correlates with production of a solution-phase Pd species, which may occur during an oxidative insertion step. It has been shown (using a three-phase test)[25] that the presence of an aryl halide in solution is necessary to generate a solution-phase active catalyst.

During its preparation, $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ is heated in oxygen at 800 °C to afford the final perovskite catalyst containing Pd^{III}. It has been demonstrated that under the conditions of the combustion engine exhaust system (that operates over 800 °C) the palladium reversibly moves out of the perovskite lattice to form a face-cen-

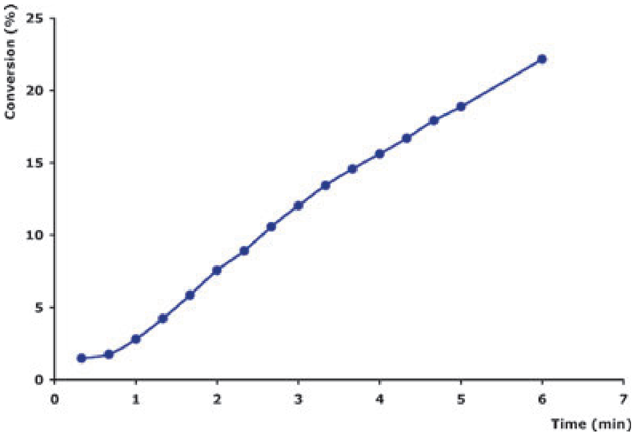


Figure 2. Kinetic investigation of $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ in the first 7 minutes of the reaction between phenylboronic acid and 4-bromoanisole.

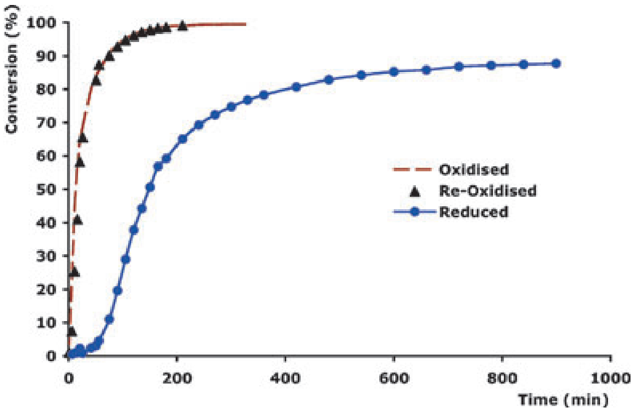


Figure 3. Kinetics of oxidized, reduced and re-oxidized $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ catalysts.

tred cubic arrangement of metallic palladium, or palladium-cobalt clusters at the surface of the perovskite.[29] These redox conditions can be mimicked by the treatment of the catalyst with hydrogen at 800 °C to produce reduced material that can be regenerated by re-oxidation in oxygen at 800 °C. Kinetic plots of the Suzuki reaction catalysed by the standard oxidized material (already described in Figure 1), reduced material and re-oxidized catalyst are pictured in Figure 3.

The reduced form of the catalyst is an active, but inferior Suzuki catalyst displaying sigmoidal kinetics with an induction period significantly longer than that displayed by the oxidized catalyst. However, it is interesting to note that this catalyst, in which the palladium is zero-valent, is a significantly worse catalyst for the Suzuki reaction than the catalyst in which the palladium is predominantly in a high-valent state (Pd^{III}). This is almost counter-intuitive as it can be expected that the palladium must be reduced from Pd^{III} prior to any oxidative insertion event; it is clear then that the Pd^0 species produced during the reaction must be distinct from that produced under the redox conditions described herein. The re-oxidized catalyst displays kinetics identical to those of the original catalyst, consistent with the reversible migration of palladium in and out of the perovskite lattice.[29]

Maitlis' Filtration Test

In order to probe the formation of soluble Pd species, Maitlis' filtration experiments were performed and the catalytic activity of the resulting solution measured.[38] This involved stopping the reaction after a range of conversions (as adjudged by LC-MS) and filtering the reaction through a 0.45 μm syringe filter to remove the bulk catalyst. It was found that the filtrates were catalytically active, and that the reactions progressed to significantly higher conversions in the absence of the solid perovskite catalyst, even when the reaction was stopped after only 4% conversion, Table 2.

Table 2. Maitlis filtration tests.

Conversion before Filtration (%)*	Maximum Conversion after Filtration (%)*
4	83
30	96
73	99
78	96

* Conversion based on LC-MS.

The results of these tests support the formation of soluble Pd and demonstrate not only that catalytic activity was partially retained after filtration but also that the active solution-phase species has a lifetime that is less than the total reaction time. This test does not preclude the presence of nanoclusters,[39,40] which would not be removed by filtration through media of this nature.

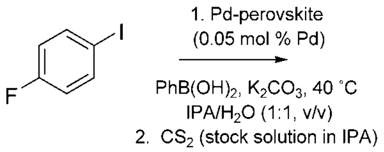
Catalyst Poisoning

CS_2 as well as other ligands like PPh_3 or thiophene bind strongly to metal centres, thereby blocking access of the substrate to the active site. This poisoning can be performed quantitatively to permit determination of the number of *active* metal atoms.[41] If the catalyst can be poisoned with less than 1.0 equiv. of the added ligand (per metal atom), that suggests that not all metal atoms are participating in catalysis. This is generally considered evidence for a heterogeneous catalyst, which usually only has a fraction of the metal atoms available for catalysis. On the contrary, more than 1.0 equiv. is usually required to completely poison a homogeneous catalyst.[42] A drawback of CS_2 poisoning experiments is that they must be performed at temperatures below 50 °C, because the ligands will begin to reversibly dissociate from the catalyst above this temperature.[36]

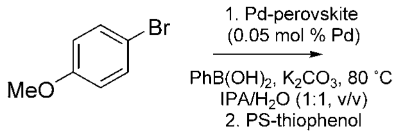
The poisoning experiment was conducted using phenylboronic acid and 1-fluoro-4-iodobenzene as coupling partners under our usual Suzuki conditions [1 mol % LaPd*, 3 equivs. K_2CO_3, 2-propanol/water (1:1, v/v)]. The activated iodide was chosen in order that the reaction could progress at the lower temperature (40 °C) necessary to prevent ligand dissociation.[41] After the reaction had proceeded 10–30% (as adjudged by LC-MS), CS_2 was added to the reaction mixture (Scheme 2).

It was found that only 0.01 equiv. of CS_2 (*vs.* palladium) was necessary to poison LaPd* (average over 39 experiments). The stoichiometry of this poisoning study indicates that the true total turnover number is significantly higher than the 243,000 originally indicated.[43]

When the kinetic experiment was repeated with the original 'oxidized' catalyst in the presence of triphenyl-



Scheme 2. CS_2 poisoning experiment.



Scheme 3. PS-thiophenol three-phase poisoning study.

phosphine (50 molar equivalents with respect to Pd), the additive was found to inhibit the reaction by prolonging the induction period by some 40 minutes (Figure 4).

However, the maximum reaction rate attained by the catalyst is still comparable to the reaction in the absence of the added ligand. This can be attributed to the phosphine competing with bromoanisole for ligation to a Pd^0 species that is still bound to the perovskite surface. The binding of the phosphine is reversible and so it is when oxidative insertion of the aryl halide occurs that the generation of a soluble Pd species is initiated.

A three-phase test designed to catch and poison a soluble Pd source was performed with polymer-supported thiophenol as the immobilized poison. It was found that if the thiol was added to a Suzuki reaction that had been started in the usual manner, the reaction progress would stop at the point of addition, Scheme 3.

Also, if the reagents were added to a sample of perovskite, which was pre-mixed with PS-thiophenol in solvent at 80 °C, no reaction occurred. Due to the site-isolation principle, this test is evidence of a catalytically active soluble Pd source that is trapped by the strongly binding sulfur ligand. This is complementary to a previous three-phase test conducted on this system.[31]

Mechanism

The reduced form of LaPd* has been shown by kinetic experiments to be a relatively poor catalyst for the Suzuki reaction but the oxidized form, which is a perovskite lattice incorporating Pd^{III} shows high activity. A mechanistic proposal that incorporates the information discussed thus far is pictured below, Figure 5.

The first step in the reaction could be expected to involve a reduction step in which Pd^{III} (or other high-valent Pd species) in the perovskite is reduced to a Pd^0 species still bound to a solid surface (possibly by the aqueous alcoholic solvent) which can then undergo oxidative addition with an aryl halide. It is thought that this oxidative addition is the step at which a soluble catalyst is produced on the basis of a previously described three-phase test. Triphenylphosphine increases the period of time it takes for the active catalyst to be produced, and hence it is believed to be competing with the aryl halide at this stage for a solid-bound Pd^0 species. The actual mechanism by which the palladium enters the solution after the oxidative insertion is unknown; the mechanism of oxidative addition itself is still the subject of much debate despite sophisticated studies.[44] Once in solution, it is envisaged that the catalyst can enter a standard cross-coupling catalytic cycle, producing a soluble Pd^0 species. It is possible that this Pd^0 intermediate may form halide-stabilized nanoparticles, which could ag-

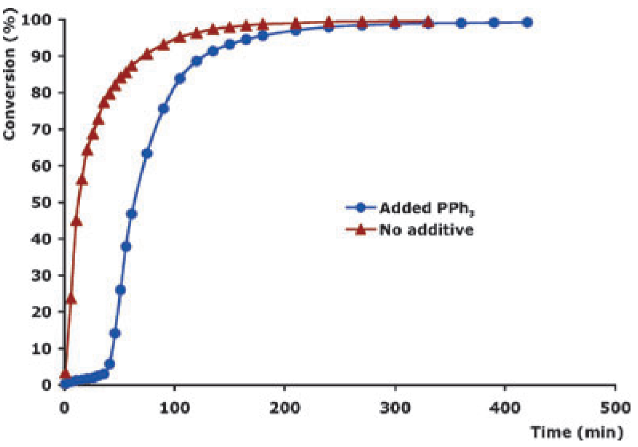


Figure 4. Comparison of the kinetics of $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ in the Suzuki reaction with and without added triphenylphosphine.

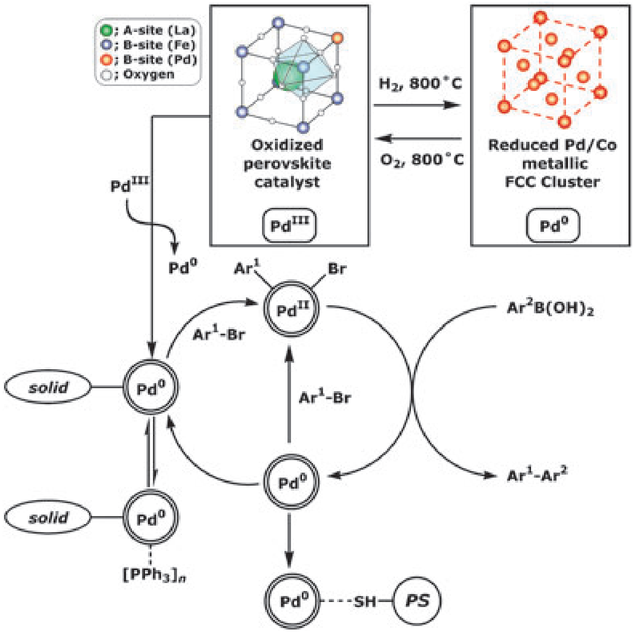


Figure 5. Putative mechanistic scheme for the generation of a soluble active catalyst (PS = polymer supported, Ar = aryl).

glomerate to generate palladium black in the absence of another oxidative addition, although these species have not been observed by TEM. This is consistent with other ligand-free systems in which high substrate to catalyst ratios produce high TONs.[45–47] The Pd^0 species can carry on the catalytic cycle or be recaptured by the bulk inorganic phase (as suggested by ICP measurements that detected a residual Pd level of approx. 2 ppm in reaction mixture filtrates). The presence of such a species in solution is indicated by the ease with which a polymer-supported thiol poison can hinder the reaction, and the prevailing catalytic activity of filtrates after solid catalyst removal.

TEM Studies

In an attempt to ascertain whether palladium was being redeposited on the surface of the perovskite after reaction a series of TEM studies was initiated. The surface of the catalyst was examined before, and after reaction, Figure 6.

Whereas the surface of the unused catalyst is relatively uniform and appears amorphous, the post-reaction catalyst has undergone a profound morphological change and appears to consist predominantly of a new crystalline phase. The identity of this crystalline material is not known at present, though preliminary X-ray diffraction data indicate that it is neither the perovskite catalyst or simple lanthanum oxide or hydroxide.

Conclusion

It has been demonstrated that palladium-containing perovskites are a general class of 'heterogeneous' reagents possessing utility in cross-coupling reactions. The mechanism by which this occurs involves the generation of a soluble, catalytically active palladium species that is desorbed from the bulk inorganic phase and probably redeposited on a modified solid phase after the reaction is complete. The nature of the soluble palladium species is not clear; attempts to observe palladium nanoclusters in these systems *via* TEM investigations have proven fruitless. Only a small number of perovskites were screened for activity in this study, but in principle a huge range of perovskite materials containing alternative metal combinations could be prepared for potential applications in organic synthesis programmes. The aptitude of different metal-containing perovskite systems is currently being explored.

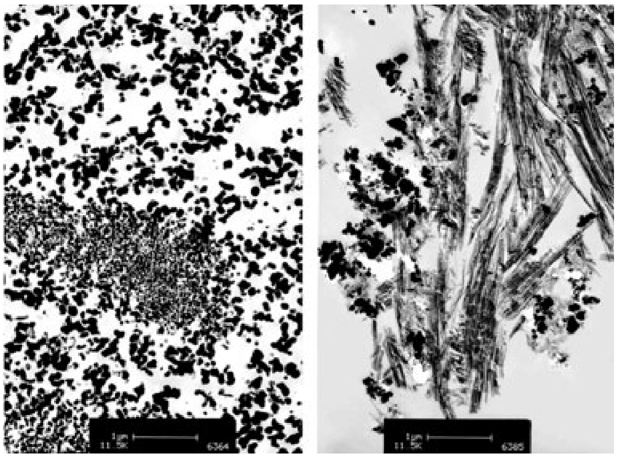


Figure 6. TEM images of the catalyst before (left) and after (right) reaction.

Experimental Section

General

All reagents and solvents were bought from commercial sources and used as supplied. Reactions were performed in Radley's Carousel™ tubes in air unless otherwise stated. Kinetic experiments were conducted with React Array™ SK233 equipment and analysed by in-line high-pressure liquid chromatography HPLC (*vide infra*). Thin layer chromatography (TLC) was performed with Merck 60 F254 silica gel plates and viewed under UV radiation (254 nm). Liquid chromatography/mass spectrometry (LC-MS) experiments were conducted on HP1100/HP MSD with diode array detection. *Column*: Mercury MS Luna 3 μm C8(2), 20 × 2.0 mm. *Eluent*: A: water, 0.1% TFA, B: acetonitrile, 0.1% TFA. *Flow rate*: 0.6 mL min^{-1}. *Method*: gradient 5–95% B in A over 2.5 minutes, run time 8 minutes. *Ionization technique*: atmospheric pressure chemical ionization (APCI).

High-resolution mass spectrometry was conducted with Kratos Concept spectrometer at the University of Cambridge. Infrared spectra were recorded by Perkin-Elmer Spectrum One spectrometer equipped with an attenuated total reflectance sampler. NMR spectra were recorded with Bruker DPX-400 spectrometer operating at 400 MHz and 100 MHz for measurement of ^1H and ^{13}C shifts, respectively, with $CDCl_3$ solvent. COSY spectra were obtained and used to assign ^1H signals. HMQC and DEPT experiments were used to aid the assignment of ^{13}C signals. All quoted ^1H and ^{13}C shifts are measured in ppm, with residual $CHCl_3$ calibrated to 7.27 and 77.0 ppm respectively.

Microwave heating was performed in 5 mL Smith vials by irradiation with a Personal Chemistry Smith Synthesiser™. TEM images were obtained at the Multi-Imaging Centre, University of Cambridge. Samples were dehydrated in three changes of dry ethanol, followed by three changes of dry acetonitrile and incubated overnight in 50/50 acetonitrile and Spurr's epoxy resin. The samples were aged for 8 hours in 25/75 acetonitrile and Spurr's resin followed by 5 days in 100 resin under vacuum and finally cured at 60 °C for 24 hours. Sections (60 nm) were cut on a Leica Ultracut UCT using a diamond knife, mounted on 400 mesh copper grids and viewed on a FEI-Philips CM100 operated at 80 kV using a 100 μm condenser aperture and a 30 μm objective aperture. Images were recorded on Kodak 4489 cut film.

Reactions were performed using a React Array™ SK233 automated workstation subjected to in-line HPLC analysis on Hewlett Packard HP1100. *Column*: Supercosil™ ABZ$^+$ 3.3 cm × 4.6 mm, 3 μm. *Eluent*: A: water, 0.1% TFA, B: 95% acetonitrile, 5% water, 0.05% TFA. *Flow rate*: 1 mL min^{-1}. *Detection*: UV (220 nm). *Method*: gradient 10–95% B in A over 7 minutes, run time 10 minutes. All solvents were commercially available and used as supplied.

All reactions were performed in air at 80 °C in 25-mL vessels with fitted condensers and stirrer bars. 10 μL aliquots were sampled at specified intervals and diluted serially by a factor of 100 before being subjected to in-line HPLC analysis. The aliquots were dispensed into 1.5-mL vials, quenched with acetonitrile (1 mL) and mixed [75% by volume, (aspirated and dispensed at 10 mL min^{-1})]. 100 μL of these solutions were transferred to clean 1.5-mL vials, diluted with acetonitrile (900 μL) and mixed [75% by volume, (aspirated and dispensed at 10 mL min^{-1})] to give analytical samples ready for analysis by HPLC (20 μL injected).

Typical Procedure for React Array™ Suzuki Study

4-Bromoanisole (500 μL, 4 mmol), phenylboronic acid (744 mg, 6 mmol), K_2CO_3 (1.66 g, 12 mmol) and naphthalene-2-carboxamide (64.8 mg, 379 μmol) were added to a reaction vessel and diluted with 2-propanol/water (12 mL, 1:1, v/v). The SK233 was initiated and once the mixture had reached 80 °C and homogeneous phase mixing, the perovskite catalyst (10 mg, 40 μmol) was added and the timer started. The reactions were run for 5 hours and 30 minutes. Aliquots (10 μL) were withdrawn automatically, diluted and injected into HP1100 for HPLC analysis at $t=1$, 6, 11, 16, 21, 26, 31, 36, 41, 46, 51, 56, 61, 75, 90, 105, 120, 135, 150, 165, 180, 210, 240, 270, 300, 330 minutes.

Typical Procedure for CS_2 Poisoning Experiment

A 20-mL tube was charged with phenylboronic acid **1** (180 mg, 1.50 mmol), 1-fluoro-4-iodobenzene **25** (0.11 mL, 1.00 mmol), $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ (3.00 mg, 1 mol %, 0.05 mol % Pd), K_2CO_3 (0.40 mg, 2.90 mmol) and water/2-propanol (1:1, v/v, 5 mL), and the mixture was stirred at 0 °C until LC indicated the reaction had proceeded 10–30%. At 0 °C CS_2 [0.05–0.4 mL of a freshly prepared 0.02 nM solution in water/2-propanol (1:1 v/v)] was then added. This mixture was stirred at 40 °C and the conversion followed by LC over 2 days.

Typical Procedure for Maitlis' Test

A 20-mL tube was charged with phenylboronic acid **1** (180 mg, 1.50 mmol), 1-fluoro-4-iodobenzene **25** (0.11 mL, 1.00 mmol), $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ (3.00 mg, 1.00 mol %, 0.05 mol % Pd), K_2CO_3 (0.40 g, 2.90 mmol) and water/2-propanol (1:1, v/v, 5 mL), and the mixture was stirred at 0 °C, room temperature or 40 °C until LC indicated the reaction had proceeded 5–70%. The mixture was then filtered through a 0.45 μm syringe filter and stirred at 40 °C. The conversion was followed by LC over 1 day.

Data Analysis

Calibration: Standard solutions of 4-bromoanisole (2.0 μL mL^{-1}), naphthalene-2-carboxamide (2.0 mg mL^{-1}) and 4-methoxybiphenyl (2.0 mg mL^{-1}) were prepared with acetonitrile in volumetric flasks and serially diluted with acetonitrile. A set of six solutions of varying concentration was thus obtained for each of the three compounds and these were injected into the HP1100 and the HPLC trace recorded at 220 nm. HPLC trace areas were plotted against sample concentration to produce a calibration curve.

Monitoring Suzuki Reaction Progress (Raw and processed data available in Supporting Information)

During the Suzuki reaction, the HPLC trace areas for naphthalene-2-carboxamide, 4-bromoanisole and 4-methoxybiphenyl were recorded and normalized with respect to the internal standard (naphthalene-2-carboxamide). Areas of 4-bromoanisole and 4-methoxybiphenyl were then extrapolated back to their concentrations using the calibration curves. Percentages of 4-bromoanisole remaining in solution and 4-methoxybiphenyl formed were calculated and reaction progress assessed by plotting *conversion* [=(% 4-methoxybiphenyl)/(% 4-bromoanisole + % 4-methoxybiphenyl)] against time.

Typical Procedure for Determination of Catalyst Turnover Number

$LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$ (0.50 mg, 2.0 μmol) was added to a stirring solution of 4-bromoanisole (10.0 g, 53.5 mmol), phenylboronic acid (9.8 g, 80 mmol) and K_2CO_3 (22.2 g, 120 mmol) in a mixture of 2-propanol/water (100 mL, 1:1, v/v) at 80 °C. The resulting mixture was stirred until LC-MS (220 nm) revealed no change in the ratio of 4-bromoanisole:4-methoxybiphenyl between two aliquots that had been removed at 24-hour intervals (this takes approximately two weeks).

Small-Scale Work-Up (1 mL of the crude reaction mixture extracted at 80 °C with vigorous stirring to maintain phase-homogeneity)

The sample was partitioned between Et_2O (10 mL) and water (5 mL). The separated aqueous phase was back-extracted with Et_2O (10 mL) and the combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), filtered and evaporated under reduced pressure. The residue was analysed by ^1H NMR and the MeO peak integrals measured and compared to provide the definitive ratio of 4-bromoanisole:4-methoxybiphenyl and from this, the catalyst turnover number.

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hatsu Motor Company for their kind gift of perovskite catalysts, Hokko Chemical Industry Co. Ltd., for their assistance in sample preparation and the Royal Society for a URF (to MDS).

References and Notes

[1] The classical, solubility-based definition equates "heterogeneous" to "insoluble" and "homogeneous" to "soluble". When referring to this definition, quotation marks will be used ('homogeneous', 'heterogeneous'). A newer definition deals with the active site of the catalytic system; see J. Schwartz, *Acc. Chem. Res.* **1985**, *18*, 302. If the active site is uniform, the system is called homogeneous; if the active site consists of irregular sites, then the catalyst is called heterogeneous. When referring to this definition no quotation marks will be used.

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[42] In cases where a heterogeneous precatalyst generates a catalytically active soluble catalyst, the stoichiometry of such poisoning studies are useful for the calculation of turnover numbers but are not particularly informative for the investigation of homogeneous versus heterogeneous mechanisms.

[43] The true turnover number takes into account the number of catalytically active metal sites in the molecule, and for the catalyst described here is 100 times greater than first indicated (giving a true turnover number of 24.3 million). For a soluble catalyst generated from an insoluble precatalyst, it is to be expected that the soluble palladium content of the reaction mixture may vary as the reaction progresses. In the studies presented herein, there was relatively little variation in the amount of CS_2 required to poison the reaction over a range of experiments, and no correlation between product conversion (when the poison was added) and the volume of CS_2 required to stop any catalysis.

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