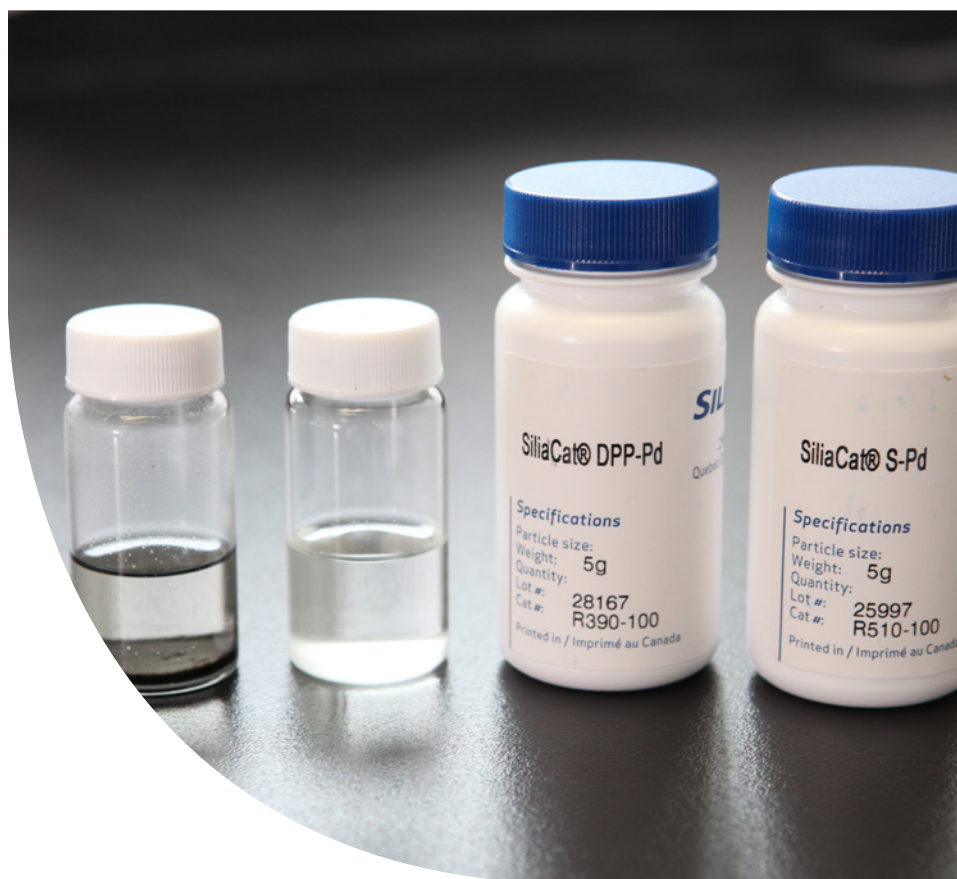


SiliaCat

Heterogeneous Catalysts 
Experimental Procedure



SILICYCLE 
UltraPure SILICA GELS

SiliaCat Palladium Cross-Coupling Catalysts Experimental Procedure Guide

Advantages of using the SiliaCat® heterogeneous catalysts over competitive products:

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



SiliaCat Palladium Cross-Coupling Catalysts Portfolio

General Description of SiliaCat Products

Organically modified silica-based **SiliaCat** DPP-Pd and **SiliaCat** S-Pd are highly reactive and reusable heterogeneous catalysts. These catalysts are widely used in palladium-catalyzed reaction such as Suzuki, Sonogashira, Heck, Still and Kumada coupling.

Characteristics

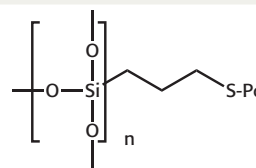
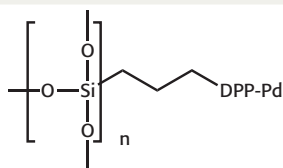
- Surface Area: 300 - 650 m²/g
- Particle Size Distribution: 60 - 250 microns
- Pore Size: 25 - 70 Å

SiliaCat® DPP-Pd (R390-100)

Loading: 0.2 - 0.4 mmol/g

SiliaCat® S-Pd (R510-100)

Loading: 0.4 - 0.6 mmol/g



Palladium-Catalyzed Coupling Reactions Presented

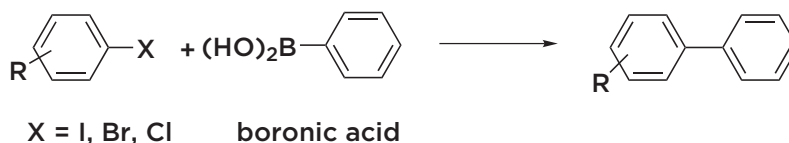
- Suzuki Coupling
- Sonogashira Coupling
- Heck Coupling
- Buchwald Coupling
- Kumada Coupling
- Stille Coupling

Note: Unless otherwise indicated, all reactions do not require inert atmosphere or dry solvents. Catalysts can be handled in open air.

***ALL THESE PRODUCTS ARE AVAILABLE IN DIFFERENT SIZES FROM LAB SCALE TO MULTI-TON SCALE (5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 5kg, 10kg, 25kg, etc.)**

Suzuki Coupling Reaction

The best catalyst for this reaction is **SiliaCat** DPP-Pd. It showed good reactivity for aryl iodides, bromides and chlorides. **SiliaCat** S-Pd showed good reactivity for aryl iodides and bromides.



Standard Conditions

Reaction

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

Work-up

Once the reaction is complete as deemed by TLC or GC-MS, the catalyst is filtered at room temperature, rinsed two times with water and three times with the solvent used in the reaction, dried and stored for reuse if desired. The reaction mixture obtained after filtration of the catalyst is evaporated and the product is extracted using ethyl acetate (AcOEt) or diethyl ether (Et₂O) and washed twice with water. Organic phase is dried using magnesium sulfate (MgSO₄), filtered and the solvent is evaporated. Crude mixture is purified using flash chromatography if needed.

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 Time: 5-15 minutes

Work-up

Once the reaction is complete as deemed by TLC or GC-MS, follow same work-up procedure as for standard conditions.

Experimental Conditions - Suzuki Coupling

Products	Standard Conditions			Microwave Conditions		
	Ar-Iodide	Ar-Bromide	Ar-Chloride	Ar-Iodide	Ar-Bromide	Ar-Chloride
Base [K ₂ CO 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.
SiliaCat 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 ₂ O (10:1, 0.1 M)	EtOH or TBAB/H ₂ O (10:1.5, 0.12 M)	MeOH (0.2 M)	MeOH (0.2 M)	EtOH/H ₂ O (10:1, 0.2 M)

*Note: molar concentration in related to the substrate.

Sonogashira Coupling Reaction

The best catalyst for this reaction is **SiliaCat** DPP-Pd with aryl iodides and bromides.



Standard Conditions

Reaction

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

Work-up

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

Microwave Conditions

Reaction

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

- **Aryl Iodide**

Power: 150 W
Temperature: 100 °C

Pressure: 150 psi
Time: 5-15 minutes

- **Aryl Bromide**

Power: 200 W
Temperature: 100-150 °C

Pressure: 200 psi
Time: 5-20 minutes

Work-up

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

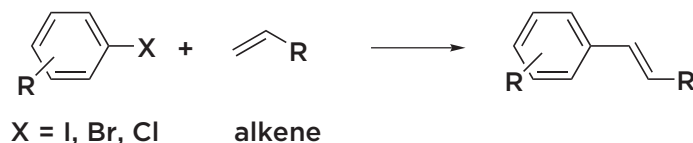
Experimental Conditions - Sonogashira Coupling

Products	Standard Conditions		Microwave Conditions	
	Ar-Iodide	Ar-Bromide	Ar-Iodide	Ar-Bromide
Base [K ₂ CO ₃]	1.5 eq.	1.5 eq.	1.5 eq.	2.0 eq.
Phenylacetylene	1.1 eq.	1.25 eq.	1.1 eq.	1.5 eq.
SiliaCat 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 => typically 0.07 M) EtOH /H ₂ O (10:1, 0.1 M)		MeOH (0.2 M)	MeOH/H ₂ O (10:1, 0.2 M)

*Note: molar concentration in related to the substrate.

Heck Coupling Reaction

The best catalyst for this reaction is **SiliaCat** DPP-Pd. It showed a good reactivity for aryl iodides, bromides and chlorides. **SiliaCat** S-Pd showed good reactivity for aryl iodides and bromides.



Standard Conditions

Reaction

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

Work-up

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

Microwave Conditions

Reaction

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

- **Aryl Iodide**

Power: 100 W

Pressure: 150 psi

Temperature: 100 °C

Time: 10 minutes

- **Aryl Bromide**

Power: 200 W

Pressure: 200 psi

Temperature: 125 °C

Time: 15 minutes

- **Aryl Chloride**

Power: 200 W

Pressure: 200 psi

Temperature: 125 °C

Time: 15 minutes

Work-up

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

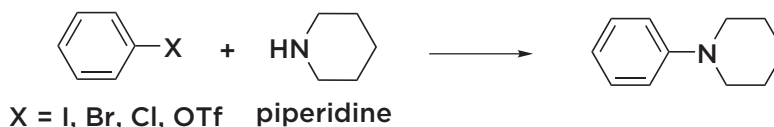
Experimental Conditions - Heck Coupling

Products	Standard Conditions			Microwave Conditions		
	Ar-Iodide	Ar-Bromide	Ar-Chloride	Ar-Iodide	Ar-Bromide	Ar-Chloride
Base [K ₂ CO ₃]	1.5 eq. [Et ₃ N or NaOAc]	1.5 eq. [NaOAc]	1.5/0.5 eq. [Ca(OH) ₂ /TBAB]	1.5 eq. [Et ₃ N or NaOAc]	1.5 eq.	2.0 eq.
Olefin	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.	1.2-2.0 eq.
SiliaCat 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 ₂ O (1:1, 1.67 M) NMP (2.0 M)	MeCN or DMF (1.2 M)	DMF (0.75-1.5 M)	NMP/H ₂ O (1:1, 1.67 M) NMP (2.0 M)

*Note: molar concentration in related to the substrate. Olefin examples: styrene, methyl acrylate, methyl methacrylate, etc.

Buchwald Coupling Reaction

SiliaCat DPP-Pd and **SiliaCat** S-Pd showed good reactivity for this reaction in the presence of iodo, bromo and chloro nitrosubstrates in standard conditions, and with chloro nitrosubstrates in microwave condition.



Standard Conditions

Reaction

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

Work-up

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

Microwave Conditions

Reaction

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

Power: 200 W

Pressure: 200 psi

Temperature: 150 °C

Time: 15 minutes

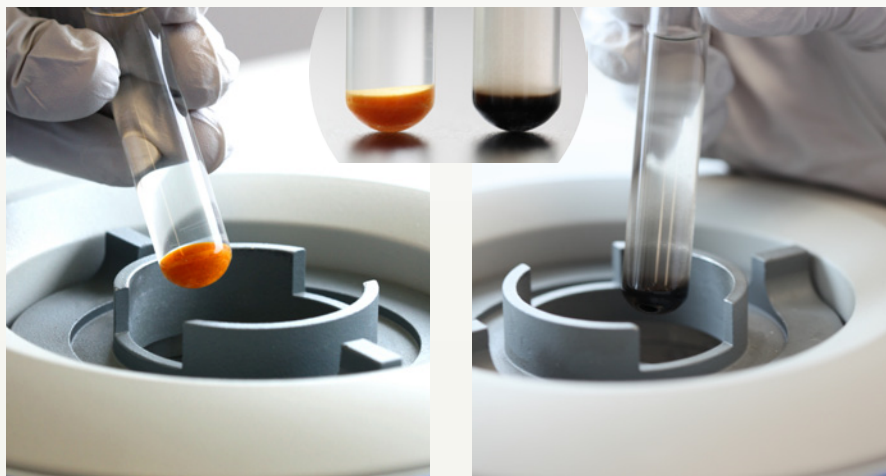
Work-up

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

Experimental Conditions - Buchwald Coupling

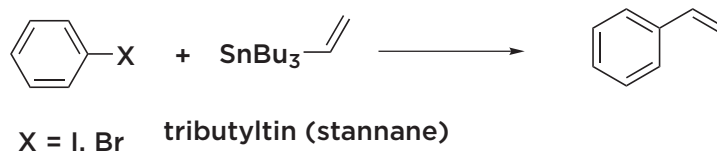
Products	Standard Conditions			Microwave Conditions		
	Ar-Iodide	Ar-Bromide	Ar-Chloride	Ar-Iodide	Ar-Bromide	Ar-Chloride
Base [NaOtBu]	1.5 eq.	1.5 eq.	-	1.5 eq.	2.0 eq.	-
Amine	1.1 eq.	1.25 eq.	-	1.1 eq.	1.5 eq.	-
SiliaCat Catalyst	0.5 mol%	1.0 mol%	-	0.5 mol%	1.0 mol%	-
Best Solvents (HPLC Grade)	For room temperature reaction: MeOH (0.02 M) For reflux reaction: MeOH (0.05-0.13 M => typically 0.07 M) EtOH /H ₂ O (10:1, 0.1 M)			MeOH (0.2 M)	MeOH/H ₂ O (10:1, 0.2 M)	-

*Note: molar concentration in related to the substrate.



Stille Coupling Reaction

SiliaCat DPP-Pd catalyst showed good reactivity for aryl iodides and bromides.



Standard Conditions

Reaction

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

Work-up

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

Experimental Conditions - Stille Coupling

Standard Conditions	
Products	Ar-Iodide & Ar-Bromide
RSnBu ₃	1.0-2.0 eq. (usually 1.1 eq.)
Additive (CsF)	Add 2.0 eq. (for higher conversion)
SiliaCat Catalyst	0.25-10.0 mol% (usually 2 mol% for Ar-I and 2-10 mol% for Ar-Br)
Best Solvents (HPLC Grade)	Dioxane (0.1 M) Toluene (0.1 M)

*Note: molar concentration in related to the substrate.

Kumada Coupling Reaction

SiliaCat DPP-Pd showed good reactivity for aryl iodides and bromides. Inert conditions are required for Kumada couplings due to the presence of Grignard reagent. Use standard Schlenk procedures or round-bottom flask equipped with a magnetic stirrer.



Standard 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 complete, inert conditions are not necessary. Follow same work-up procedure as for Suzuki coupling standard conditions.

Experimental Conditions - Kumada Coupling

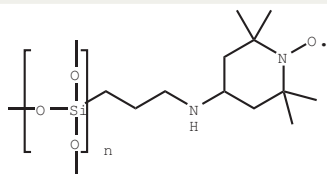
Standard Conditions	
Products	Ar-Iodide & Ar-Bromide
RMgBr	2.0 eq.
SiliaCat Catalyst	2.0-10.0 mol% (usually 5 mol%)
Best Solvent (HPLC Grade)	Tetrahydrofuran, room temperature (0.05-0.08 M, usually 0.08 M)

*Note: molar concentration in related to the substrate.

SiliaCat TEMPO - Oxidizing Catalyst Experimental Procedure Guide

SiliaCat TEMPO (R723-100)

Loading: 0.8 - 0.9 mmol/g



General Description of SiliaCat TEMPO

SiliaCat TEMPO is an effective and useful oxidizing catalyst for delicate primary and secondary alcohol substrates into valued carbonyl derivatives. SiliaCat TEMPO can be used for solid-state synthesis in which no contamination of the product and high selectivity are required.

Oxidation of Alcohols (or Aldehydes) to Carboxylic Acid

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

Typical Experimental Conditions

Reaction

Under mechanical agitation, a 0.4M solution of the 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 SiliaCat TEMPO was added, followed by an aqueous solution of NaOCl (from commercial 10-13% bleach) buffered at pH 9 (using NaHCO₃) or pH 6.7 (using NaH₂PO₄/Na₂HPO₄). NaOCl was added slowly over a 10 minute period as the reaction is exothermic. The mixture was warmed to room temperature (20°C) and was stirred between 1300-1500 rpm. The temperature can be increased to 35°C if necessary.

- 1.2-5 eq of NaOCl_{aq} (typically start with 3 eq and if necessary, after all of the alcohol is consumed add another 2 equivalent of NaOCl via an addition funnel)
- 0.1 eq of potassium bromide (KBr) (prepared as a 0.5 M solution)
- pH 9 is achieved using a NaHCO₃ buffer or pH of 6.7 is achieved using a sodium phosphate buffer (1:1 mixture of 0.67M NaH₂PO₄ and 0.67M Na₂HPO₄)
- 0.01-1 mol% of SiliaCat TEMPO (typically 1 mol%)
- The best solvents are water, ACN/water or DCM/water, typically at 0.4 M (molar concentration is with respect to the substrate).

Work-up

Once the reaction is complete as deemed by TLC or GC-MS, the catalyst is filtered at room temperature, pH was adjusted at 12 with aqueous NaOH (2N). The aqueous phase was separated, acidified with HCl 6N and extracted with CH₂Cl₂. The organic phase was dried over MgSO₄ and evaporated. The residue was purified by crystallization or column chromatography on silica gel.

Note: Unless otherwise indicated, all reactions do not require inert atmosphere or dry solvents. Catalysts can be handled in open air. Strong agitation is suggested during SiliaCat TEMPO oxidations due to the hydrophobic nature of organosilica material and the fact that most reactions are in water or biphasic media. We recommend 1300-1500 rpm for mechanical stirring. Oxidation of alcohols to aldehydes/ketones by SiliaCat TEMPO and NaOCl is generally performed between pH 8 and 10. For the oxidation of alcohols to acid, the pH can be brought down to approximately 5 to 7 to decrease reaction times (chlorination of substrate may occur but lower pH should speed up formation of acid). For sluggish reactions and more difficult substrates, phase transfer catalyst Aliquat 336 (Triocylmethylammonium chloride), can be used to increase aldehyde¹ yields and formation of acid².

¹ Tetrahedron Lett., 1990, 31, 2177.

² J. Org. Chem., 1989, 54, 2970.

***ALL THESE PRODUCTS ARE AVAILABLE IN DIFFERENT SIZES FROM LAB SCALE TO MULTI-TON SCALE**

(5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 5kg, 10kg, 25kg, etc.)



Oxidation of Primary or Secondary Alcohols

Under Montanari-Anelli Conditions (using NaOCl)

Typical Experimental Conditions

Reaction

Under mechanical agitation, a 0.4M solution of the alcohol in dichloromethane was mixed with a 0.5 M aqueous solution of KBr and cooled at 0°C in an ice bath. The desired amount of SiliaCat TEMPO was added, followed by an aqueous solution of NaOCl (from commercial 10-13% bleach) buffered at pH 9 (using NaHCO₃). NaOCl solution was added slowly over a 10 minute period as the reaction is exothermic. The mixture was stirred between 1300-1500 rpm.

Work-up

Once the reaction is complete as deemed by TLC or GC-MS, the catalyst is filtered at room temperature, the organic phase was dried over MgSO₄ and evaporated. Crude mixture is purified using flash chromatography if needed.

- 1.2-5 eq of NaOCl_{aq} (typically 2.5 eq)
- 0.1 eq of KBr (prepared as a 0.5 M solution)
- 0.001-1 mol% of SiliaCat TEMPO (typically 1 mol%)
- The best solvents are DCM, EtOAc or ACN/ water (HPLC grade), typically at 0.4 M (molar concentration is with respect to the substrate).

Under Miller Conditions (using I₂ co-catalyst)

Typical Experimental Conditions

Reaction

Under mechanic agitation, a 0.4M solution of alcohol in toluene was mixed at room temperature (20°C) with a 0.3 M aqueous solution of NaHCO₃. Solid iodine was then added in one portion to the mixture followed by the desired amount of SiliaCat TEMPO. The mixture was stirred between 1300-1500 rpm at 20°C.

Work-up

Once the reaction is complete as deemed by TLC or GC-MS, the catalyst is filtered at room temperature. the mixture was cooled to 5°C, diluted with ethyl acetate, and quenched with a 0.8 M aqueous solution of Na₂SO₃. The uncolored organic phase was then washed with a saturated aqueous solution of NaHCO₃ followed by brine and dried over MgSO₄. After filtration and evaporation of the solvents, crude mixture can be purified using flash chromatography.

- 1.2-5 eq of NaOCl_{aq} (typically 2.5 eq)
- 0.1 eq of KBr (prepared as a 0.5 M solution)
- 0.001-1 mol% of SiliaCat TEMPO (typically 1 mol%)
- The best solvents are DCM, EtOAc or ACN/ water (HPLC grade), typically at 0.4 M (molar concentration is with respect to the substrate).



As a recognized industry leader in the development, manufacturing and commercialization of innovative silica gel products, and with multi-ton manufacturing capability, SiliCycle® is your partner of choice for all your **metal removal**, **catalysis**, **synthesis**, and **purification** requirements.

SiliaBond® Functionalized Silica Gels



- Highly efficient and selective **metal scavengers**
- No leaching (chemical stability)
- Selective nucleophile and electrophile scavengers
 - High resolution chromatographic phases
- **Supported reagents** for organic synthesis
 - Thermally stable and microwave compatible
 - Available in large quantities (**multi-ton scale**)

SiliaCat® Heterogeneous Catalysts



- Wide range of organic coupling and hydrogenation reactions (**Suzuki, Sonogashira, Heck, and Stille**)
- **SiliaCat** silica-supported catalysts for cleaner products and cleaner waste streams
 - Ideal for batch or flowthrough applications
- Cost efficient and highly stable
- Reusable and leach proof
- Available in sizes ranging from grams to multi-kilograms quantities

SiliaSep™ Flash Cartridges



- High resolution & reproducibility
- Ultra high performance cartridges available (**SiliaSep HP**)
- Compatible with all commercial systems
- Reversed and specialty phases available

SiliaPrep™ Solid Phase Extraction



- Wide choice of SPE cartridge formats, 96-well plates
 - Normal, reversed, fluorinated, and ion exchange phases
- Mixed-mode phases available
 - Specialty phases (scavengers, reagents, etc.)
- Certified SPE available

SiliaFlash® Irregular Silica Gels



- High purity irregular silica gel
 - Tight particle size distribution
- Very low level of fines
 - Neutral pH
- Controlled water level content
- Lot-to-lot reproducibility
 - Low metal content

SiliaSphere™ Spherical Silica Gels



- Very high purity
 - Tight particle size distribution
- Low metal content to avoid undesired interactions
- High mechanical stability
 - Wide choice of phases available (normal, reversed & specialty)

SiliaPlate™ TLC Plates



- Analytical and preparative TLC plates
- Different sizes and choice of backings
 - Normal, reversed and specialty phases

SiliaChrom® HPLC Columns



- Broad pH range (0,8-12,0)
 - Compatible with 100% aqueous mobile phase
 - High surface coverage
 - Wide variety of chemistries available
- Excellent column efficiency
 - Long column lifetime
 - Minimum buffer concentration needed
 - Low bleed