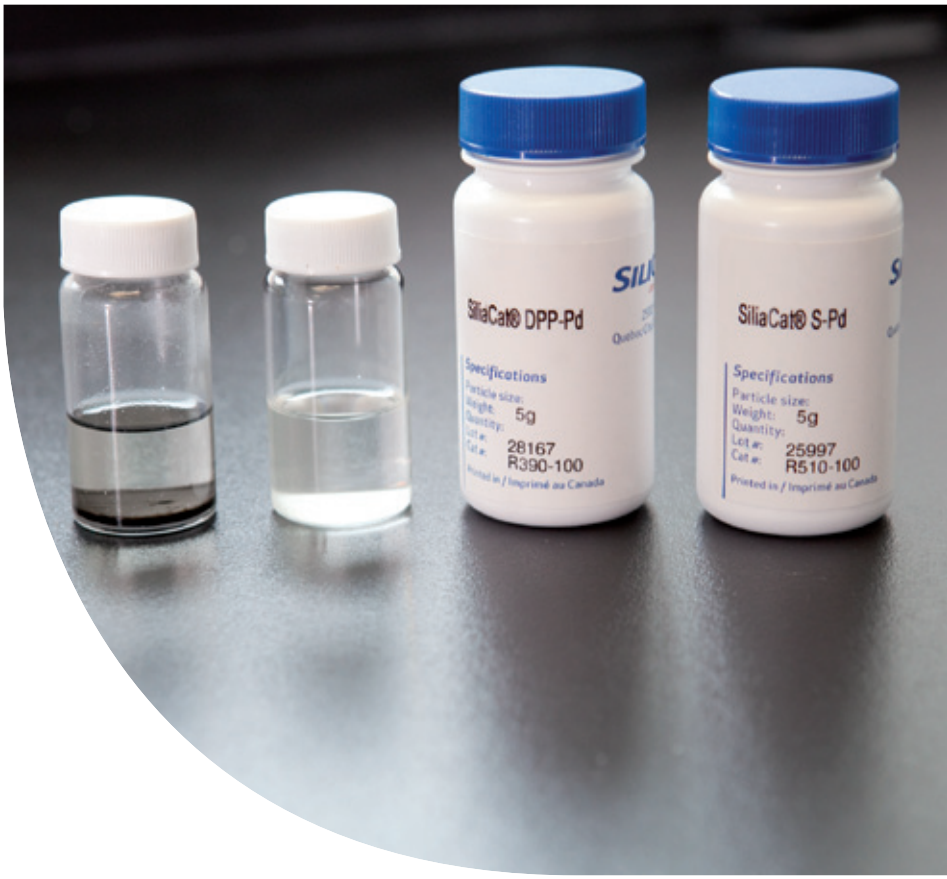
SiliaCat®

Heterogeneous Catalysts



SILICYCLE Inc.
UltraPure SILICA GELS

Importance of Quality Control

The Quality Control Department's objective is to provide default-free products. In light of this goal, we have determined the critical points that need to be addressed for each product line. These points are based on customer's and Account Managers' recommendations as well as on our employees' scientific knowledge.

Each product family has its own quality control procedures, which are strictly adhered to. QC test results are checked and confirmed by the person in charge of them before being cleared for shipping. Complete procedures for each product line are available upon request.

Thus, SiliCycle is committed to high quality standards. In doing so, every product meets the quality specifications our customers demand. All products are shipped with a Certificate of Analysis (*CofA*) and a sample from every batch is kept for subsequent analysis. If you feel that the product you have received does not meet these specifications, please contact us and we will make sure you are satisfied.

Bare Silica Gel

The backbone of most of SiliCycle's products is Silia*Flash* F60 (*40-63* µm, *60 Å*) silica gel. It provides superior performance for chromatographic applications due to its narrow particle size distribution and high purity.

Before functionalization, every silica is rigorously characterized and analyzed by the procedures below to ensure lot-to-lot reproducibility.

Functionalized Silica Gel

The process for functionalizing the silica is highly dependent on the group being attached. However, it is still possible to functionalize 90% of the surface, verified by ^{29}Si MAS NMR. The remaining 10% of the surface may be endcapped to provide a completely inert support. After being functionalized, the product is submitted to further analysis and quality control as outlined below.

Quality Control

Type of Analysis	Performed by:
Bare Silica Gel	
Carbon, nitrogen & sulfur content	Elemental analyzer
Total trace metal	ICP-OES
Surface area & porosity	Nitrogen adsorption analyzer
Particle size distribution	Laser light diffraction
Tapped density analysis	Density measurement
Water content	Moisture balance
pH	pH-meter
Functionalized Silica Gel	
Residual solvent content	Moisture balance
Specific reactivity analysis	GC-FID, GC-MS, LC-MS/MS, ICP-OES
Organic function signature	Infrared spectroscopy
Purity analysis	GC-MS

Analysis Descriptions

Elemental Analysis of Organic Compounds

Silia*Flash* silica gel has a very low organic content. All lots are subjected to elemental analysis to determine the carbon, nitrogen and sulfur levels.

Total Trace Metal Analysis

To improve the quality of the separation, SiliCycle manufactures silica gels with very low traces of metal content. All silica gels are analyzed for more than 45 metals by ICP-OES down to ppm, and reach up to 99.4% silica purity. This removes any issues from metal oxides that may act as Lewis acids and prevents «Tailing» of most polar compounds (*frequently ionizable*) that can be caused by silica with a high metal content.

Surface Area and Porosity Analysis

The efficiency and reliability of silica gel depend on its surface condition. We use the Brunauer, Emmet, and, Teller analysis to determine the surface area, and the Barret-Joyner-Hatenda method to determine the pore diameter and pore volume. A larger surface area results in more contact or interaction with the analyte, thereby increasing the segregation of different products. Pore diameter and pore volume permit semi-exclusion chromatography where smaller molecules fit into pores more easily than larger ones. This justifies the use of several types of silica to achieve better discrimination in chromatographic separations.

Particle Size Distribution Analysis

Particle size distribution is determined by laser diffraction. Usually, more than 90% of the silica gel is kept within the appropriate range.

Water Content Analysis (*silica gel activity*)

The amount of water on the silica's surface affects chromatographic performance. An anhydrous silica gel will be extremely polar, while a wetted one will be considerably less polar. Every batch is carefully adjusted to a specific percentage of water content.

pH Analysis

The pH can increase the retention of some ionizable compounds. However, some products can become hydrolyzed or rearranged when in contact with acidic silica. A neutral pH, with a range between 6.5 and 7.5, is the most important factor in determining the reliability and inert behavior of the silica. This pH test involves suspending the silica gel in pure water (*5% w/w*).

TEL.: 1 418 874.0054 FAX: 1 418 874.0355 TOLL-FREE: 1 877.SILICYCLE (NORTH AMERICA ONLY) WWW.SILICYCLE.COM INFO@SILICYCLE.COM

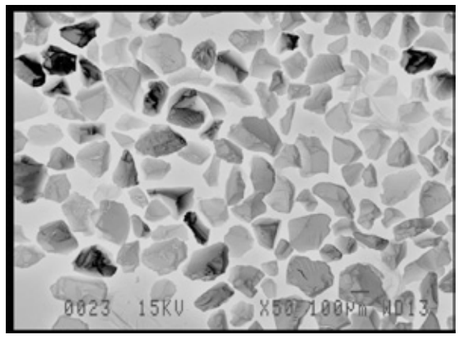
Catalytic Reactions with Silia*Cat*®

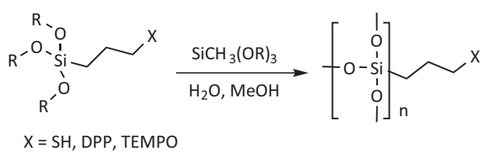
Advantages of using Silia*Cat*® heterogeneous catalysts over competitive products include:

- High stability
- Rigid & Porous Structure (*no swelling*)
- Compatibility with a wide range of solvents
- Ease of use: no swelling or static charge
- Leach-proof
- High turnover number (*TON*)
- Fast kinetics
- Accurate loading

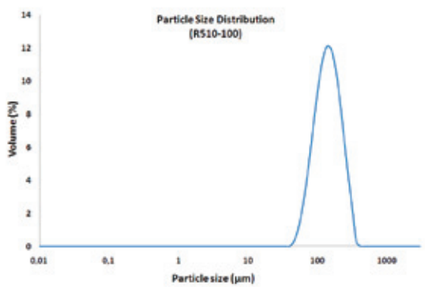
The Silia*Cat* Matrix

Inspired by the ORganically MOdified SILica (*ORMOSIL*) technology, the Silia*Cat* family is composed by new and innovative catalysts. Resulting from the co-condensation of two organosilane monomers by the sol-gel process (*confer condensation mechanism below*), the hybrid organic-inorganic materials present the highest stability and reactivity available with heterogeneous catalysts. Furthermore, the high cross linked framework presents an unmatched resistance, significantly better than the usual post-synthesis functionalized ligand.





X = SH, DPP, TEMPO

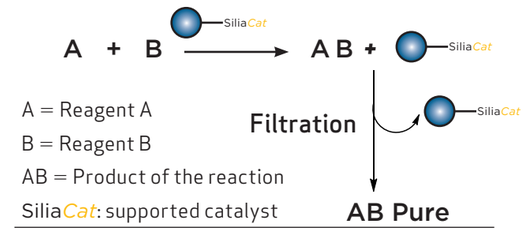


What are Silia*Cat* Heterogeneous Catalyst?

Usually, heterogeneous catalysts supported on a silica matrix are immobilized by post-modification of the inorganic support. These supports, however, present a high degree of leaching due to the poor stability of the immobilized phase. With Silia*Cat* Heterogeneous Catalysts, the ligand is directly cross linked in an organic-inorganic framework. This results a high degree of stability of the catalysts. Compared to homogeneous catalysts, Silia*Cat* exhibits a good reactivity and selectivity with one of the major advantages being that the catalyst is eliminated from the reaction mixture by a simple filtration. Forget your purification problems with our Silia*Cat* catalysts family.

The process for using Silia*Cat* Heterogeneous Catalysts is outlined in the scheme below.

What is Silia*Cat* Heterogeneous Catalyst?



Features and Benefits of Silia*Cat* Catalysts

Features & Benefits of Silia*Cat*	
Features	**Benefits**
Inertness within entrapped molecules	High conversion and yield
Reagent concentrated at the surface of the material	Reliable and reproducible synthesis
Robustness	High thermal and mechanical stabilities
Rigid and porous structure	No swelling, solvent independent and air stable Conditions do not have to be inert
Leach-proof organoceramic matrix	No contamination of APIs
High and accurate catalyst loading	Less catalyst required over competitive products
High turnover number (*TON*)	Catalytic amount (*< 1 mol %*)
Reusability	Multi-uses possible
Ease of handling and purification	Free flowing, no static charge Easily removed by simple filtration
Ease of scalability	Scalable from mg up to multi-ton scale
Flexible formats	Amenable to use in Silia*Sep* & Silia*Prep* Cartridges
Available in bulk quantities	Can be delivered in large quantities and always in stock

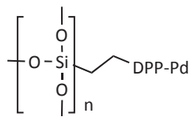
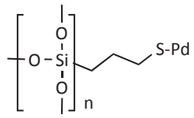
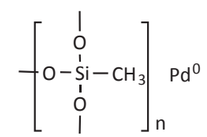
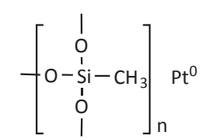
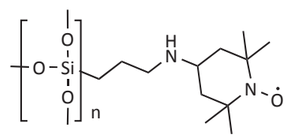
TEL.: 1 418 874.0054 FAX: 1 418 874.0355 TOLL-FREE: 1 877.SILICYCLE (NORTH AMERICA ONLY) WWW.SILICYCLE.COM INFO@SILICYCLE.COM

SiliaCat Heterogeneous Catalysts Product Range

SiliCycle, a leader in functionalized silica gels, has developed various catalysts at competitive prices.

SiliaCat Heterogeneous Catalysts Portfolio*

SiliaCat Heterogeneous Catalysts Portfolio

SiliaCat Name	Product Number	Structure	Brief Description	Typical Applications	SiliaCat Typical Characteristics: Color	Endcapping	Molecular Loading	Typical Tap Density	Solvent Compatibility	Prolonged Storage	SiliaCat Name
SiliaCat DPP-Pd	R390-100		The significant costs associated with precious metal catalysts and their tendency to remain in organic products has generated interest for solutions that increase reactivity and can enable the recovery and reuse of these metals. SiliaCat DPP-Pd is a unique diphenylphosphine palladium (II) heterogeneous catalyst made from a leach-resistant organoceramic matrix.	Suzuki, Heck Sonogashira, Kumada, Stille	Yellow	Yes	≥ 0.2 mmol/g	415 g/L	All solvents, aqueous and organic	Keep dry	SiliaCat DPP-Pd
SiliaCat S-Pd	R510-100		The significant costs associated with precious metal catalysts and their tendency to remain in organic products has generated interest for solutions that increase reactivity and can enable the recovery and reuse of these metals. SiliaCat S-Pd is a unique thiol-based palladium (II) heterogeneous catalysts made from a leach-resistant organoceramic matrix.	Suzuki, Heck Sonogashira, Kumada, Stille	Red - Orange	Yes	≥ 0.3 mmol/g	550 g/L	All organic solvents	Keep dry	SiliaCat S-Pd
NEW PRODUCT SiliaCat Pd^0	R815-100		SiliaCat Pd^0 is a new series of patent-protected sol–gel-entrapped Pd nanocatalysts. It is made from highly dispersed Pd nanoparticles (*uniformly in the range 4.0–6.0 nm*) encapsulated within an organosilica matrix.	Suzuki, Heck Sonogashira, Kumada, Stille, Selective debenzylation, Selective hydrogenation	Dark brown to black	Yes	-	-	All solvents, aqueous and organic	Keep cool (< 8 °C) Under Argon	SiliaCat Pd^0
NEW PRODUCT SiliaCat Pt^0	R820-100		SiliaCat Pt^0 is made of organosilica physically doped with nanostructured platinum (0), and is both stable and efficient. This catalyst was successfully prepared by a novel and simple sol-gel route. In the new procedure, Pt nanoparticles (*uniformly in the range 1.7–3.15 nm*) are encapsulated via an alcohol-free sol-gel process typical of enzyme sol-gel encapsulation.	Selective reduction of nitroarenes, Hydrosilylation	Dark brown to black	Yes	-	-	All solvents, aqueous and organic	Keep dry Under Argon	SiliaCat Pt^0
SiliaCat TEMPO	R723-100		SiliaCat TEMPO is a new oxidizing catalyst made from a proprietary class of organosilica-entrapped radicals. This encapsulation process confers enhanced reactivity and properties. The leach-resistant organoceramic matrix makes SiliaCat TEMPO highly efficient and selective compared to homogeneous TEMPO reagents. It also has a superior performance compared to polymer-supported TEMPO and silica-supported TEMPO in terms of both selectivity and stability. With SiliaCat TEMPO, no activation is required prior to use and selective aldehyde vs acid oxidation is possible. *U.S.Patent: 6,797,773 B1,2004*	Oxidation of alcohols or Aldehydes	Orange	Yes	≥ 0.70 mmol/g	639 g/L	All solvents, aqueous and organic	Keep dry	SiliaCat TEMPO

Formats: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 5kg, 10kg, 25kg, ...

TEL.: 1 418 874.0054 FAX: 1 418 874.0355 TOLL-FREE: 1 877.SILICYCLE (NORTH AMERICA ONLY) WWW.SILICYCLE.COM INFO@SILICYCLE.COM

Catalyst Screening Service

CONFIDENTIALITY ASSURED

Looking for the right Silia*Cat* Heterogeneous Catalyst to use? Contact us to take advantage of SiliCycle's expertise in catalysis. Our R&D team can find the optimal conditions for you.

Our Catalyst Screening Service is innovative because it provides a turn key solution to the pharmaceutical and manufacturing industries. Working with the substrates you identify, SiliCycle's chemists will quickly develop the most efficient catalysis process (*which catalyst and solvent to use, optimal concentrations, etc*).

We guarantee confidentiality, since in most cases our screening service requires us to work with APIs or other patented materials. This will ensure an easy technology transfer.

Make the call many major pharmaceutical companies have already made. Contact us to discuss how we can help you to reach your goals. Many screening services are available to fit your needs and budget.

Silia*Cat* - Regulatory Information

Silia*Cat* Heterogeneous Catalysts are being used more and more by GMP pharmaceutical, biotechnology, and fine chemical industries as well as contract research and manufacturing organizations. Many have run their own analysis proving Silia*Cat* can safely be used without compromising the purity of their compounds due to leaching.

Need specific regulatory files? SiliCycle can work with you to fulfill your requirements. We can provide custom regulatory documentations that include specific analytical tests in line with your needs.

SiliCycle is committed to high quality standards and strives to provide default-free products. In doing so, all products are manufactured in an ISO 9001:2008 compliant facility and submitted to a stringent quality control. Every lot must meet the quality specifications to be released for sale and a sample from every batch is kept for subsequent analysis. All products are shipped with the following information:

- Certificate of Analysis
  - Purity (*Leachables and extractables*)
  - Molecular loading
  - Surface Coverage
  - Volatile Content
- Material Safety Data Sheets (*MSDS*)
- BSE/TSE Declaration (*no animal origin*)
- Relevant Technical Information

Experimental Procedures and Optimization

Typical experimental procedures can be found for each catalytic reaction. Please note that these procedures are the starting suggestions meant to be starting points. Sometimes, optimization steps need to be undertaken to optimize yields and increase selectivity. Various parameters can be changed, one at a time or simultaneously, to improve results.

Number of mol % of Silia*Cat* Catalysts

For each new experiment, we suggest using a molar percent of Silia*Cat* with respect to the substrate. This quantity has to then be optimized in order to obtain a good catalytic activity with the lowest consumption of the Silia*Cat*. For initial experiments we suggest to use an higher mol % of Silia*Cat* Catalyst in respect to the substrate and then decrease the quantity if yield and kinetics are already in line with your needs. During development applications work at SiliCycle, we always start using 1 mol % of catalyst.

Solvent

Silia*Cat* can safely be used in a wide range of organic and aqueous solvents commonly used in laboratory and in process work, such as DMF, DMSO, THF, ACN, alcohols, ethers, chlorinated solvents, water, etc. The nature of the solvent does sometimes influence the catalytic efficiency, however. If yield is low or kinetics are too slow, changing solvent or adding a co-solvent should be considered.

Solution Concentration

At low substrate concentration, the activity of the catalyst will be directly proportional to the number of moles of substrate available. If you increase the concentration of the substrate, the activity will increase until the active sites become saturated. So the substrate concentration is a parameter that needs to be optimized to develop your catalytic conditions.

Temperature

A catalyst's purpose is to enhance the kinetics of a reaction, so we recommend running the experiments at room temperature. In the optimization step, the temperature could be adjusted, if it is needed.

Reaction Time

In the case that the TOF is low, and increasing the temperature to increase the kinetics is not possible, we recommend increasing the contact time with the catalyst to complete the reaction. Also, in this case, increasing of the amount of catalyst is an option.

TEL.: 1 418 874.0054 FAX: 1 418 874.0355 TOLL-FREE: 1 877.SILICYCLE (NORTH AMERICA ONLY) WWW.SILICYCLE.COM INFO@SILICYCLE.COM

Silia*Cat*'s Compatibility with New Technologies

Silia*Cat* In Flow Chemistry and Microwave Assisted Experiments

Silia*Cat* can also be used in flow chemistry and under microwave radiation. In flow chemistry, simply place the Silia*Cat* inside the solid-phase reactor included in the flow system (*i.e. Syrris Asia® Solid Phase Chemistry Reactor*) and run the reaction. See page 78 for more details.

In microwave experiments, Silia*Cat* showed excellent catalytic efficiency in a short period of time. See following pages for the different applications developed.

Catalysis Definitions and Calculation

Silia*Cat* Heterogeneous Catalysts are sol-gel silica-supported catalysts that can be used to replace homogeneous catalysts. The process for using Silia*Cat* is outlined in the scheme page 21.

What is a Turnover Number (TON)?

In catalysis, the term turnover number has two meanings: the number of moles of substrate that a mole of catalyst can convert before becoming inactivated and is the amount of substrate converted per the amount of catalyst used.

In theory, the Ideal catalyst would have an infinite turnover number and would never be consumed. In practice, turnover numbers begin at 100 and can go up to a million, more so in some cases.

What is a Turnover Frequency (TOF)?

A catalyst's turnover frequency number, or turnover number per time unit, characterizes its level of activity. So the TOF is the total number of moles transformed into the desired product by one mole of active site per hour. The larger the TOF, the more active the catalyst.

TOF = TON/hour

How to Calculate the Amount of Silia*Cat* Needed Based on Mol %?

One mol % (1 mol %) means 0.01 molar equivalent. If 3 mmol of the substrate is used, then 0.03 mmol of Silia*Cat* catalyst is required. To determine the weight of the catalyst needed, simply divide this value by the loading of the catalyst. For example, Silia*Cat* DPP-Pd typical loading is 0.2 mmol/g, so 0.15 g is needed.

Solvent Molar Concentration

A 1.2 M solvent concentration means:

1.2 mmol of substrate per mL of solvent
(*or 1.2 mol of substrate per L of solvent*)

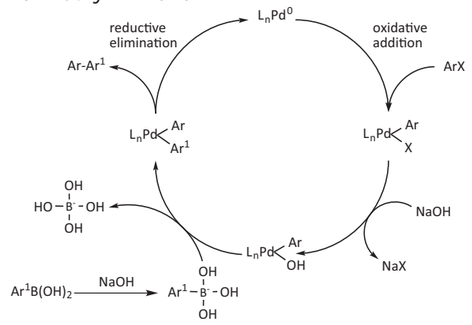
Volume of solvent needed = $\frac{\text{mmol of substrate used}}{\text{molar concentration desired}}$

For example, if 3 mmol of the substrate is used, then, 2.5 mL of solvent is necessary to reach a 1.2 M concentration.

Suzuki Coupling Using Pd-based Silia*Cat*

The Suzuki coupling (*also called Suzuki-Miyaura reaction*) is the reaction between a boronic acid and a halide catalyzed by a palladium (0) catalyst widely used in organic synthesis. At first, only aryl and vinyl substrates could undergo Suzuki coupling. Now, catalysts are becoming so powerful that the substrate scope has broadened to include: alkyl-, alkenyl- & alkynyl- halides, triflates and organoboranes, trifluoroborates or borate esters.

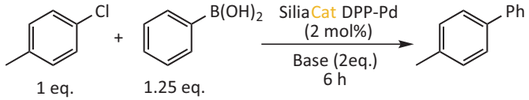
Its discovery was awarded the Nobel Prize in Chemistry in 2010.



Solvent and Base Effects

The choice of solvent and base play an important part in the Suzuki reaction. Different solvents and bases were tested to find the most suitable combination. Total conversion was obtained in both ethanol and propanol. With THF, dioxane, toluene and DMF, the kinetics were lower.

For the base, potassium carbonate (K_2CO_3) is the best. However, in some cases, Na_2CO_3 and NaOAc can also be used.



Solvent and Base Effects

Solvent	Temp. (°C)	Conversion / Selectivity (%)					
		K_2CO_3	Na_2CO_3	KOAc	NaOAc	K_2HPO_4	Et_3N
MeOH	64	74 / 95	69 / 99	63 / 98	63 / 98	73 / 100	72 / 93
EtOH	77	100 / 98	100 / 97	82 / 99	85 / 100	79 / 100	77 / 93
EtOH/H_2O (15%)	77	100 / 100	82 / 100	78 / 100	88 / 100	86 / 98	89 / 95
1-PrOH	90	100 / 95	70 / 97	90 / 99	91 / 99	15 / 100	20 / 95
2-PrOH	77	100 / 100	43 / 93	90 / 99	72 / 100	50 / 100	20 / 100
THF	64	30 / 93	15 / -	45 / 89	35 / 94	37 / 95	5 / -
MeTHF	77	40 / 95	33 / 100	39 / 100	56 / 100	30 / 97	4 / -
Dioxane	90	50 / 90	30 / 93	56 / 93	35 / 94	20 / 90	No reaction
Toluene	90	47 / 98	23 / 87	49 / 96	10 / 90	65 / 95	No reaction
DMF	90	50 / 100	30 / 100	15 / 100	17 / 100	7 / 100	No reaction

Catalyst Concentration Effect

Decreasing the mol % of the catalyst lowers the kinetics of the reaction, but the total conversion can still be achieved. In this example, the addition of water significantly improves catalyst activity. Even if the catalyst amount is divided by 10, the TOF is still increased by a factor of five.

(*Cdns: Silia*Cat* DPP-Pd, $PhB(OH)_2$ (1.1 eq.), K_2CO_3 (1.5 eq.) RT*).

Catalyst Concentration Effect

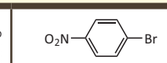
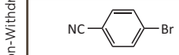
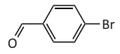
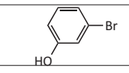
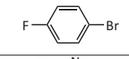
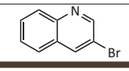
mol %	Solvent (M)	Time (h)	Conv. (%)	TON	TOF
0.2	EtOH (0.05)	0.5	100	500	1,000
0.1	EtOH (0.05)	1	100	1,000	1,000
0.01	EtOH/H_2O (0.08)	2	100	10,000	5,000
0.002	EtOH/H_2O (0.08)	16	100	50,000	3,125

Pd-Based Silia*Cat*'s Catalytic Performance Comparison and Reusability

All Silia*Cat* Pd-based catalysts can be used for Suzuki coupling. The table below presents the best conditions for bromo- substrates. It can be seen that even with half the catalyst amount, Silia*Cat* Pd^0 is the more active catalyst.

For substrates with electron-withdrawing groups, Silia*Cat* catalysts can be reused more than 5 times with a minimal loss of activity and leaching. For substrates containing an electron-donating group, Silia*Cat* catalysts can be used up to 3 times with only a small effect on activity.

Pd-Based Silia*Cat*'s Catalytic Performance Comparison and Reusability

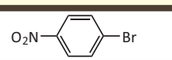
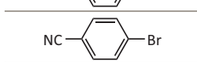
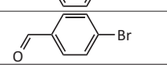
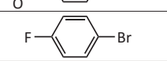
	Substrate (R)	Silia*Cat* Performance Comparison [Conversion / Selectivity (%)]			Reusability [Conversion / Selectivity (%)] Pd & Si Leaching (ppm)[1]			
		DPP-Pd (1 mol %)[a-b]	S-Pd (1 mol %)[c]	Pd^0 (0.5 mol %)[d]	Run 2	Run 3	Run 4	Run 5
Electron-Withdrawing		100 / 100 Pd: 0.1, Si: 2	100 / 99	100 / 99	100 / 100 Pd: 0.05, Si: 1	100 / 100 Pd: 0.08, Si: 1.5	100 / 100 Pd: 0.1, Si: 3	99 / 98 Pd: 0.1, Si: 3.5
		100 / 97 Pd: 0.1, Si: 3	100 / 99	99 / 97	98 / 99 Pd: 0.1, Si: 8	98 / 99 Pd: 0.07, Si: 5	100 / 99 Pd: 0.1, Si: 6	99 / 98 Pd: 0.1, Si: 5
		100 / 97 Pd: 0.1, Si: 6	94 /88	95 / 98	99 / 90 Pd: 0.2, Si: 7	97 / 92 Pd: 0.2, Si: 8	99 / 98 Pd: 0.1, Si: 4	98 / 97 Pd: 0.1, Si: 5
Electron-Donating		100 / 99 Pd: 0.9, Si: 5	82 / 100	83 / 100	100 / 100 Pd: 0.6, Si: 9	100 / 98 Pd: 0.4, Si: 7	60 / 97 Pd: 0.05, Si: 6	-
		100 / 80 Pd: 0.07, Si: 3	94 / 100	98 / 99	99 / 99 Pd: 0.04, Si: 1.5	98 / 98 Pd: 0.1, Si: 2	81 / 94 Pd: 0.06, Si: 2	73 / 95 Pd: 0.03, Si: 7
		100 / 99 Pd: 2.1, Si: 10	72 / 95	97 / 95	88 / 90 Pd: 0.3, Si: 7	75 / 95 Pd: 4, Si: 9	87 / 99 Pd: 0.6, Si: 10	68 / 96 Pd: 04, Si: 11

[a] Corresponds to "Run 1" in the reusability study.
General exp. cond.: 1 eq. substrate, 1.2 eq. $PhB(OH)_2$, 2 eq. K_2CO_3; [b] MeOH (0.1 M), 2 h, 65°C; [c] $EtOH/H_2O$ (0.12 M) 4h, 77°C; [d] EtOH (0.12 M) 2h, 77°C.

[1] Using Silia*Cat* DPP-Pd as catalyst under the same conditions previously described. Run #1 is the result presented in the performance comparison section of the table.

The performance of the Silia*Cat* DPP-Pd and S-Pd catalysts for Suzuki coupling was also compared in microwave assisted experiments for brominated substrates. Both products exhibit a very high performance in microwave experiments. After only 5 minutes, 100% of the product is obtained in most experiments. Both also present high selectivity, with yields nearly reaching 100%. The products were also tested for chlorinated substrates as presented on the following page.

Catalytic Performance in Microwave

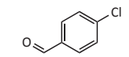
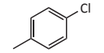
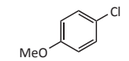
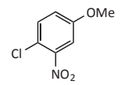
Substrate (R)	Conversion (%) / Yield (%)	
	Silia*Cat* DPP-Pd (0.5 mol %)[a-b]	Silia*Cat* S-Pd (0.5 mol %)[c]
	100 / 99.5	100 / 99.3
	100 / 99.4	100 / -
	100 / 88	100 / -
	98 / 97.3	72 / -

General exp. cond.: 1 eq. substrate, 1.1 eq. $PhB(OH)_2$, 1.5 eq. K_2CO_3;
[a] MeOH (0.2 M), 5 min, 75°C, 150 W, 150 psi; [b] MeOH (0.2 M), 5 min, 75°C, 200 W, 200 psi, [c] 15 min.

Pd-based Silia*Cat*'s Catalytic Performance Comparison (con't)

The Silia*Cat* Pd-based catalysts can also be used for Suzuki coupling with chlorinated substrates in both conventional and microwave conditions. We have chosen to do this study with Silia*Cat* DPP-Pd.

Catalytic Performance of Chlorinated Substrates

Substrate (R)	Conversion /Yield (%)[a]	Substrate (R)	Conversion /Yield (%)[a]
	98 / 93		99 / -
	98 / 96		Bulk: 100 / 98 MW[b]: 100 / 95

[a]Exp. cond. in bulk: 1.5 mol % of Silia*Cat*, 1 eq. substrate, 1.5 eq. $PhB(OH)_2$, 2 eq. K_2CO_3, $EtOH/H_2O$ 15% (0.12M), 6 h, reflux. [b] Microwave: 1 mol % of Silia*Cat*, 15 min, 125°C.

Conclusion for Suzuki Coupling

In conclusion, Silia*Cat*, can be used successfuly for Suzuki coupling reactions with iodide, bromide and chloride aryl substrates in conventional or in microwaves conditions. The Silia*Cat* DPP-Pd gives better performance versus the Silia*Cat* S-Pd and nearly equivalent to the Silia*Cat* Pd^0 for the substrates presented.

Suzuki Coupling Typical Experimental Condition

Conventional Experimental Conditions

Reaction

All products except the catalyst are added to a round bottom flask equipped with a condenser and a magnetic stirrer. Bring mixture to reflux and, after 10 minutes (*when the solution is homogeneous*), add the required quantity of catalyst.

Work-up

Once the reaction is complete (*determined by TLC or GC-MS*), the catalyst is filtered at room temperature, rinsed twice with water and three times with the solvent used in the reaction, and finally dried and stored for future use. The reaction mixture obtained after filtration of the catalyst is evaporated, and the product is extracted using ethyl acetate (AcOEt) or diethyl ether (Et_2O) and washed twice with water. The organic phase is dried using magnesium sulfate ($MgSO_4$), and filtered, and the solvent is evaporated. The crude mixture is purified using flash chromatography, if needed. Also applicable to microwave conditions.

Microwave Conditions

Reaction

All products are added to a microwave tube equipped with a magnetic stirrer. Set microwave conditions to:

- Power: 150 W
- Pressure: 150 psi
- Temperature: 75 - 150°C
- Reaction Time: 5 - 15 min

Suzuki Coupling Typical Experimental Conditions

Products	Conventional Conditions			Microwave Conditions		
	Ar-Iodide	Ar-Bromide	Ar-Chloride	Ar-Iodide	Ar-Bromide	Ar-Chloride
Base [K_2CO_3]	1.5 eq.	1.5 eq.	2.0 eq.	1.5 eq.	1.5 eq.	2.0 eq.
Boronic Acid	1.2 eq.	1.2 eq.	1.5 eq.	1.2 eq.	1.2 eq.	1.5 eq.
Silia*Cat* Catalyst	≥ 0.5 mol %	≥ 0.5 mol %	≥ 1.0 mol %	≥ 0.5 mol %	≥ 0.5 mol %	≥ 1.0 mol %
Best Solvents (HPLC Grade)	MeOH (0.05 - 0.1 M)	$EtOH/H_2O$ (10:1, 0.12 M)	EtOH or TBA/H_2O (10:1.5, 0.12 M)	MeOH (0.2 M)	MeOH (0.2 M)	$EtOH/H_2O$ (10:1, 0.2 M)

***Note: molar concentration is related to the substrate.**

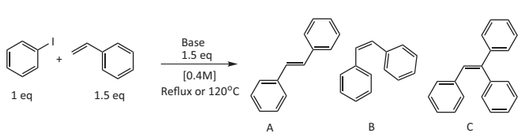
Heck Coupling Using Silia*Cat* DPP-Pd & S-Pd

The Heck reaction, also known as the Mizoroki-Heck reaction, is the coupling of a halide with an alkene in the presence of a base and a palladium catalyst. This coupling allows a substitution reaction on alkenes and is of great importance in pharmaceutical research. We determined that the best catalyst for this reaction is Silia*Cat* DPP-Pd. It showed good reactivity for aryl iodides, bromides and chlorides.

Note: Silia*Cat* Pd^0 results were not available at the time of printing. Contact us for details.

Base and Solvent Effects

The Heck coupling between iodobenzene and styrene was used to evaluate the influence of solvent and base. The best combinations are KOAc/DMF, Et_3N/MeCN and Pr_3N/neat. Using these systems, high yields and great selectivity in favor of product A were obtained.

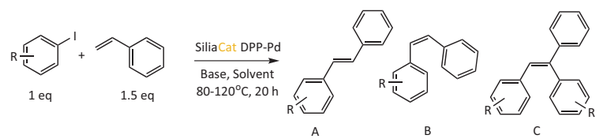


Base and Solvent Effects (Silia*Cat* DPP-Pd)

Silia*Cat* (mol %)	Base	Solvent (0.4 M)	Time (h)	Conversion A / B / C (%)
0.5	KOAc	DMF	24	100 (90 / 9.5 / 0.5)
0.5	Na_2CO_3	DMF	24	67 (62 / 47 / 0)
0.1	Et_3N	MeCN	24	93 (77 / 6 / 11)
0.1	Et_3N	H_2O	24	75 (70 / 5 / 0)
0.1	Pr_3N	(neat)	20	100 (95 / 5 / 0)

Catalytic Performance and Comparison vs Homogeneous Catalyst

Silia*Cat* DPP-Pd is a very efficient catalyst for the Heck coupling and allows greater selectivity over homogeneous Pd catalyst (*TPP is required*). In addition to higher yield of the desired product, the catalyst left minimal residual Pd, TPP or TPPO in solution that would have otherwise required the use of a metal scavenger, chromatography or trituration to remove.

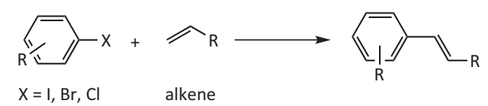


Catalytic Performance and Comparaison vs Homogeneous

Substrate R	Substrate X	Silia*Cat* DPP-Pd (mol %)	Base	Solvent (0.4 M)	Conversion A / B / C (%)	Phosphine Leaching (ppm)
4-CN	Br	0.25	NaOAc	DMF	100 (95 / 5 / -)	-
4-NO_2	Br	0.25	NaOAc	DMF	99 (97 / 2 / -)	-
2-CH_3	Br	0.25	Et_3N	MeCN	71 (67 / 5 / -)	-
4-OMe	I	0.25	Et_3N	MeCN	75 (60 / 15 / -)	-
H	I	0.1	Et_3N	MeCN	100 (98 / 2 / -)	0
H	I	1.0 $Pd(OAc)_2$ PPh_3	Et_3N	MeCN	100 (70 / 22 / 8)	6,030

Substrate Scope, Leaching and Microwave Compatibility

Silia*Cat* catalysts are efficient in the Heck coupling with different substrates. In all cases, conversion and selectivities were excellent. Leaching results were all below FDA regulations, and no further metal removal was needed. Microwave technology allows faster kinetics with good yields.



Substrate Scope, Leaching and Microwave (MW) Compatibility

Rn	Mode	Silia*Cat* DPP-Pd mol %	Time	Temp.	Conv./Sel.(%)	Leaching (ppm)	Silia*Cat* S-Pd mol %	Time	Temp.	Conv./Sel.(%)	Leaching (ppm)
1	Batch	0.5	24 h	120°C	100 / 97	-	0.5	24 h	120°C	98 / 92	-
	MW	0.2	10 m	125°C	93 / 85	P: 0.3, Pd: 0.02, Si: 0.8	0.2	15 m	125°C	97 / 93	Pd: 3.8, Si: 1.9
2	Batch	0.2	24 h	135°C	100 / 98	-	0.25	24 h	120°C	85 / 75	-
	MW	0.2 0.5[1]	10 m 30 m[1]	125°C 150°C[1]	92 / 81 99 / 93[1]	- P: 0.7, Pd: 0.02, Si: 1.6	0.2	15 m	125°C	87 / 76	Pd: 0.3, Si: 0.8

[1] Et_3N in water

Heck Coupling Typical Experimental Procedure

Conventional Experimental Conditions

Reaction

All products except the catalyst are added to a round bottom flask equipped with a condenser and a magnetic stirrer. Bring mixture to reflux (MeCN) or to 120°C (DMF or NMP) and after 10 minutes (*when solution is homogeneous*) add the desired quantity of catalyst.

Work-up

Once the reaction is complete (*determined by TLC or GC-MS*), follow the same work-up procedure as for Suzuki coupling conventional experimental conditions as they are applicable to microwave conditions.

Microwave Conditions

Reaction

All products are added to a microwave tube equipped with a magnetic stirrer. Set microwave conditions to:

- Power: 100 W (I-) or 200 W (Br-, Cl-)
- Pressure: 150 psi (I-) or 200 psi (Br-, Cl-)
- Temperature: 100°C (I-) or 125°C (Br-, Cl-)
- Reaction Time: 10 min (I-) or 15 min (Br-, Cl-)

Heck Coupling Typical Experimental Conditions

Products	Conventional Conditions for 1 eq of: Ar-Iodide	Ar-Bromide	Ar-Chloride	Microwave Conditions for 1 eq of: Ar-Iodide	Ar-Bromide	Ar-Chloride
Base	1.5 eq. [Et_3N or NaOAc]	1.5 eq. [NaOAc]	1.5/0.5 eq. [$Ca(OH)_2$/TBAB]	1.5 eq. [Et_3N or NaOAc]	1.5 eq. [K_2CO_3]	2.0 eq. [K_2CO_3]
Olefin	1.2 eq.	1.2 - 2.0 eq.	1.2 - 2.0 eq.	1.2 - 2.0 eq.	1.2 - 2.0 eq.	1.2 - 2.0 eq.
Silia*Cat* Catalyst	≥ 0.5 mol %	≥ 0.5 mol %	≥ 1.0 mol %	≥ 0.2 mol %	≥ 0.2 mol %	≥ 1.0 mol %
Best Solvents (HPLC Grade)	MeCN (1.2 M) DMF (0.75 M)	DMF (0.75 - 1.5 M)	NMP/H_2O (1:1, 1.67 M)	MeOH (0.2 M)	MeOH (0.2 M)	EtOH/H_2O (10:1, 0.2 M)

*Note: molar concentration is related to the substrate.

Sonogashira Coupling Using Silia*Cat* Catalysts

The Sonogashira coupling reaction of aryl halides and terminal acetylenes is an effective method for the formation of substituted acetylenes. This reaction is frequently utilized as a key step in natural product chemistry and for the synthesis of acetylene compounds, which have several applications.

Catalyst Concentration and Solvent Effects

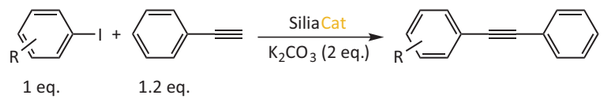
Sonogashira coupling between iodonitrobenzene and phenylacetylene was achieved easily and without the need for co-catalysts to activate the alkyne, making the use of Silia*Cat* an efficient method for the formation of substituted acetylenes. All catalysts screened presented excellent efficiency, even in low amounts.

Catalyst Concentration and Solvent Effects

Silia*Cat* DPP-Pd					Silia*Cat* S-Pd					Silia*Cat* Pd^0				
mol %	Solvent (M)	Time (min)	Conv. (%)	TON (TOF)	mol %	Solvent (M)	Time (min)	Conv. (%)	TON (TOF)	mol %	Solvent (M)	Time (min)	Conv. (%)	TON (TOF)
0.5	EtOH/H_2O (0.07)	30	100	200 (400)	0.5	EtOH/H_2O (0.07)	5	100	200 (2,500)	0.1	EtOH (0.1)	2 h	100	1,000 (500)
0.5	MeOH/H_2O (0.07)	5	100	200 (2500)	0.5	MeOH/H_2O (0.07)	1 h	100	200 (200)	0.1	EtOH (0.05)	30	100	1,000 (2,000)
0.1	EtOH/H_2O (0.07)	1 h	100	1,000 (1,000)	0.1	EtOH/H_2O (0.07)	1 h	100	1,000 (1,000)					
0.1	MeOH/H_2O (0.07)	15	100	1,000 (4,000)										
0.01	EtOH/H_2O (0.13)	3 h	100	10,000 (4,000)										
0.002	EtOH/H_2O (0.13)	8 h	100	50,000										

Iodo-Substrate Scope and Microwave Compatibility

Sonogashira couplings between iodoaryls and phenylacetylene are achieved with ease and without the need for co-catalysts to activate the alkyne.This shows that Silia*Cat* is an efficient tool for the formation of substituted acetylenes.



1 eq. 1.2 eq.

Iodo- Substrate Scope and Microwave Compatibility

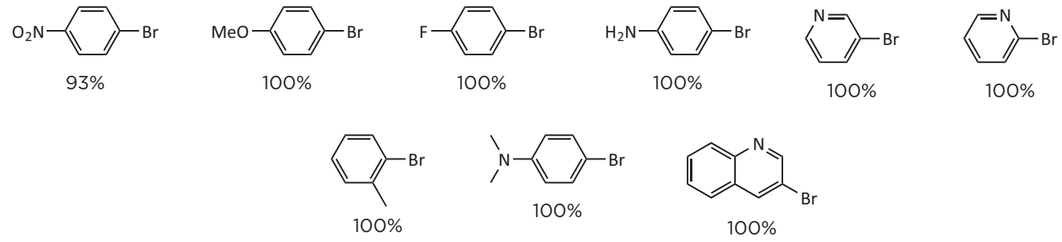
R	Mode	Silia*Cat* DPP-Pd			Silia*Cat* S-Pd			Silia*Cat* Pd^0		
		mol %	Conditions	Conv. / Sel. (%)	mol %	Conditions	Conv. / Sel. (%)	mol %	Conditions	Conv. / Sel.(%)
4-NO_2	Batch	1	EtOH (0.08 M) 77°C, 4 h	100 / 100	1	EtOH (0.08 M) 77°C, 4 h	100 / 100	1	EtOH (0.08 M) 77°C, 4 h	100 / 100
	MW	0.6	MeOH/H_2O (0.2 M) 100°C, 2 min	100 / -	0.6	MeOH/H_2O (0.2 M) 100°C, 2 min	100 / -	0.1	MeOH (0.1 M) 75°C, 5 min	100 / -
4-OMe	Batch	1	EtOH (0.08 M) 77°C, 4 h	99 / 98	1	EtOH (0.08 M) 77°C, 4 h	100 / 100	1	EtOH (0.08 M) 77°C, 4 h	99 / 98
4-CH_3	Batch	1	EtOH (0.08 M) 77°C, 4 h	100 / 100	1	EtOH (0.08 M) 77°C, 4 h	100 / 99	1	EtOH (0.08 M) 77°C, 4 h	100 / 100
	MW	0.5	MeOH/H_2O (0.2 M) 100°C, 2 min	90 / -	1	MeOH/H_2O (0.2 M) 100°C, 2 min	88 / -	0.1	MeOH (0.2 M) 75°C, 5 min	100 / -

Bromo- Substrate Scope and Microwave Compatibility

Silia*Cat* DPP-Pd and Pd^0 are also efficient catalysts for use with bromo substrates. A few examples of the Sonogashira coupling between various bromoaryls substrates (1 eq.) and phenylacetylene (1.25 eq.) using K_2CO_3 (2 eq.) in MeOH (0.2 M) are shown below.

Conversions obtained with 1 mol % of Silia*Cat* DPP-Pd under microwave irradiation are presented below. Conventional methodology is also possible, but kinetics are significantly lower (*a few hours compared to 15 minutes*).

Bromo- Substrate Scope Conversion (%) Results using Silia*Cat* DPP-Pd



Sonogashira Coupling Typical Experimental Procedure

Conventional Experimental Conditions

Reaction

All products except the catalyst are added to a round bottom flask equipped with a condenser and a magnetic stirrer. Bring mixture to reflux, and after 10 minutes (*when the solution is homogeneous*) add the required quantity of catalyst.

Work-up

Once the reaction is complete (*determined by TLC or GC-MS*), follow the same work-up procedure as for Suzuki coupling conventional experimental conditions as they are applicable to microwave conditions.

Microwave Conditions

Reaction

All products are added to a microwave tube equipped with a magnetic stirrer. Set microwave conditions to:

- Power: 150 W (I-) or 200 W (Br-)
- Pressure: 150 psi (I-) or 200 psi (Br-)
- Temperature: 100°C (I-) or 100 - 150°C (Br-)
- Reaction Time: 5 - 15 min (I-) or 5 - 20 min (Br-)

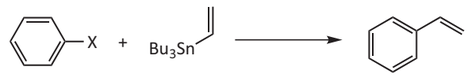
Sonogashira Coupling Typical Experimental Conditions

Products	Standard Conditions for 1 eq of:		Microwave Conditions for 1 eq of:	
	Ar-Iodide	Ar-Bromide	Ar-Iodide	Ar-Bromide
Base [K_2CO_3]	1.5 eq.	1.5 eq.	1.5 eq.	2.0 eq.
Alkyne	1.1 eq.	1.2 5 eq.	1.10 eq.	1.5 eq.
Silia*Cat* Catalyst	≥ 0.5 mol %	≥ 1.0 mol %	≥ 0.5 mol %	≥ 1.0 mol %
Best Solvents (HPLC Grade)	For room temperature reaction: MeOH (0.02 M) For reflux reaction: MeOH (0.05 - 0.13 M, typ.: 0.07 M) or EtOH/H_2O (10:1, 0.1 M)		MeOH (0.2M)	MeOH/H_2O (10:1, 0.2 M)

*Note: molar concentration is related to the substrate.

Stille Coupling Using Silia*Cat* Pd Catalysts

The Stille coupling is a versatile reaction for C-C bond formation. It is a coupling between a halide and an organotin compound. This reaction is widely used in synthesis, but a major drawback is the toxicity of the tin compounds involved. In Stille couplings, a Pd^0 or Pd^{II} catalyst is required, and it must be compatible with a wide variety of functional groups (*very few limitation on the R-group*). SiliCycle has developed catalysts that are highly efficient for Stille couplings, as shown below.



Note: Silia*Cat* Pd^0 results were not available at the time of printing.

Catalyst Concentration and Solvent Effects

Increasing the amount of the catalyst, for the same solvent and at a constant substrate concentration, improves kinetics (*see table below*). With a mol % of 0.25, the reaction was not completed in 22 h. With a mol % of 2.0, the reaction was completed in 17 h.

As a general rule, if the solvent and the concentration of the substrate are kept constant, increasing the amount of the catalyst, thus increasing the member of the active sites, will speed up the kinetics of the reaction.

This table also shows the importance of the solvent. At low catalyst concentration, 0.25 mol % in dioxane, the reaction was not completed in 22 h. However, under the same conditions but with toluene as the solvent, the reaction was completed in 16 h. In dioxane, the same activity is observed for a concentration of 2.0 mol %. The solvent is responsible for diffusion of the substrate to the active sites, so the better the diffusion, the higher the kinetics will be.

In all experiments, determining the optimal quantity of Silia*Cat* in respect to the solvent should be done.

Catalyst Concentration and Solvent Effects

Silia*Cat* DPP-Pd (mol %)	Solvent (M)	Time (h)	Conversion (%)
2.0	Dioxane (0.1 M)	17	99
0.5	Dioxane (0.1 M)	20	100
0.25	Dioxane (0.1 M)	22	74
0.25	Toluene (0.1 M)	16	99

Silia*Cat* DPP-Pd Reusability and Leaching

The minimal leaching and the robustness of the organoceramic matrix are important factors that allow Silia*Cat* DPP-Pd to be reused several times.

Silia*Cat* DPP-Pd Reusability and Leaching

Reusability	Conversion (%)	Pd Leaching (ppm)
1st	100	3.0
2nd	100	1.7
3rd	100	2.3
4th	100	2.3

Catalytic Activity and Additive CsF Influence

Reactions were performed at reflux until the GC/MS analysis showed maximum conversion. Anhydrous conditions are not required.

Catalytic Activity and Additive CsF Influence

Substrate (R)	Halide (X)	Silia*Cat* DPP-Pd (mol %)	Additive (eq.)	Solvent (M)	Time (h)	Conversion (%)
4-CN	Br	2	-	Dioxane (0.1 M)	18	87
4-F	Br	10	-	Dioxane (0.1 M)	24	99
4-F	Br	10	CsF (2)	Toluene (0.1 M)	24	100
H	Br	10	-	Toluene (0.1 M)	24	100
4-CH_3	Br	10	CsF (2)	Dioxane (0.1 M)	24	100
4-OCH_3	Br	10	CsF (2)	Dioxane (0.1 M)	24	100
H	I	10	CsF (2)	Toluene (0.1 M)	24	100
4-NO_2	I	2	-	Dioxane (0.1 M)	18	88

Note: $R'SnBu_3$ was vinyl (1.1 eq.)

Silia*Cat* DPP-Pd vs Competitive Catalysts

Comparative analysis with other Pd catalysts available on the market demonstrates the Silia*Cat* DPP-Pd to be comparable or better in standard Stille conditions. Table at right shows conversion %.

Silia*Cat* DPP-Pd vs Competitive Catalysts

Silia*Cat* DPP-Pd	Escat 1351	Encat 30	Royer Catalyst	$Pd(PPh_3)_4$	$Pd(OAc)_2$
99	44	95	90	72	20

Stille Coupling Typical Experimental Procedure

Conventional Experimental Conditions

Reaction

All products except the catalyst are added to a round bottom flask equipped with a condenser and a magnetic stirrer. Bring mixture to reflux, and after 10 minutes (*when the solution is homogeneous*) add the required quantity of catalyst.

Work-up

Once the reaction is complete (*determined by TLC or GC-MS*), follow the same work-up procedure as for Suzuki coupling standard conditions.

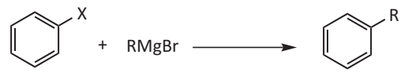
Experimental Conditions - Stille Coupling

Products	Standard Conditions for 1 eq of: Ar-Iodide & Ar-Bromide
Base [K_2CO_3]	1.0- 2.0 eq. (usually 1.1 eq.)
Additive (CsF)	If needed, add 2.0 eq. for higher conversion
Silia*Cat* Catalyst	0.25 - 10.0 mol % (typ.: 2 mol % for -I and 2 - 10 mol % for -Br)
Best Solvents (HPLC Grade)	Dioxane (0.1 M) or Toluene (0.1 M)

*__Note__: molar concentration is related to the substrate.

Kumada Coupling Using Silia*Cat* Pd Catalysts

The Kumada coupling is the direct cross-coupling between an alkyl or an aryl Grignard and a halocarbon. It can be catalyzed by a Pd or a Ni catalyst.

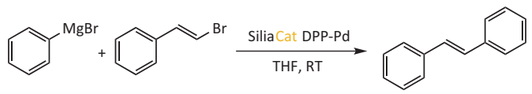


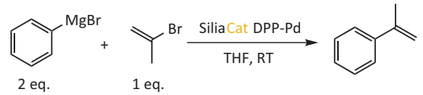
Note: Silia*Cat* Pd^0 results were not available at the time of printing.

Catalyst Concentration Effect

At a constant concentration of substrate, an increase of the amount of Silia*Cat* from 0.1 (or 0.2) to 1.0 will increase the kinetics (*completed in only 15 minutes*).

By increasing the concentration of the catalyst, thus thereby increasing the number of active sites, conversion of the substrate will be favored.





Catalyst Concentration Effect

Silia*Cat* DPP-Pd (mol %)	Solvent (M)	Time (min)	Conversion (%)
1.0	THF (0.07 M)	15	96
0.5	THF (0.07 M)	15	95
0.2	THF (0.08 M)	2 h	94

Catalyst Concentration Effect

Silia*Cat* DPP-Pd (mol %)	Solvent (M)	Time (min)	Conversion (%)
1.0	THF (0.08 M)	15	98
0.5	THF (0.08 M)	90	96
0.2	THF (0.08 M)	4 h	98

Catalyst Reusability and Leaching

Minimal leaching and the robustness of the organoceramic matrix are important factors that allow it to be reused several times.

Silia*Cat* Reusability and Leaching

Reusability	Conversion (%)	Leaching (ppm) Pd	Leaching (ppm) Si
1st	98	0.20	1.5
2nd	95	0.20	2.3
3rd	94	0.50	1.7
4th	77	0.02	1.9

Catalytic Activity and Leaching

Silia*Cat* DPP-Pd showed good reactivity for aryl iodides and bromides. Inert conditions are required for Kumada couplings due to the presence of Grignard reagent.

Catalytic Activity and Leaching

Substrate (R) / Halide (X)	R-MgBr (2 eq.)	Solvent (M)	Time (h)	Conversion (%)	Leaching (ppm) Pd	Leaching (ppm) Si
4-OCH_3 / Br	Ph-MgBr	THF (0.05 M)	18	98	0.3	0.2
4-OCH_3 / Br	i-Bu-MgBr	THF (0.05 M)	18	95	-	-
4-CH_3 / Br	Ph-MgBr	THF (0.05 M)	18	96	-	-
4-CH_3 / Br	i-Bu-MgBr	THF (0.05 M)	18	98	-	-
4-F / Br	Ph-MgBr	THF (0.08 M)	24	94	< 0.01	1.5
H / I	Ph-MgBr	THF (0.08 M)	24	99	-	-
4-OCH_3 / I	Ph-MgBr	THF (0.08 M)	24	94	-	-
4-CH_3 / I	Ph-MgBr	THF (0.08 M)	24	95	< 0.01	1.0

Kumada Coupling Typical Experimental Procedure

Conventional Experimental Conditions

Reaction

All products under inert conditions (*catalyst, solvent, substrates, and Grignard reagent*) are added to a Schlenk or a dry round bottom flask equipped with a magnetic stirrer. The mixture was stirred at room temperature until the TLC or GC-MS analysis confirmed reaction completion (18-24h).

Work-up

Once the reaction is completed, inert conditions are not necessary. Follow same work-up procedure as for Suzuki coupling conventional experimental conditions.

Experimental Conditions - Kumada Coupling

Products	Standard Conditions for 1 eq of: Ar-Iodide & Ar-Bromide
R-MgBr	2.0 eq.
Silia*Cat* Catalyst	2.0 - 10.0 mol % (usually 5 mol %)
Best Solvents (HPLC Grade)	Tetrahydrofuran (0.05 - 0.08 M) (usually 0.08 M)

*Note: molar concentration is related to the substrate. Reaction need to be done at room temperature under inert atmosphere.

Selective Hydrogenation of Nitroarenes Using Silia*Cat* Pt^0

Functionalized anilines are important intermediates in various industries such as pharmaceuticals, polymers, and dyes. Simple aromatic amines are generally obtained by catalytic hydrogenation of nitroarene compounds with various heterogeneous commercial catalysts (*supported nickel, copper, cobalt*) including Pt/C. Yet, the selective reduction of a nitro group with H_2 when other reducible groups are present in the same molecule is generally not feasible with these catalytic materials and requires the use of advanced heterogeneous catalysts. Silia*Cat* Pt^0 exhibits chemoselective catalytic activity for the hydrogenation reaction of a series of substituted nitro compounds under remarkably mild conditions, namely at room temperature with 1 bar H_2 in a simple hydrogen balloon, using a modest 0.5 mol % catalyst amount.

Solvent and Catalyst Concentration Effects

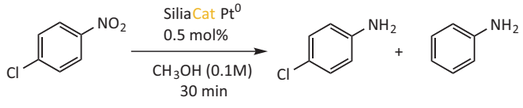
The best results were obtained using methanol as solvent at 0.1 M concentration with respect to substrate. Even if the use of EtOAc results in high selectivities, the reaction times are generally much longer. Complete conversion is obtained after 1 hour in hexane using 0.5 or 0.1 mol % catalyst, but the selectivity to 4-chloroaniline was generally low.

Solvent and Catalyst Concentration Effects

Silia*Cat* Pt^0 (mol %)	Time (h)	Solvent (M)	Yield (%)	
			Product	Aniline
1.0	0.5	MeOH (0.1 M)	92	8
0.5	0.5	MeOH (0.1 M)	87	13
0.2	1	MeOH (0.1 M)	84	13
0.1	2	MeOH (0.1 M)	90	10
0.5	4	EtOAc (0.1 M)	55	0.5
1.0	4	EtOAc (0.1 M)	75	1
1.0	1	THF (0.1 M)	45	17

Silia*Cat* Pt^0 Reusability and Leaching

The reusability test of Silia*Cat* Pt^0 was studied using 4-chloronitrobenzene as substrate under the optimal reaction conditions identified above. Reusing the catalyst in 7 consecutive cycles did not result in any loss of catalytic activity and leaching of Pt and Si (*assessed by ICP-MS*) was minimal. Complete substrate conversion was obtained even after the seventh cycle, with 99% selectivity. The selectivity of the reaction even improves with each subsequent cycle going from 84% in the first run up to 99% in run 7. The positive-feedback phenomenon of effective selectivity in consecutive reaction cycles is probably attributed to the silica matrix alkylation.



Silia*Cat* Pt^0 Reusability and Leaching

Reusability	Yield (%)		Leaching (ppm)	
	Product	Aniline	Pt	Si
1	84	12	0.20	1.20
2	89	11	0.04	0.40
3	90	10	0.02	0.08
4	92	8	0.17	0.10
5	98	2	0.01	0.10
6	99	1	0.01	0.12
7	99	1	0.01	0.08

Silia*Cat* Pt^0 vs Competitive Catalysts

Other commercially available Pt heterogeneous catalysts [Pt/C, Pt/SiO_2 and Reaxa Pt(0)EnCat40] were tested in the selective reduction of 4-chloro-nitrobenzene. In comparison to other Pt(0) heterogeneous catalysts, the Silia*Cat* Pt^0 catalyst proved to be much more reactive, with complete conversion after 0.5 h with just 0.5 mol %. Furthermore, selectivity was significantly higher with only 4% aniline formed as by-product. No secondary product was observed in solution.

Silia*Cat* Pt^0 vs Competitive Catalysts

Catalyst	Pt/C			Pt/SiO_2			Reaxa Pt(0)EnCat40 wet			Reaxa Pt(0)EnCat40 dry		
Mol %	5	1	0.5	5	1	0.5	5	1	0.5	5	1	0.5
Time (h)	1	1	1	1	2	2	1	2	2	0.5	2	2
Product (%)	82	65	43	84	88	48	75	78	72	87	90	86
Aniline (%)	14	4	0	13	10	2	18	14	12	13	10	13

Exp. conditions: 2 mol substrate in 20 mL MeOH under hydrogen balloon at room temperature.

Substrate Scope and Selectivity

The Hydrogenation of different nitro compounds, including those nitro compounds containing different functionalities, was attempted to demonstrate the selectivity of Silia*Cat* Pt^0 catalyst in a wide range of reactions. The material was tested under hydrogen balloon, at room temperature conditions in methanol solvent with 0.5 – 1 mol % Pt catalyst.

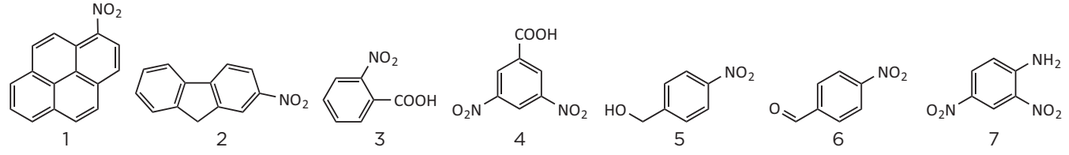
Note: look at our publication in *Adv. Synth. Catal.*, **2011**, *353*, 1306-1316 for more examples.

Substrate Scope and Selectivity

Substrate	Silia*Cat* Pt^0 (mol %)	Solvent (M)	Time (h)	Conversion (%)	Selectivity (%)
Structure #1	0.5	MeOH (0.05 M)	1	100	98 (5% pyrene)
Structure #2	0.5	MeOH (0.05 M)	1	98	100
Structure #3	0.5	MeOH (0.1 M)	1	100	100
Structure #4	0.5 / 1.0	MeOH (0.1 M)	2	100 / 100[1]	98 / 100[1]
Structure #5	0.5	MeOH (0.1 M)	1	100	100
Structure #6	0.5	MeOH (0.1 M)	1	100	95
Structure #7	0.5	MeOH (0.07 M)	2	100	100

[1] If 0.5 mol % was used only one NH_2 group was reduced. If 1 mol % was used, both nitro groups were reduced.

Substrate Structures



Conclusion of Selective Hydrogenation of Nitroarenes

The hydrogenation of different nitro compounds and the selective hydrogenation of different nitro compounds in the presence of different functionalities, including reducible carbonyl, amide, ester, amine and halide groups was achieved with Silia*Cat* Pt^0 catalyst in methanol at room temperature and under 1 bar H_2 pressure. Given the broad applicability of Pt-based catalysts to widely different chemical reactions, it is envisaged that these catalysts, now commercially available, will be used in numerous fields of chemical synthesis as well as in energy generation applications.

Selective Hydrogenation of Nitroarenes Typical Experimental Procedure

Conventional Experimental Conditions

Reaction

Typical reactions are performed on a 2 mmol scale. The substrate is dissolved in 20 mL of MeOH and then treated with 0.1 – 1 mol % of Silia*Cat* Pt^0 catalyst. The mixture is degassed twice, replacing the vacuum by hydrogen each time. The reaction mixture, connected to a balloon of hydrogen, is stirred at room temperature until it shows maximum conversion.

Work-up

Once the reaction is complete (*determined by TLC or GC-MS*), the catalyst is filtered off and washed with EtOH or MeOH. The filtrate is concentrated to give a crude product, and the conversion to the desired product is determined by GC/MS analysis.

Reusability

To reuse the catalyst, after completion of the reaction remove the catalyst by filtration, rinse with MeOH/THF solvents and dry under vacuum.

Selective Debenzylation Using Silia*Cat* Pd^0

The selective debenzylation of aryl benzyl ethers, benzyl esters, and benzyl amines, while leaving other sensitive groups intact, can be carried out in high yield under remarkably mild conditions (*namely at room temperature under 1 bar H_2 in a simple hydrogen balloon, using a modest 0.5 mol % catalyst amount*) using Silia*Cat* Pd^0 (*note that Silia*Cat* Pt^0 can also be used but reaction times are longer and concentrations are higher*).

Selective and smooth deprotection is critical. The commonly used method makes use of catalytic hydrogenolysis to protect benzylic groups with H_2 under pressure and in the presence of a heterogeneous catalyst such as Pd/C or Raney Ni. Often, however, the deprotection reaction conditions are not compatible with other functional groups, such as nitro, unsaturated bonds, and halogen groups.

Silia*Cat* hydrogenation catalysts offer a number of additional advantages over traditional Pd/C. They are non pyrophoric, and have a higher density and lower catalytic consumption (*<1 mol % vs 5 - 10% for Pd/C*) due to fast kinetics and high turnover.

Note: refer you to our publication called “Selective Debenzylation of Benzyl Protected Groups with Silia*Cat* Pd^0 under Mild Conditions” in *ChemCatChem,* **2011**, *3*, 1–5.

Solvent Effect

Solvent choice is critical for any debenzylation reaction. Therefore, in order to optimize the reaction conditions, 1-(benzyloxy)-4-methoxybenzene was used as our substrate of choice. A series of commonly employed solvents (*THF, methanol, ethanol, ethyl acetate, and hexane*) were screened under a hydrogen balloon at room temperature and at different solvent concentrations. The best results were achieved with methanol and ethanol (*HPLC grade*).

Solvent Effect

Silia*Cat* Pd^0 (mol %)	Time (h)	Solvent (M)	Conversion (%)
2	16	EtOH (0.1 M)	17
2	16	MeOH (0.1 M)	15
2	4	EtOH (0.07 M)	100
2	0.5	MeOH (0.07 M)	100
2	20	THF (0.07 M)	10
2	20	THF (0.07 M)	15
2	20	EtOAc (0.07 M)	20
2	20	Hexane (0.07 M)	21

Catalyst Concentration Effect

The molar concentration of the solvent with respect to the substrate is crucial with higher concentrations, slowing or even preventing reaction. The best results were achieved by using a methanol concentration of 0.07 M and 0.5 – 1 mol % Silia*Cat* Pd^0, with complete conversion obtained after 1 – 2 hours.

Catalyst Concentration Effect

Silia*Cat* Pd^0 (mol %)	Time (h)	Solvent (M)	Conversion (%)
2	0.5	MeOH (0.07 M)	100
1	1	MeOH (0.07 M)	100
0.5	2	MeOH (0.07 M)	100

Silia*Cat* Pd^0 Reusability and Leaching

Catalyst stability and reusability are crucial features of any catalyst seeking commercial applications. The Silia*Cat* Pd^0 was thus reused six consecutive times in the O-debenzylation reaction of 1-(benzyloxy)-4-methoxybenzene under the standard mild conditions developed in our laboratory (*reaction shown on previous page using 1 mol % of catalyst*).

After six runs, the catalyst exhibits only a slight loss in activity compared with that of a catalyst run three times. However, the activity remained approximately constant, and it was enough to expand the reaction time to 1 h and 30 min to gain complete debenzylation of the substrate.

Silia*Cat* Pd^0 Reusability and Leaching

Reusability	Time (h)	Conversion (%)	Leaching (ppm)	
			Pd	Si
1st	1	100	0.7	2.5
2nd	1	100	0.3	1.3
3rd	1	95	-	-
	1.5	100	0.3	2.3
4th	1	95	-	-
	1.5	100	0.2	1.4
5th	1	94	-	-
	1.5	99	0.2	0.8
6th	1	94	-	-
	1.5	100	0.1	0.5

TEL.: 1 418 874.0054 FAX: 1 418 874.0355 TOLL-FREE: 1 877.SILICYCLE (NORTH AMERICA ONLY) WWW.SILICYCLE.COM INFO@SILICYCLE.COM

Silia*Cat* Pd⁰ vs a Competitive Catalyst

Using the same reaction as that used to demonstrate the reusability of Silia*Cat* Pd⁰ in the O-debenzylation reaction of 1-(benzyloxy)-4-methoxybenzene, we also tested the commercial catalyst Pd0 EnCat, a polyurea-entrapped catalyst.

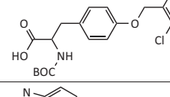
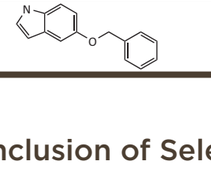
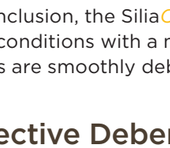
Silia*Cat* Pd⁰ vs a Competitive Catalyst

Catalyst (mol %)	Time (h)	Conversion (%)	Selectivity (%)
Silia*Cat* Pd⁰ (0.5)	1 / 2	95 / 100	- / 100
Silia*Cat* Pd⁰ (1.0)	0.5 / 1	75 / 100	- / 100
Pd0 EnCat (10)	16	100	100

Substrate Scope and Selectivity

Silia*Cat* Pd⁰ is an efficient catalyst for the selective debenzylation of different aryl benzyl ethers, benzyl amino-acids, and benzylprotected sugars leaving other sensitive groups intact. Refer to our publication in *ChemCatChem,* **2011**, *3*, 1–5 for more examples.

Substrate Scope & Selectivity

Substrate	Silia*Cat* Pd⁰ (mol %)	Time (h)	Conversion [Yield] (%)	Leaching (ppm) Pd	Leaching (ppm) Si
	1	1	100 [99.7]	3.4	1.3
	1	1	100 [98.6]	1.7	5.0
	1	20	100 [98.0]	0.4	7.0

Conclusion of Selective Debenzylation

In conclusion, the Silia*Cat* Pd⁰ catalyst is suitable for the selective debenzylation of numerous substrates under mild conditions with a modest 1 – 2 mol % catalyst amount. Benzyl-protected sugars, amino acids, ethers, and esters are smoothly debenzylated under 0.1 MPa H_2 at room temperature.

Selective Debenzylation Typical Experimental Procedure

Conventional Experimental Conditions

Reaction

Typical reactions were performed on a 1 mmol scale. The substrate was dissolved in 15 mL of MeOH or EtOH (0.07 M) and 1 or 2 mol % of the Silia*Cat* Pd⁰ catalyst was added. The mixture was degassed twice and each time replacing the vacuum by hydrogen. The reaction mixture, connected to a balloon filled with hydrogen, was stirred at room temperature until GC/MS analysis showed maximum conversion.

Work-up

Once the reaction is complete as deemed by TLC or GC-MS, the catalyst was filtered off and washed with EtOH or MeOH. The filtrate was concentrated to give a crude product. The conversion in the desired product was determined by GC/MS analysis and by ^{1}H NMR.

Reusability

To reuse the catalyst, after completion of the reaction, remove the catalyst by filtration, rinse with MeOH/THF solvents and dry under vacuum.

Hydrosilylation Using Silia*Cat* Pt⁰

Hydrosilylation reactions (*or catalytic hydrosilation*) are a widely used method to prepare organosilicon products. The reaction consists of the addition of *Si*-H bonds on unsaturated bonds like alkenes, alkynes or ketones, where catalysts are often required (usually H_2PtCl_6). Silia*Cat* Pt⁰ can be used for hydrosilylation reactions. Some examples are shown to the right.

Hydrosilylation using Silia*Cat* Pt⁰

Substrate	Time (h)	Temp. (°C)	Conversion (%)	Selectivity (%)
1-octene	5	22 / 60	88 / 99	98 / 99
1-decene	5	22 / 60	100 / 100	97 / 98
1-octadecene	5	22 / 60	95 / 98	56 / 83
4-vinyl-benzamine	5 / 24	60	47 / 80	96 / 96
3,3-diethoxy-prop-1-ene	5	22 / 60	94 / 100	93 / 81

Hydrosilylation Typical Experimental Procedure

Conventional Experimental Conditions

Reaction

A 100 ml two neck dry round bottom flask equipped with a condenser and a rubber septum is filled with 1 mol % Silia*Cat* Pt⁰ and was degassed two times for 15 minutes kept under argon conditions. The anhydrous solvent, the silane (*95% pure*) and the olefin (*previously degassed for 15 minutes under argon*) were added using a syringe. The reaction mixture was either stirred at room temperature or heated at 60°C until the GC/MS analysis showed maximum conversion

Work-up

Once the reaction is complete the catalyst was filtered off and washed with toluene. The filtrate was concentrated to give a crude product. The conversion in the desired product was determined by GC/MS.

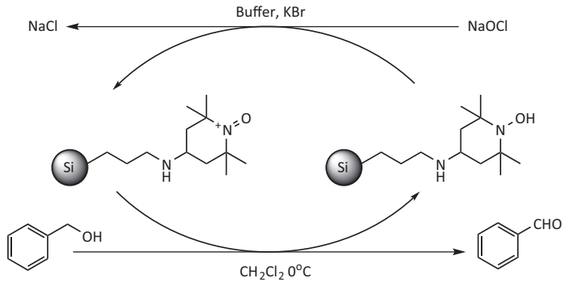
Note: Unless otherwise indicated, all manipulations were carried out under argon conditions. In general, reactions were performed on a 2 mmol scale in 15 ml anhydrous toluene.

TEL.: 1 418 874.0054 FAX: 1 418 874.0355 TOLL-FREE: 1 877.SILICYCLE (NORTH AMERICA ONLY) WWW.SILICYCLE.COM INFO@SILICYCLE.COM

Oxidation Using Silia*Cat* TEMPO

Aldehydes and ketones, either as starting materials, synthetic intermediates, or final products, are of great interest in synthetic chemistry. Such carbonyl-containing products can lead to carbon–carbon (*i.e. Wittig, Aldol, alkylation*) or carbon–nitrogen bond formation. Over the years, chemists have discovered various oxidizing agents such as pyridinium chlorochromate (PCC), MnO2, Dess-Martin periodinane, or Swern oxidation conditions. Although all these methods lead to the aldehyde (*limited oxidation of the aldehyde to the carboxylic acid*), they have drawbacks such as the hazards and toxicity associated with residual metal contamination.

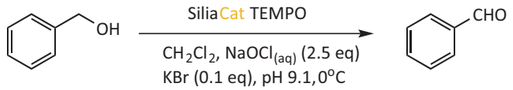
Development of environmentally friendly methods such as selective catalytic oxidation of alcohol substrates to aldehydes and ketones can have significant impact on modern methods of chemical synthesis. Silia*Cat* TEMPO is the oxidation solution of choice.



Catalytic Performance and Leaching

Silia*Cat* TEMPO was investigated in the Montanari-Anelli conditions. The catalytic cycle involves regeneration of the oxidative species with NaOCl (*commercially available bleach*) in presence of KBr as co-catalyst to form the stronger anion OBr-.

Unless otherwise stated, the reaction shown below was used for the demonstration.



Catalytic Performance and Leaching

Silia*Cat* (mol %)	Time (h)	Conversion (%)	TON	Si Leaching (ppm)
0.1	1	95	950	-
0.01	2	83	8,300	3
0.01	3	95	9,500	1.6
0.01	4	97	9,650	1.5
0.02	2	96	4,800	-
0.02	3	100	5,000	2

Silia*Cat* TEMPO can be used with as low as 0.01 mol % quantity to provide the desired aldehyde in short reaction times. ICP analysis confirms that the material is leach-resistant ([Si] ≤ 3 ppm).

Silia*Cat* TEMPO Reusability

Minimal leaching and the robustness of Silia*Cat* TEMPO's organoceramic matrix allow it to be reused several times for further uses.

Silia*Cat* TEMPO Reusability

Reusability	Time (min)	Conversion (%)	Reusability	Time (min)	Conversion (%)	Reusability	Time (min)	Conversion (%)
1st	30	100	...	...	...	9th	30 / 60	97 / 100
2nd	30	100	8th	30 / 60	95 / 100	10th	30 / 60	90 / 100

[a]Silia*Cat* TEMPO is recycled by post-reaction filtration, DCM washes and air drying.

Influence of Co-Catalyst KBr and Temperature

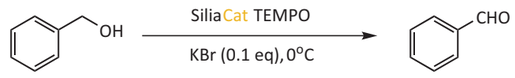
SiliCycle investigated wether it was necessary to use a co-catalyst (KBr) for the reaction to proceed effectively. As shown in the table, although KBr is not required for the reaction, it does have a significant impact on the kinetics. The reaction can still proceed to completion without KBr but requires longer time and/or more Silia*Cat* TEMPO. It was also demonstrated that the reaction can be carried out at room temperature without KBr.

Influence of KBr and Temperature

Silia*Cat* (mol %)	KBr (eq.)	Temp. (°C)	Time (min)	Conversion (%)
0.1	0.1	0	60	95
0.1	0	0	60	80
0.1	0	0	210	100
0.2	0	0	105	96
0.2	0	22	60	76
0.2	0	22	90	87

Influence of Solvents, pH and NaOCl

As shown on the right, the reaction can be carried out at pH 9.0 or at pH 7.5 in DCM with high conversion yields. The catalytic conditions are selective towards the aldehyde, rather than the carboxylic acid, even with 10 equiv of NaOCl. At pH 7 in water, the reaction is slower, but this can be overcome by using more $NaOCl_{(aq)}$. At pH 9, the conversion is high, but too much bleach and the long reaction time in the aqueous media will lead to the corresponding carboxylic acid. The reaction can also be pursued in other organic solvents.



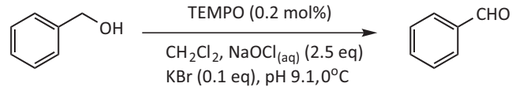
Influence of Solvent, pH and $NaOCl_{(aq)}$

Silia*Cat* (mol %)	$NaOCl_{(aq)}$ (eq.)	Solvent	pH	Time (min)	Conversion (%)
0.2	2.50	DCM	9.0	60	98
0.2	10.00	DCM	9.0	90	98
0.2	1.25	DCM	7.5	60 / 90	83 / 86
0.2	2.50	DCM	7.5	60 / 90	94 / 98
0.2	1.25	H_2O	7.5	60 / 90	57 / 65
0.2	2.50	H_2O	7.5	60 / 90	87 / 88
0.7	1.20	H_2O	9.0	60 / 150	83 / 89
0.8	5.00	H_2O	9.0	60 / 18 h	60 (19)/ 7 (89)[1]
0.2	1.25	EtOAc	9.0	60 / 90	95 / 96

[1] In parenthesis = conversion to carboxylic acid.

Silia*Cat* TEMPO vs Homogeneous TEMPOs

Comparative analysis versus homogeneous TEMPOs demonstrates the Silia*Cat* TEMPO to be comparable or better at neutral pH and significantly superior in basic conditions.



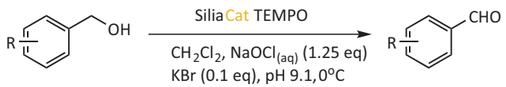
Silia*Cat* TEMPO vs Homogeneous TEMPOs

pH	Silia*Cat* TEMPO	4-MeO-TEMPO	4-Oxo-TEMPO
7.5	91	99	45
9.0	98	55 (40)[1]	73

[1] In parenthesis = conversion to carboxylic acid.

Substrate Scope with Silia*Cat* TEMPO

Silia*Cat* TEMPO is efficient with different substrates and can be used with phase a transfer agents such as Aliquat 336. When an electron-rich benzylic alcohol cannot be oxidized successfully with NaOCl, conditions involving I_2 in toluene, at room temperature, will yield the desired product.



Substrate Scope with Silia*Cat* TEMPO

Substrate (R)	Catalyst (mol %)	Time (min)	Conversion (%)
3-NO_2	0.4	90	100
4-NO_2	0.4	90	98
4-OCH_3	0.4	90	36
4-OCH_3	0.4 (0.05 eq. Aliquat 336)	60	79
4-Cl	0.4	90	95
3-phenyl-1-propanol	0.4	60	97
1-phenyl-3-propanol	0.4	180	95
4-OCH_3	8.2	16 h	99[1]
3-OCH_3	7.8	16 h	96[1]
Piperonal	10.0	20 h	100[1]

[1]Exp. Cond.: I_2 (1.8 eq.), $NaHCO_3$(aq), pH 8, toluene, 22°C.

Conclusion of Oxidation

In conclusion, the Silia*Cat* TEMPO is an effective oxidizing catalyst presenting unique advantages such as high activity, robustness, leach-proof properties and selectivity toward the oxidation of alcohols into aldehydes and ketones, both very valuable products in organic chemistry.

Oxidation Typical Experimental Procedure

Oxidation of Alcohols or Aldehydes to Carboxylic Acid

Note: changing the solvent to water, increasing temperature and the amount of bleach will all favor the acid formation.

Conventional Experimental Conditions

Reaction

Under mechanical agitation, a 0.4M solution of alcohol in water and a 0.5 M aqueous solution of KBr were cooled at 0°C in an ice bath. The desired amount of Silia*Cat* TEMPO was added, followed by an aqueous solution of NaOCl (*from 10-13% bleach*) buffered at pH 9 (*using* $NaHCO_3$) or pH 6.7 (*using* NaH_2PO_4/Na_2HPO_4). NaOCl was added slowly over a 10 minute period as the reaction is exothermic. The mixture was warmed to room temperature (20°C) and stirred between 1,300-1,500 rpm. The temperature can be increased to 35°C if necessary.

Work-up

Once the reaction was complete (*determined by TLC or GC-MS*), the catalyst was filtered at room temperature, and the pH was adjusted to 12 with aqueous NaOH (2N). The aqueous phase was separated, acidified with HCl 6N and extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$ and evaporated. The residue was purified by crystallization or column chromatography on silica gel.

- 1.2 - 5 eq. of $NaOCl_{(aq)}$ (*typically start with 3 eq. and, if necessary, add another 2 eq. of* NaOCl *via an addition funnel after all of alcohol is consumed*)
- 0.1 eq. of potassium bromide (KBr) (*prepared as a 0.5 M solution*)
- pH 9 is achieved using a $NaHCO_3$ buffer or a pH of 6.7 is achieved using a sodium phosphate buffer (*1:1 mixture of 0.67 M* NaH_2PO_4 *and 0.67 M* Na_2HPO_4)
- 0.01 - 1 mol % of Silia*Cat* TEMPO (*typically 1 mol %*)
- The best solvents are H_2O, ACN/H_2O or DCM/H_2O, typically at 0.4 M (*molar concentration with respect to the substrate*)

Oxidation of Primary or Secondary Alcohols

Under Montanari-Anelli Conditions (using NaOCl)

Conventional Experimental Conditions

Reaction

Under mechanical agitation, a 0.4M solution of the alcohol in dichloromethane is mixed with a 0.5M aqueous solution of KBr and cooled at 0°C in an ice bath. The desired amount of Silia*Cat* TEMPO is then added, followed by an aqueous solution of NaOCl (*from commercially available 10-13% bleach*), then the solution is buffered at pH 9 (*using* $NaHCO_3$). NaOCl solution is added slowly over a 10 minute period as the reaction is exothermic. The mixture is then stirred between 1,300-1,500 rpm.

Work-up

Once the reaction is complete (*determined by TLC or GC-MS*), the catalyst is filtered at room temperature, and the organic phase is dried over $MgSO_4$ and evaporated. Crude mixture is purified using flash chromatography, if needed.

Under Miller Conditions (using I_2 co-catalyst)

Conventional Experimental Conditions

Reaction

Under mechanical agitation, a 0.4M solution of alcohol in toluene is mixed at room temperature (20°C) with a 0.3 M aqueous solution of $NaHCO_3$. Solid iodine is then added in one portion to the mixture, followed by the desired amount of Silia*Cat* TEMPO.

Work-up

Once the reaction is complete (*determined by TLC or GC-MS*), the catalyst is filtered at room temperature. The mixture should then be cooled to 5°C, diluted with ethyl acetate, and quenched with a 0.8M aqueous solution of Na_2SO_3. The uncolored organic phase is then washed with a saturated aqueous solution of $NaHCO_3$ followed by brine and dried over $MgSO_4$. After filtration and evaporation of the solvents, the crude mixture can be purified using flash chromatography.

- For Montanari-Anelli conditions: 1.2 - 5 eq. of $NaOCl_{(aq)}$ (*typically 2.5 eq.*) and 0.1 eq. of KBr (*prepared as a 0.5 M solution*)
- For Miller conditions: 1.8 eq. of solid iodine (I_2)
- 0.001 - 1 mol % of Silia*Cat* TEMPO (*typically 1 mol %*)
- The best solvents are DCM, EtOAc or ACN/H_2O (*HPLC grade*), typically at 0.4 M (*molar concentration is with respect to the substrate*)

SiliCycle Publications

Silia*Cat* TEMPO Oxydation

Topics in Catalysis, **2010**, *53*, 1110-1113
Organic Process Research & Development, **2010**, *14*, 245–251
Chemistry Today, **2009**, *27*, 13-16
Organic Process Research and Developement, **2007**, *11*, 766-768

Hydrogenation of nitroarenes with Silia*Cat* Pt⁰

Advanced Synthesis & Catalysis, **2011**, *353*, 1306–1316
Catal. Sci. Technol., **2011**, Advance Article, DOI: 10.1039/C1CY00097G

Suzuki coupling with Silia*Cat*

Catal. Sci. Technol., **2011**, Advance Article, DOI: 10.1039/C1CY00119A
Topics in Catalysis, **2010**, *53*, 1059-1062

Selective debenzylation with Silia*Cat* Pd⁰

ChemCatChem, **2011**, *3*, 1146-1150