SOLUTIONS FOR SCAVENGING OF METAL AND ORGANIC IMPURITIES

SiliCycle

Founded in 1995, SiliCycle is specialized in the development, manufacturing and commercialization of high value silica gels and specialty products for chromatography, purification and synthesis.

Scavenging Solutions

SiliCycle Scavenging Solutions

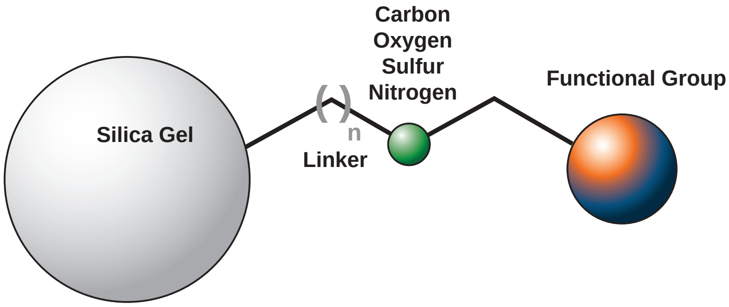
- Increased R&D and manufacturing productivity
- Versatile (*solvents, pH, compatible in batch flow, microwave, etc.*)
- Green and environmentaly friendly technology
- Broad scope of metals and organics to be scavenged

Silia*MetS* & Silia*Bond* Silica-Based Scavengers

Chemists have been searching for techniques and tools to separate, isolate and purify chemical substances from one to another to improve the quality of the synthesized molecules. SiliCycle grafted technology enables more powerful purification processes to help reach new purity standards. Our solutions are extremely versatile and customizable, hence suitable for a use in a vast array of industries facing different contamination issues.

Easier & Faster Purification Processes Using Scavengers

- Broadest portfolio of scavengers with associated applications
- Great variety of formats for all purifications scales: from laboratory to plant scale
- Successful technology for a variety of fields, such as pharmaceuticals, organic chemistry labs, agrochemicals and fine chemicals
- Great compatibility with a myriad of experimental conditions, solvents, pH and temperatures
- Strong chemical, physical, thermal and mechanical stability



Typical Structure of our Functionalized Silicas with Various Organic Groups

You Can Benefit From Our Scavenging Expertise

At SiliCycle, silica gels are functionalized with various molecules featuring scavenging properties toward different metals and / or organics.

We name our metal scavengers Silia*MetS* and our organic scavengers Silia*Bond*.

This technology combines the benefits of classical purification techniques, while integrating new assets that are becoming more and more critical in modern industries. New purification procedures need to be more selective, more efficient, faster and greener.

It is because of today's strive for greater performance while respecting environmental concerns that silica-based scavengers were developed; they are a powerful tool with an eco-friendly twist:

- Reduced purification steps
- No swelling
- No cross-contamination
- Less solvent needed
- Efficient precious metal recovery

Why Choose Silica-Based vs Polymer-Based Scavengers?

Silica-based scavengers have been proven to be one of the purification solution of choice.
Silica matrices show advantages over polymeric resins in purification, such as:

- No swelling
- Faster kinetics
- Solvent independence
- Mechanical & thermal stability
- Ease of use
- Controlled & precise loading

Regulatory Information

Regulatory Documents & Information

Certificate of analysis
iol Functionalized Silica
TION
4-0054 FAX: (418) 874-0355
riday 8:00 a.m.-5:00 p.m. (ES

The SiliCycle scavengers have been used for over decades in pilot plants and production units under GMP conditions by the pharmaceutical industry as well as CMOs and CROs. They have ran their own analysis proving that silica-based scavengers can safely be used, both in reactors or cartridges to purify their compounds.

SiliCycle is committed to high quality standards and always strives to provide superior quality products. In doing so, all products are manufactured in an ISO 9001:2015 compliant facility and subjected to stringent quality control.

SiliCycle provides a Certificate of Analysis with all its products, certifying that every lot has been manufactured and tested in accordance with SiliCycle specifications. Moreover, samples from every lot are kept for subsequent analysis.

<u>All products are shipped with the following information</u>:

- Certificate of Analysis (*molecular loading, surface coverage, volatile content, etc.*)
- Safety Data Sheet (*SDS*)
- Technical information

<u>All products can be shipped with the following information, under request</u>:

- BSE / TSE declaration (*non animal-derived*)
- GMO-Free Certificate
- Melamine-Free Certificate

Regulatory Support File

SiliCycle can work with you to fill and provide customized regulatory documents, including specific analytical tests in line with your needs.

Our Regulatory Support Files (*RSF*) are documents that include both proprietary and non-proprietary information on performance, chemical / thermal / mechanical stability, extractable & leachable compounds, SOPs, scale-up procedures, batch history, analytical methods and more. RSF documentation can be obtained through a Non-Disclosure Agreement (*NDA*).

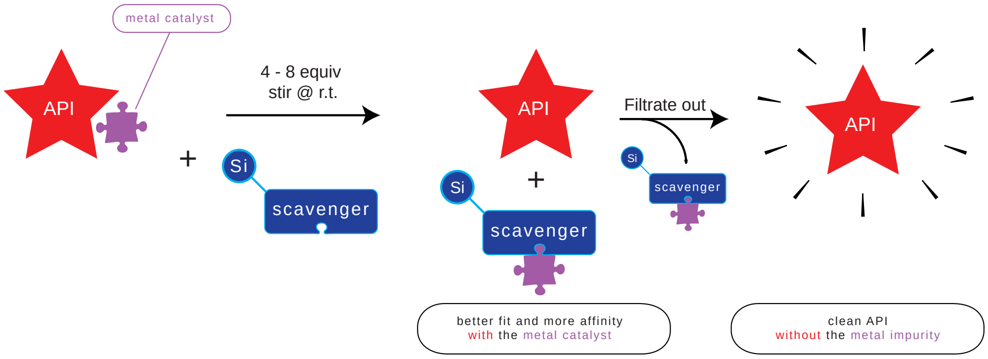
For any inquiries, please contact: regulatorysupport@silicycle.com

Silia*MetS*: Scavengers for Metal Impurities

SiliCycle Helps You Achieve Your Goals

In recent years, the time pressure associated with quickly bringing drug candidates to market has increased the number of transition metal-catalysed reactions progressing from lead optimisation to early scale-up. The removal of post-reaction metal residues has become a major issue in the pharmaceutical industry.

Purification of APIs (*Active Pharmaceutical Ingredients*), or Product of Interest from residual metal catalyst by traditional methods (*chromatography, activated carbon, distillation, etc.*) often leads to problems such as high costs, time loss, low efficiency and reduced API yields. To overcome these limitations, SiliCycle's Scavenger Solutions have changed how chemists can purify APIs. Here is the scavenging mechanism:

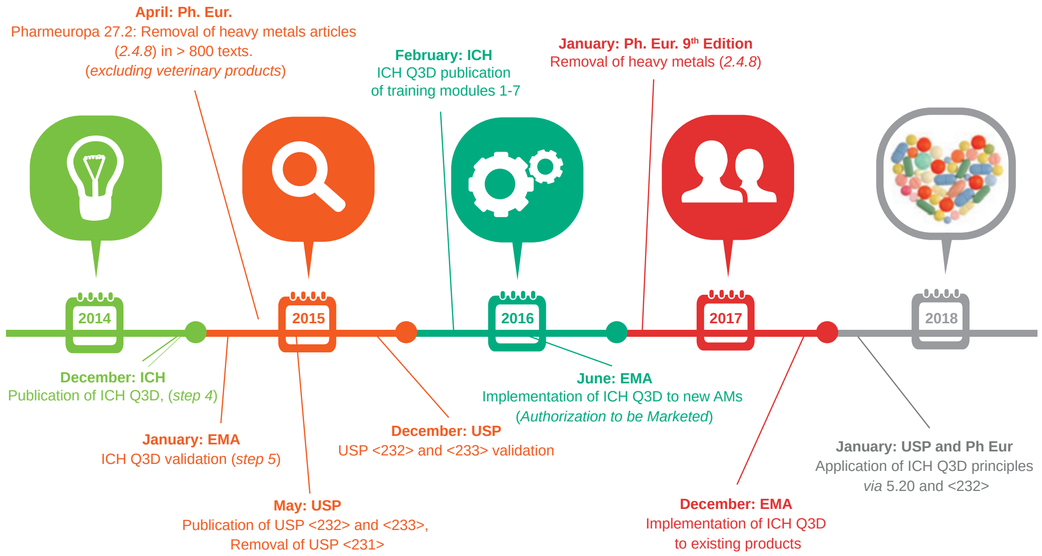


Pharmaceutical Challenges in Purification

ICH-Q3D Heavy Metal Regulation in the Pharmaceutical Industry

Since June 2013, the International Conference on Harmonisation (*ICH*) has been working on its Q3D guidelines on metal elemental impurities in new drugs and new formulations containing known ingredients. After many revisions and improvements, the final version of the Q3D guidelines was finally accepted and signed off by the ICH Steering Committee in December 2014, hence requiring the entire manufacturing industry and supply chain to meet more stringent regulations.

Since December 2015, twenty-four (*24*) metals - well-known to act as catalysts or present in solvents - have been indicted and associated with great health risks, and have been assigned distinctive PDE (*Permitted Daily Exposure*) limits. For example, now that ICH Q3D contains Lithium and Barium, we no longer talk of heavy metals impurities but elemental impurities.



December: ICH
Publication of ICH Q3D, (*step 4*)

January: EMA
ICH Q3D validation (*step 5*)

April: Ph. Eur.
Pharmeuropa 27.2: Removal of heavy metals articles
(*2.4.8*) in > 800 texts.
(*excluding veterinary products*)

May: USP
Publication of USP <232> and <233>,
Removal of USP <231>

December: USP
USP <232> and <233> validation

February: ICH
ICH Q3D publication
of training modules 1-7

June: EMA
Implementation of ICH Q3D to new AMs
(*Authorization to be Marketed*)

January: Ph. Eur. 9th Edition
Removal of heavy metals (*2.4.8*)

December: EMA
Implementation of ICH Q3D
to existing products

January: USP and Ph Eur
Application of ICH Q3D principles
via 5.20 and <232>

Take advantage of SiliCycle's expertise and knowledge in the field of grafting technologies to efficiently address this regulation.

Silia*Bond*: Scavengers for Organic Impurities

The Importance of Organic Contaminant Removal From APIs

Using excess reagents in organic synthesis is a very common strategy to maximise conversion and product yield. But the benefits of this approach can be outshined when comes the need to purify the final reaction mixture from excess reagents.

In addition, even reagents used in stoechiometric amounts can lead to an uncomplete reaction, and this is far more common than the other way around.

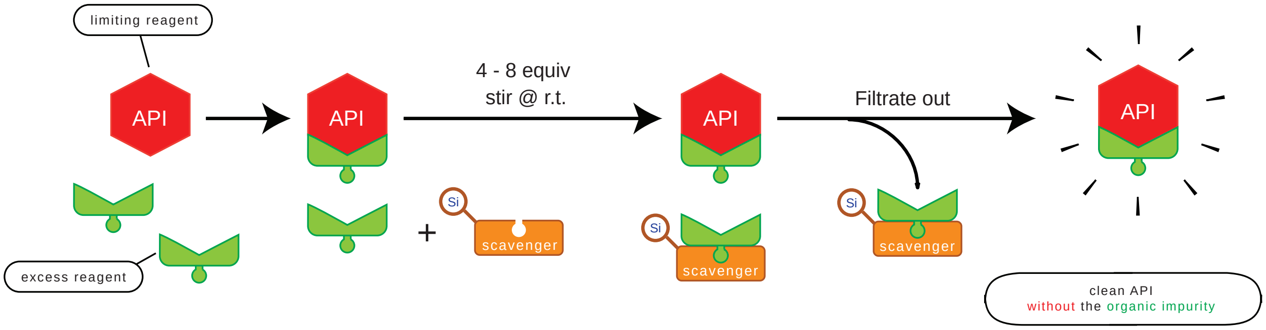
These reagents can either contaminate the API with potentially genotoxic impurities or environmental hazards, or jeopardize subsequent reactions by their reactivity. Indeed, such reagents usually bear nucleophilic, electrophilic, acidic or basic functional groups.

There is a need for simpler work-up and purification processes and our range of organic scavengers can help you from R&D up to manufacturing steps.

Two Ways to Purify API from Organic Contaminants using Silia*Bond* Organic Scavengers

Method 1: Direct scavenging of the undesired compound to isolate the API

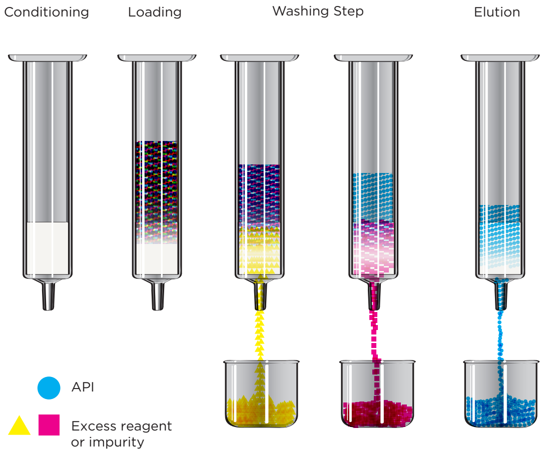
- Silica is bound with a functional group, that will specifically react with a product: either excess reagents (*unreacted*) or impurities.
- The API is recovered by simple filtration as demonstrated on the following scheme:



Method 2: Catch and release of the API

Silia*Bond* scavenger is packed in a SPE cartridge:

- **Conditioning step:** with six to ten hold-up volumes of solvent
- **Loading step:** API is loaded and trapped onto the cartridge bed
- **Washing step:** cartridge is washed to filter excess reagents and / or other impurities
- **Elution step:** API is eluted, recovered and purified



Removal of Potential Genotoxic Impurities (*PGI*)

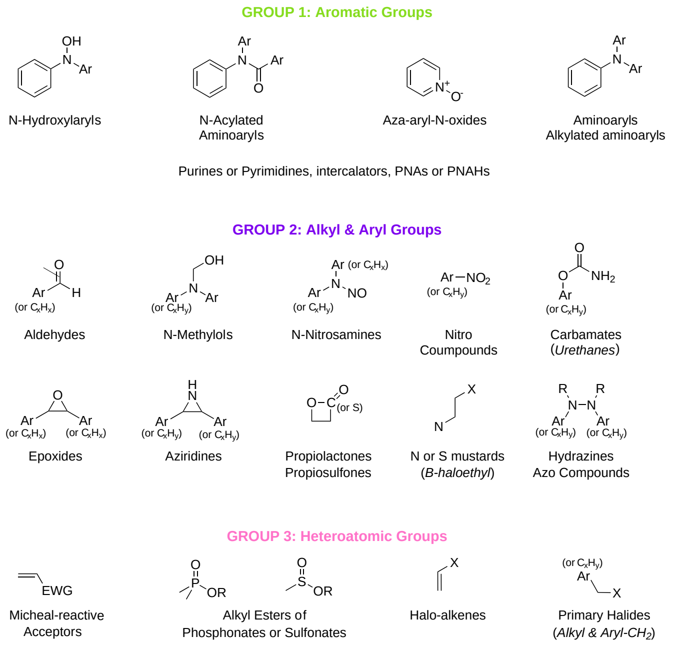
Potential Genotoxic Impurities (*PGI*) have gained attention due to their carcinogenic character to induce genetic mutations and / or chromosomal rearrangements. These compounds cause DNA damage by various mechanisms such as alkylation or other interactions and lead to mutation of the genetic code.

In situations where formation of PGIs cannot be avoided, an ideal solution would be to perform complete removal of PGIs after the synthesis is completed. For example, recrystallization, preparative chromatography or other downstream processing approaches might be considered. Many disadvantages of using such approaches include: potential yield loss, high solvent consumption, additional time and resources required for process development.

If you want to learn more about these impurity regulations, here are regularly updated websites and work of reference you may rely on:

- **International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human**
  http://www.ich.org
- **The European Medicines Agency**
  http://www.ema.europa.eu/
- **References and On-Going Updates from Regulatory Authorities and Industry Practices Related to Genotoxic Impurities**
  http://www.labcompliance.com/info/links/impurities/genotoxins

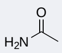
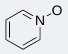
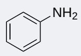
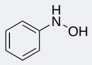
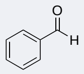
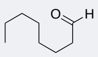
Alerting Structures Examples (*ICH*)



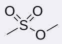
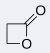
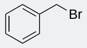
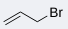
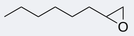
SiliCycle's PGI Scavengers

Eleven compounds containing structurally alerting functional groups were studied in SiliCycle labs, and scavenged by at least one of our grafted silica:

Scavenging Affinity for Various Potentially Genotoxic Impurities

Alerting Functional Groups	Acetamide 	Pyridine N-oxide 	Aniline 	Phenyl-hydroxylamine 	Benzaldehyde 	Octaldehyde 
Silia*MetS* DMT					●	●
Silia*MetS* Triamine					■	■
Silia*MetS* TAAcOH		●				
Silia*Bond* Tosic Acid	■	■	■	■		
Silia*Bond* Tosyl Chloride	●	■	●	●		

Scavenging Affinity for Various Potentially Genotoxic Impurities

Alerting Functional Groups	Methylmethane sulfonate 	Propiolactone 	Benzyl bromide 	Allyl bromide 	1,2-epoxyoctane 
Silia*MetS* DMT	■	■	■	■	
Silia*MetS* Thiourea		●	●	●	
Silia*MetS* Triamine	●	■			
Silia*MetS* TAAcONa	●	■			
Silia*Bond* Tosic Acid					■
Silia*Bond* Tosyl Chloride					■

Best scavenger: ■ Good scavenger: ●

Metal & Organic Scavenging Screening Services

CONFIDENTIALITY GUARANTEED

This service was specially designed for scientists that are either confronted with a residual impurity that needs to be discarded, or in lower in concentration.

With increasing regulatory requirements (*FDA, ICH*) for residual levels of metal catalysts and organic potentially genotoxic impurities (*PGI compounds*), the removal of post-reaction metal residues has become a major issue in the industry. SiliCycle offers a wide range of metal scavengers with its Silia*MetS* line, which significantly facilitates this purification process.

Our scavenging screening services provide solutions to quickly develop the most efficient metal scavenging process providing both time and cost savings. Confidentiality is assured, as in most cases the solution involves working with API and other patented materials, and easy technology transfers are guaranteed.

We will be working with you, in function of your needs. This process optimization work can be carried out and optimized as a slurry in your reactor followed by filtration (*bulk mode*), or via a cartridge in a flow design.

Over the years, SiliCycle has developed a number of screening services to assist customers in their project and help identify solutions for purification problems, at all stages & scales, from R&D to production.

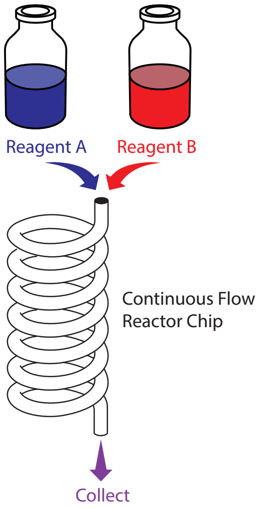
Contact us: **services@silicycle.com**

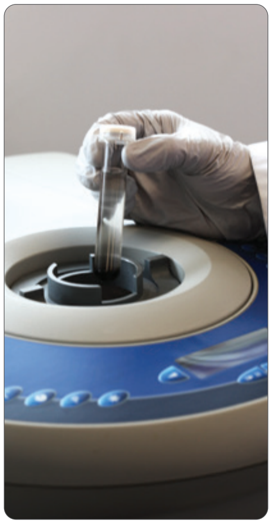
1. NDA signed for confidentiality purpose
2. Scavenging questionnaire completed by customer and revised by our experts
3. Communications to determine the objectives of the service
4. Customer's sample sent to SiliCycle
5. Initial lab-scale screening to select the most efficient scavengers and generate data
6. Optimization of the conditions
7. Scale-up trials and purity evaluation
8. Preparation of the report and wrap up meeting to present results to customer
9. Detailed experimental procedure for easy technology transfer & plant trials

Compatibility with Flow & Microwave-Assisted Chemistries

Scavenging can be achieved using Silia*MetS* or Silia*Bond* in flow or microwave chemistry applications. Simply place the silica-based scavenger inside the solid-phase reactors and let the solution to be purified flow through these reactors. Multiple reactors can be placed in series and reactors can be heated to obtain optimum scavenging results.

Metal and organic removal impurity using Silia*MetS* and Silia*Bond* can also be done under microwave irradiation to provide excellent scavenging efficiency in just minutes. Simply mix into a microwave tube the scavenger, the API dissolved in a suitable solvent, and set-up the system with chosen parameters. Usually, five minutes are sufficient for complete scavenging.





Different Formats for Different Applications

Scavengers as Bulk Silica

All our scavengers can be used in bulk directly in your reaction flask or reactor.

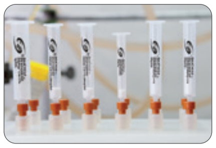
All scavengers are available in the following format size: 5 g, 10 g, 25 g, 50 g, 100 g, 250 g, 500 g, 1 kg, 5 kg, 10 kg, 25 kg, etc. Up to multi-ton scale!

- All our scavengers have, by default, the same silica backbone: our Silia*Flash* R10030B.
  - Particle Size: 40 - 63 µm
  - Pore Size: 60 Å
- All our Silia*Flash* silica gels of various particle sizes and pore sizes are available as silica backbones upon request.

Scavengers in Silia*Prep* SPE Cartridges

All our scavengers are available in pre-packed SPE cartridges, from 3 mL / 200 mg to 6 mL / 2 g.

Please refer to our Silia*Prep* Ordering Information p. 78 to learn about the different formats available.



Scavengers in Silia*Sep* Flash Cartridges

All our scavengers are available pre-packed in Flash cartridges.

- **Silia*Sep* flash cartridges**
  From 4 g to 1.6 kg bed weight
- **Silia*Sep* OT (*Open Top*) flash cartridges**
  From 12 mL / 200 g to 276 mL / 100 g formats
- **Silia*Sep* Industrial Scale cartridges**
  From 2.5 to 41 kg bed weight

Packings can also be tailored to your available equipment & scales.

Scavengers in E-PAK® Fixed Bed Flow-Through Cartridges

E-PAK is a family of radial flow adsorption cartridges developed specifically for pharmaceutical processings.

A proven radial technology that offers high adsorption capacity and flow rate!

E-PAK cartridges are offered in different formats for easy scale up:

- **Lab Scale -** from 8 g to 200 g media weight.
  Designed to facilitate evaluation of small samples.
- **Pilot Scale -** from 875 g to 1.75 kg media weight
  Provide rapid processing for volumes from 10 to hundreds of liters, and can establish the parameters upon moving to larger scales.
- **Commercial Scale -** from 3.5 to 7 kg media weight.
  Designed for manufacturing operations needing to process batch sizes of > 10,000 liters.

Scavengers in Silia*Chrom* Guard Cartridges

Protect your HPLC columns and system from damageable metallic impurities!

EXCLUSIVE
EXCLUSIVE
TO SILICYCLE

Scavengers as Guard Cartridges (*for HPLC*)

EXCLUSIVE
EXCLUSIVE TO SILICYCLE

Silia*Chrom* HPLC Guard Cartridges are designed to effectively protect both analytical and preparative HPLC columns. The usage of this shorter column is highly recommended to prolong column lifetime and does not alter chromatography. All metals can be prejudicial and very damaging to your column and detector, complicating purification steps, often making them longer, more laborious and less effective.

Crude reaction mixtures can now directly be injected without further metal removal, which will save precious time for the chemist. Another great benefit is that there is much less risk of corroding the equipment by injecting dirty samples.

Silia*Chrom* Guard Cartridges are cost effective and easy to use as a pre-filter to remove contaminants prior to injection.

SiliCycle is the only one on the market to offer protective guard cartridges filled with metal scavengers to protect your HPLC columns and system from damageable metallic impurities.

Silia*Chrom* Guard Cartridges Dimensions

Silia*Chrom* Guard Cartridges are available in lengths of 10 - 20 mm and three internal diameters (*ID: 4.0, 10 and 21.2 mm*).
The Guard Column internal diameter should be the same as the HPLC column or one size smaller.
Never use a guard column with a larger ID than the HPLC column (*risk of efficiency loss*).

Silia*Chrom* Scavenger Guard Cartridges

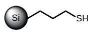
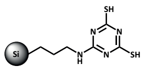
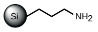
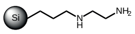
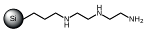
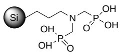
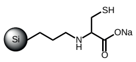
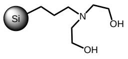
Guard Column Name	Favorite Metal Guard Column
Scavenger Packing #	K346
Effective Scavenger for:	**Pd, Ag, Hg, Ir, Ni, Os, Pt, Rh, Ru**
Can also Remove:	Cd, Co, Cu, Fe, Pb, Sc, Sn, Zn

Silia*Chrom* Scavenger Guard Cartridges Formats

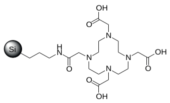
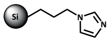
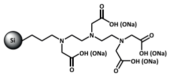
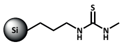
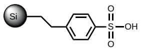
Particle Size of Sorbent (*µm*)	Formats Available (*internal diameter x length in mm*)			
	4.0 x 10	4.0 x 20	10 x 10	21.2 x 10
5	05E-A-N010	05E-A-N020	05E-A-Q010	05E-A-T010
10	07E-A-N010	07E-A-N020	07E-A-Q010	07E-A-T010

Silia*MetS* Metal Scavengers Portfolio

Silia*MetS* Metal Scavengers Technical Information

Scavengers	Structure	Brief Description	Metals Removed [1]	Typical Characteristics [2, 3]
PGI-S **Silia*MetS* Thiol** PN: R51030B Loading: ≥ 1.20 mmol/g Endcapping: Yes		Silia*MetS* Thiol is our most versatile and robust metal scavenger for a variety of metals under a wide range of conditions.	**Ag, Hg, Os, Pd & Ru** Cu, Ir, Pb, Rh & Sn	Color: White Density: 0.682 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
PGI-S **Silia*MetS* DMT** PN: R79030B Loading: ≥ 0.50 mmol/g Endcapping: Yes		Silia*MetS* DMT is the silica-bound equivalent of 2,4,6-trimercaptotriazine (*trithiocyanuric acid, TMT*). It is a versatile metal scavenger for a variety of metals and the preferred metal scavenger for ruthenium catalysts and hindered Pd complexes (*i.e. Pd(dppf)*Cl_2).	**Ir, Ni, Os, Pd, Pt, Rh & Ru** Cd, Co, Cu, Fe, Sc & Zn	Color: Light brown Density: 0.732 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
Silia*Bond* Amine PN: R52030B Loading: ≥ 1.20 mmol/g Endcapping: Yes		Also known for their electrophile scavenging efficiencies and their base reagent qualities, Silia*MetS* Amine, Diamine and Triamine have also proven to be very useful for the scavenging of the following metals: Pd, Pt, Cr, W and Zn.	**Cd, Cr, Pd, Pt, Rh & Ru** Co, Cu, Fe, Hg, Pb, W & Zn	Color: Off-white Density: 0.700 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
Silia*MetS* Diamine PN: R49030B Loading: ≥ 1.28 mmol/g Endcapping: Yes			**Cr, Pd, Pt, W & Zn** Cd, Co, Cu, Fe, Hg, Ni, Pb, Ru, V & Sc	Color: Off-white Density: 0.728 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
PGI-S **Silia*MetS* Triamine** PN: R48030B Loading: ≥ 1.11 mmol/g Endcapping: Yes			**Cr, Pd, Pt, W & Zn** Ag, Cd, Co, Cu, Fe, Hg, Ni, Os, Pb, Rh, Ru & Sc	Color: Off-white Density: 0.736 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
Silia*MetS* AMPA PN: R85130B Loading: ≥ 0.80 mmol/g Endcapping: Yes		Silia*MetS* AMPA is an aminomethyl-alkylphosphonic acid ligand known for its excellent metal-bonding properties. It is particularly efficient to remove Al, Sb, Ni, La, and also very effective for Co, Cu, Fe, Mg and Zn scavenging from reaction intermediates or final APIs.	**Al, Ce, Dy, Er, Eu, Gd, Ho, La, Lu, Mg, Nd, Ni, Pm, Pr, Sb, Sm, Tb, Tm, V & Yb** Co, Cu, Fe, Mg & Zn	Color: Yellow Density: 0.707 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 1 Year
Silia*MetS* Cysteine PN: R80530B Loading: ≥ 0.30 mmol/g Endcapping: Yes		Silia*MetS* Cysteine is the silica-bound equivalent of the amino acid cysteine. It is a versatile scavenger for a variety of metals and the preferred metal scavenger for tin residues. By attaching the molecule to the backbone via the amino group, the thiol group remains free and accessible for higher metal scavenging efficiency.	**Cd, Fe, Ir, Os, Ru, Sc & Sn** Ca, Cr, Cs, Cu, La, Mg, Pd, Pt, Rh & Zn	Color: Orange Density: 0.665 g/mL Solvent Compatibility: 1 (*although we recommend organic solvent when possible*) Prolonged Storage: 1 Shelf Life: 1 Year
PGI-S **Silia*MetS* DEAM** PN: R54430B Loading: ≥ 0.85 mmol/g Endcapping: Yes		Silia*MetS* DEAM is a versatile scavenger designed to remove trace metal of Ti, Zn, Fe and Ag as well as boronic acids from reaction intermediates or final APIs.	**Ag, Fe, Sn, Ti & Zn**	Color: Off-white Density: 0.691 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years

Silia*MetS* Metal Scavengers Technical Information

Scavengers	Structure	Brief Description	Metals Removed [1]	Typical Characteristics [2, 3]
PGI-S **Silia*MetS* DOTA** PN: R91030B Loading: ≥ 0.38 mmol/g Endcapping: Yes		Silia*MetS* DOTA is a silica-supported tetracarboxylic acid and its various conjugate bases. DOTA molecule is a well-adopted complexing agent. Linked to various metals, so formed-complexes are used as contrast agents in cancer treatments or other medical applications.	**Ca, Cu, Gd, La, Ni & Zn** Co, Fe, Mg, Pd, Pt & Rh	Color: Light yellow Density: 0.681 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 1 Year
Silia*MetS* Imidazole PN: R79230B Loading: ≥ 0.96 mmol/g Endcapping: Yes		Silia*MetS* Imidazole is a versatile metal scavenger for a variety of metals including Cd, Co, Cu, Fe, Ni, Os, Pd and Rh.	**Cd, Co, Cu, Fe, Ir, Li, Mg, Ni, Os, W & Zn** Cr, Pd & Rh	Color: Off-white Density: 0.681 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
PGI-S **Silia*MetS* TAAcOH** PN: R69030B Loading: ≥ 0.41 mmol/g Endcapping: No		Silia*MetS* TAAcOH & TAAcONa are supported versions of EDTA in their acid and sodium salt forms. These two products are effective metal scavengers for Ca, Mg, Li, Ir, Cs, Os, Sn, Pd, Ni and Cu. Silia*MetS* TAAcOH is effective for metals in low or zero oxidation states, compared to Silia*MetS* TAAcONa which is useful for metals in higher oxidation states (≥ *2*).	**Ca, Co, Ir, Li, Mg, Ni, Os, Ru & Sc** Cr, Cs, Fe, Pd, Rh & Sn	Color: Off-white Density: 0.635 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
Silia*MetS* TAAcONa PN: R69230B Loading: ≥ 0.41 mmol/g Endcapping: No			**Ca, Cd, Cs, Cu, Fe, Ir, La, Li, Mg, Ni, Os, Rh, Sc & Sn** Cr, Pd, Ru & Zn	Color: Off-white Density: 0.712 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
Silia*MetS* Thiourea PN: R69530B Loading: ≥ 1.07 mmol/g Endcapping: Yes		Silia*MetS* Thiourea is a versatile metal scavenger for all forms of palladium and is widely used in the pharmaceutical industry. Once complexed with a transition metal, it has been reported to be an effective catalyst.	**Pd & Ru** Ag, Cu, Fe, Os, Rh, Sc & Sn	Color: Off-white Density: 0.767 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
PGI-S **Silia*Bond* Tosic Acid** PN: R60530B Capacity: ≥ 0.54 meq/g Endcapping: Yes		Silia*Bond* Tosic Acid is in a class of strong acids used in different fields of synthetic organic chemistry. The aromatic ring makes it slightly more acidic than other supported sulfonic acids.	**Fe, Rh & Sn** Ag, Cu, Ni, Pd, Pt, Ru & Zn	Color: Off-white Density: 0.698 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years

[1] **Scavenging Efficiency:**

- Best scavenger for the removal of a particular metal is indicated in **Navy Blue**
- Good scavenger indicated in Pale Blue

[2] **Solvent Compatibility:**

1- All solvents, aqueous and organic

2- All organic solvents

[3] **Prolonged Storage:**

1- Keep dry

2- Keep cool (< *8°C*) and dry

3- Keep cool (< *8°C*), dry and under inert atmosphere

PGI-S Potentially Genotoxic Impurities (*PGI*) Scavenger
Contact us for more information

Silia*MetS* Metal Scavengers Selection Table

When selecting a metal scavenger, every parameter must be considered: metal catalyst, solvent, residual reagents, by-products, structure of the API (*or molecule of interest*) and temperature.

The following table will help in selecting the most efficient scavenger for a specific metal and application. However, since some parameters may affect the efficiency of the scavenging, we highly recommend performing a preliminary screening experiment using the Silia*MetS* Metal Scavenger Kit.

SiliCycle also offers a confidential Metal Scavenger Screening Service. Contact us to take advantage of our expertise in metal removal.

Best scavenger: ■ Good scavenger: ●

Silia*MetS* Metal Scavengers Selection Table

	Scavenger	Silia*MetS* Thiol (*Si-Thiol*)	Silia*MetS* DMT (*Si-DMT*)	Silia*Bond* Amine (*Si-WAX*)	Silia*MetS* AMPA (*Si-AMPA*)	Silia*MetS* Cysteine (*Si-CYS*)	Silia*MetS* DEAM (*Si-DEAM*)	Silia*MetS* Diamine (*Si-DIA*)
	PN	R51030B	R79030B	R52030B	R85130B	R80530B	R54430B	R49030B
	Loading (*mmol/g*)	≥ 1.20	≥ 0.50	≥ 1.20	≥ 0.80	≥ 0.30	≥ 0.85	≥ 1.28
	Typical Tap Density (*g/mL*)	0.682	0.732	0.700	0.707	0.665	0.691	0.728
Metals to be scavenged	**Ag**	■					■	
	Al				■			
	Ar					■		
	As	●			■			
	Ca					●		
	Cd		●	■		■		●
	Ce				■			
	Co		●	●	●			●
	Cr			■		●		■
	Cs					●		
	Cu	●	●	●	●	●		●
	Fe		●	●	●	■	■	●
	Gd				■			
	Hg	■		●				●
	Ir	●	■			■		
	La				■	●		
	Li							
	Mg				●	●		
	Ni		■		■			●
	Os	■	■			■		
	Pb	●		●				●
	Pd	■	■	■		●		■
	Pt		■	■		●		■
	Rh	●	■	■		●		
	Ru	■	■	■		■		●
	Sc		●			■		●
	Se	●	■			●	●	●
	Sn	●				■	■	
	Ti						■	
	W			●				■
	Zn		●	●	●	●	■	■

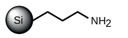
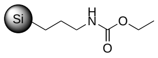
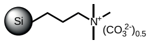
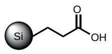
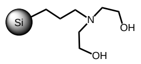
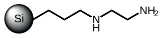
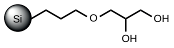
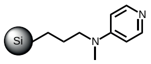
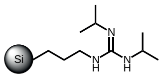
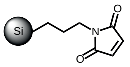
Silia*MetS* Metal Scavengers Selection Table

Silia*MetS* DOTA (*Si-DOTA*)	Silia*MetS* Imidazole (*Si-IMI*)	Silia*MetS* TAAcOH (*Si-TAAcOH*)	Silia*MetS* TAAcONa (*Si-TAAcONa*)	Silia*MetS* Thiourea (*Si-THU*)	Silia*MetS* Triamine (*Si-TRI*)	Silia*Bond* Tosic Acid (*Si-SCX*)	Scavenger
R91030B	R79230B	R69030B	R69230B	R69530B	R48030B	R60530B	**PN**
≥ 0.38	≥ 0.96	≥ 0.41	≥ 0.41	≥ 1.07	≥ 1.11	≥ 0.54 meq/g	**Loading (*mmol/g*)**
0.681	0.681	0.635	0.712	0.767	0.736	0.698	**Typical Tap Density (*g/mL*)**
				●	●	●	**Ag**
							Al
■							**Ar**
■							**As**
■		■	■				**Ca**
	■		■		●		**Cd**
							Ce
●	■	■			●		**Co**
	●	●	●		■		**Cr**
		●	■				**Cs**
■	■		■	●	●	●	**Cu**
●	■	●	■	●	●	■	**Fe**
■							**Gd**
					●		**Hg**
	■	■	■				**Ir**
■			■				**La**
	■	■	■				**Li**
●	■	■	■				**Mg**
■	■	■	■		●	●	**Ni**
	■	■	■	●	●		**Os**
					●		**Pb**
●	●	●	●	■	■	●	**Pd**
●					■	●	**Pt**
●	●	●	■	●	●	■	**Rh**
		■	●	■	●	●	**Ru**
		■	■	●	●		**Sc**
■			●		●		**Se**
		●	■	●		■	**Sn**
							Ti
	■				■		**W**
■	■		●		■	●	**Zn**

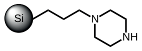
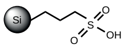
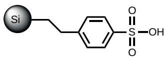
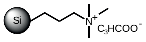
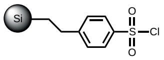
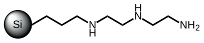
Metals to be scavenged

Silia*Bond* Organic Scavengers Portfolio

Silia*Bond* Organic Scavengers Technical Information

Scavengers	Structure	Nature	Molecules Removed	Typical Characteristics [1, 2]
Silia*Bond* Amine PN: R52030B Loading: ≥ 1.20 mmol/g Endcapping: Yes		Scavenger for Electrophiles (*Covalent Bonding*)	Acyl Chlorides, Aldehydes, Anhydrides, Chloroformates, Isocyanates, Ketones & Sulfonyl Chlorides	Color: Off-white Density: 0.700 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
		Scavenger for Acids (*Ionic Bonding*) Catch & Release	Acids & Acidic Phenols	
Silia*Bond* Carbamate PN: R50130B Loading: ≥ 1.16 mmol/g Endcapping: Yes		Scavenger for Nucleophiles (*Covalent Bonding*)	Alcohols, Alkoxides, Amines, Anilines, Hydrazines, Organometallics, Thiols & Thiolates	Color: Off-white Density: 0.741 g/mL Solvent Compatibility: 3 Prolonged Storage: 2 Shelf Life: 2 Years
Silia*Bond* Carbonate PN: R66030B Loading: ≥ 0.46 mmol/g Endcapping: Yes		Scavenger for Acids (*Ionic Bonding*) Catch & Release	Acids, Acidic Phenols & Boronic Acids	Color: Off-white Density: 0.608 g/mL Solvent Compatibility: 3 Prolonged Storage: 1 Shelf Life: 1 Years
Silia*Bond* Carboxylic Acid PN: R70030B Loading: ≥ 0.92 mmol/g Endcapping: Yes		Scavenger for Bases (*Ionic Bonding*) Catch & Release	Primary / Secondary Amines & Anilines	Color: Off-white Density: 0.687 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
PGI-S **Silia*MetS* DEAM** PN: R54430B Loading: ≥ 0.85 mmol/g Endcapping: Yes		Scavenger for Electrophiles & Lewis Acids (*Covalent & Ionic Bonding*) Catch & Release	Boronic Acids	Color: Off-white Density: 0.691 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
Silia*MetS* Diamine PN: R49030B Loading: ≥ 1.28 mmol/g Endcapping: Yes		Scavenger for Electrophiles (*Covalent Bonding*)	Acyl Chlorides, Aldehydes, Anhydrides, Chloroformates, Isocyanates, Ketones & Sulfonyl Chlorides	Color: Off-white Density: 0.728 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
		Scavenger for Acids (*Ionic Bonding*) Catch & Release	Acids & Acidic phenols	
Silia*Bond* Diol PN: R35030B Loading: ≥ 0.97 mmol/g Endcapping: No		Scavenger for Electrophiles & Lewis Acids (*Covalent & Ionic Bonding*) Catch & Release	Boronic Acids	Color: Off-white Density: 0.687 g/mL Solvent Compatibility: 2 Prolonged Storage: 1 Shelf Life: 2 Years
Silia*Bond* DMAP PN: R75630B Loading: ≥ 0.53 mmol/g Endcapping: Yes		Scavenger for Electrophiles (*Covalent Bonding*)	Acyl Chlorides & Sulfonyl Chlorides	Color: Light brown to brown Density: 0.674 g/mL Solvent Compatibility: 1 Prolonged Storage: 3 Shelf Life: 1 Years
Silia*Bond* Guanidine PN: R68230B Loading: ≥ 0.80 mmol/g Endcapping: Yes		Scavenger for Acids (*Ionic Bonding*) Catch & Release	Acids, Acidic Phenols & Boronic Acids	Color: Light yellow Density: 0.732 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
Silia*Bond* Maleimide PN: R71030B Loading: ≥ 0.64 mmol/g Endcapping: Yes		Scavenger for Nucleophiles (*Covalent Bonding*)	Thiols & Thiolates	Color: Off-white Density: 0.644 g/mL Solvent Compatibility: 5 Prolonged Storage: 3 Shelf Life: 2 Years

Silia*Bond* Organic Scavengers Technical Information

Scavengers	Structure	Nature	Molecules Removed	Typical Characteristics [1, 2]
PGI-S **Silia*Bond* Piperazine** PN: R60030B Loading: ≥ 0.83 mmol/g Endcapping: Yes		Scavenger for Electrophiles (*Covalent Bonding*)	Acyl Chlorides, Aldehydes, Anhydrides, Chloroformates, Isocyanates, Ketones & Sulfonyl Chlorides	Color: Off-white Density: 0.671 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
		Scavenger for Acids (*Ionic Bonding*) Catch & Release	Acids & Acidic Phenols	
PGI-S **Silia*Bond* Propylsulfonic Acid** PN: R51230B Loading: ≥ 0.63 mmol/g Endcapping: Yes		Scavenger for Bases (*Ionic Bonding*) Catch & Release	Amines & Anilines	Color: Off-white Density: 0.728 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
PGI-S **Silia*Bond* Tosic Acid** PN: R60530B Loading: ≥ 0.54 meq/g Endcapping: Yes				Color: Off-white Density: 0.698 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
Silia*Bond* TMA Acetate PN: R66430B Loading: ≥ 0.71 mmol/g Endcapping: No		Scavenger for Acids (*Ionic Bonding*) Catch & Release	Carboxylic Acids	Color: Off-white Density: 0.665 g/mL Solvent Compatibility: 1 Prolonged Storage: 1 Shelf Life: 2 Years
Silia*Bond* Tosyl Chloride PN: R44030B Loading: ≥ 0.63 mmol/g Endcapping: Yes		Scavenger for Nucleophiles (*Covalent Bonding*)	Alcohols, Alkoxides, Amines, Anilines, Hydrazines, Organometallics, Thiols & Thiolates	Color: Off-white Density: 0.761 g/mL Solvent Compatibility: 4 Prolonged Storage: 3 Shelf Life: 6 months
PGI-S **Silia*MetS* Triamine** PN: R48030B Loading: ≥ 1.11 mmol/g Endcapping: Yes		Scavenger for Electrophiles (*Covalent Bonding*)	Acyl Chlorides, Aldehydes, Anhydrides, Chloroformates, Isocyanates, Ketones & Sulfonyl Chlorides	Color: Off-white Density: 0.736 g/mL Solvent Compatibility: 1 Prolonged Storage: 2 Shelf Life: 2 Years
		Scavenger for Acids (*Ionic Bonding*) Catch & Release	Acids & Acidic Phenols	

[1] **Solvent Compatibility:**

1- All solvents, aqueous and organic

2- All organic solvents

3- Anhydrous aprotic solvents

4- Anhydrous aprotic solvents, unstable in DMF

5- Polar solvents (*DMF, MeOH,* H_2O)

[2] **Prolonged Storage:**

1- Keep dry

2- Keep cool (< *8°C*) and dry

3- Keep cool (< *8°C*), dry and under inert atmosphere

PGI-S Potentially Genotoxic Impurities (*PGI*) Scavenger
Contact us for more information

Silia*Bond* Organic Scavengers Selection Table

Silia*Bond* Organic Scavengers can help you purify your API. Functional group is bound to silica, that will specifically react with a given product. Use the double-entry chart below to choose the best match between the impurity you are dealing with or the scavenger you already have in hand.

Electrophile scavenger (*Covalent Bonding*): ◆

Nucleophile scavenger (*Covalent Bonding*): ▼

Ionic bonding: ●

Catch & release: ⬢

Silia*Bond* Organic Scavengers Selection Table

Organic Scavenger	Silia*Bond* Amine (*Si-WAX*)	Silia*Bond* Carbamate (*Si-CAR*)	Silia*Bond* Carbonate (*Si-CO$_3$*)	Silia*Bond* Carboxylic Acid (*Si-WCX*)	Silia*MetS* DEAM (*Si-DEAM*)	Silia*MetS* Diamine (*Si-DIA*)	Silia*Bond* Diol *nec* (*Si-Diol*)
Product Number	R52030B	R50130B	R66030B	R70030B	R54430B	R49030B	R35030B
Loading	≥ 1.20 mmol/g	≥ 1.16 mmol/g	≥ 0.46 mmol/g	≥ 0.92 mmol/g	≥ 0.85 mmol/g	≥ 1.28 mmol/g	≥ 0.97 mmol/g
Typical Density	0.700 g/mL	0.741 g/mL	0.608 g/mL	0.687 g/mL	0.691 g/mL	0.728 g/mL	0.687 g/mL
Solvent Compatibility	All aqueous & organic solvents	Anhydrous aprotic solvents	Anhydrous aprotic solvents	All aqueous & organic solvents	All aqueous & organic solvents	All aqueous & organic solvents	All organic solvents
Functionalities to be scavenged							
Acids & Acidic Phenols	● ⬢	▼	● ⬢			● ⬢	
Acyl & Sulfonyl Chlorides	◆					◆	
Alcohols & Alkoxides		▼					
Aldehydes, Anhydrides, Chloroformates, Isocyanates & Ketones	◆					◆	
Amines & Anilines		▼		● ⬢			
Boronic Acids			● ⬢		◆ ⬢		◆ ⬢
Carboxylic Acids							
Hydrazines		▼					
Organometallics, Thiols & Thiolates		▼					

Silia*Bond* Organic Scavengers Selection Table

Silia*Bond* DMAP (*Si-DMAP*)	Silia*Bond* Guanidine (*Si-GUA*)	Silia*Bond* Maleimide (*Si-MAL*)	Silia*Bond* Piperazine (*Si-PPZ*)	Silia*Bond* Propylsulfonic Acid (*Si-SCX-2*)	Silia*Bond* Tosic Acid (*Si-SCX*)	Silia*Bond* TMA Acetate *nec* (*Si-SAX$_2$*)	Silia*Bond* Tosyl Chloride *nec* (*Si-TsCl*)	Silia*MetS* Triamine (*Si-TRI*)
R75630B	R68230B	R71030B	R60030B	R51230B	R60530B	R66430B	R44030B	R48030B
≥ 0.53 mmol/g	≥ 0.80 mmol/g	≥ 0.64 mmol/g	≥ 0.83 mmol/g	≥ 0.63 meq/g	≥ 0.54 meq/g	≥ 0.71 mmol/g	≥ 0.63 mmol/g	≥ 1.11 mmol/g
0.674 g/mL	0.732 g/mL	0.644 g/mL	0.671 g/mL	0.728 g/mL	0.698 g/mL	0.665 g/mL	0.761 g/mL	0.736 g/mL
All aqueous & organic solvents	All aqueous & organic solvents	Polar solvents (*DMF, MeOH, H_2O*)	All aqueous & organic solvents	All aqueous & organic solvents	All aqueous & organic solvents	All aqueous & organic solvents	Anhydrous aprotic solvents, unstable in DMF	All aqueous & organic solvents
	● ⬢		● ⬢					● ⬢
◆			◆					◆
							▼	
			◆					◆
				● ⬢	● ⬢		▼	
	● ⬢							
						● ⬢		
							▼	
		▼					▼	

Silia*MetS* E-PAK Cartridges

E-PAK is a family of radial flow adsorption cartridges developed specifically for pharmaceutical processing.

Created with proprietary technology, E-PAK cartridges provide rapid adsorption kinetics at flow rates and processing capacities suitable for laboratory, pilot and commercial operations. They are designed for use with both organic and aqueous solvents, and incorporate design features useful for the production of active pharmaceutical ingredients (*API*).

Features & Benefits

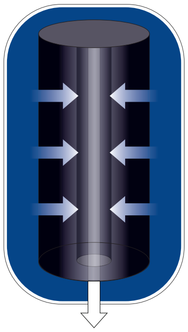
- Proven cartridge design ensures rapid, simple & reliable technology
- High adsorption capacity and flow rate
- Fixed-bed design ensuring safer handling, clean-up and disposal
- Large adsorbent capacity in small area footprint increases product recovery & reduces solvent requirements

Sorbents for E-PAK Cartridges

E-PAK cartridges are available in a range of sorbents to accommodate the broad range of processing requirements. Other adsorbents are available under request.

Sorbents for E-PAK

Active Adsorbents	For Removal and/or Recovery of :	pH Operation
Silia*MetS* Thiol	**Pd, Ag, Hg, Os, Ru,** Cu, Ir, Pb, Rh, Se & Sn	2 to 10
Silia*MetS* DMT	**Pd, As, Ir, Ni, Os, Pt, Rh, Ru, Se,** Cd, Co, Cu, Fe, Sc & Zn	
Silia*MetS* Imidazole	**Cd, Co, Cu, Fe, Ir, Li, Mg, Ni, Os, W, Zn,** Cr, Pd & Rh	
Silia*Bond* Amine	**Pd, Cr, Pt, W, Zn,** Cd, Co, Cu, Fe, Hg, Ni, Pb, Ru, Sc & Se	
Silia*MetS* Diamine		
Silia*MetS* Triamine		
Silia*Flash* Bare Silica	Very vast range of organic impurities, metals, pigments...	2 to 9
Activated Carbons	Precious metal catalysts & colors	1 to 13



Out-to-in radial flow-through fixed porous adsorbent media

Chemical Compatibility

E-PAK cartridges are formed using a proprietary technology and chemically stable materials in common organic solvents. They have been tested and found satisfactory for use with the following commonly used solvents, such as: Methanol, Dichloromethane, Ethyl acetate, Tetrahydrofuran, Toluene & N-ethyl-2-pyrolidone.

Various Ways of Using E-PAK

Depending on the application and how you prefer to work, E-PAK cartridges can be used in different ways as shown below.

For a single pass usage, we suggest to run at very low flow rate compared to recirculation process, which can be run at higher flow rate.

Single Pass

Recirculation

Multiple Sequential Passes

2 Cartridges Method

Case Study

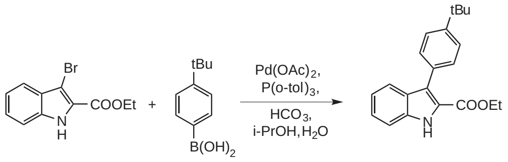
Get your copy of our new Case Study!

« Two-Steps Purification with E-PAK® Cartridges Following a Direct Pd-Catalyzed Borylation »

Contact us: scavengers@silicycle.com

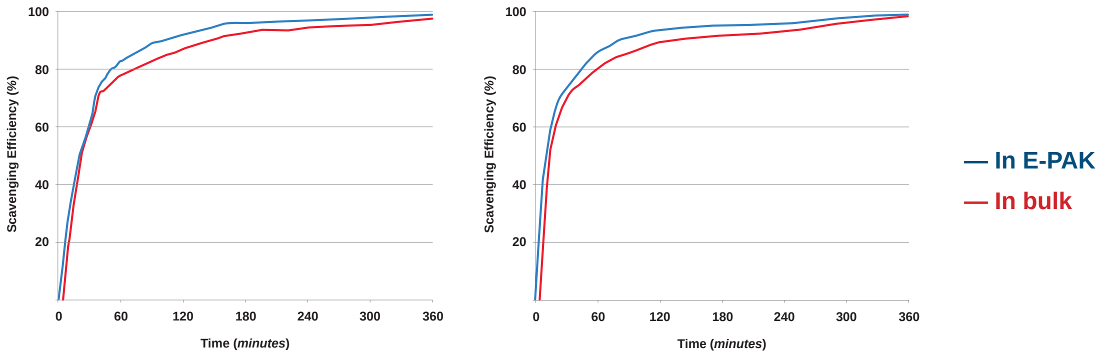
Pd Scavening: Bulk vs E-PAK

A typical Suzuki-Miyaura reaction was performed (*right*).



Silia*MetS* in a 5 x 1 cm E-PAK and bulk (≈ *8 molar equiv.*), solution recirculated at 50 mL/min for E-PAK, contact time of 6 h for both.

No backpressure was observed for E-PAK with a slightly faster scavenging efficiency versus bulk.



Portfolio

Lab Scale

Lab scale cartridges are designed to facilitate the evaluations of small samples. Testing with loose media can be done with samples as small as a few milliliters and are normally done in advance of cartridge testing to identify the formula with the highest capacity to remove contaminants with the highest recovery.

Lab Scale Cartridges

Cartridge Size Diameter x Height	Flow Rate Range	Pressure Drop ΔP (Psig) with w/1 cps Fluid	Media Weight	
			Silia*MetS* & Silia*Bond*	Silia*Flash* & Activated Carbons
5 x 1 cm	1 - 20 mL/min	≤ 5 psig	8 g	5 g
5 x 10 cm	10 - 200 mL/min	≤ 5 psig	75 g	50 g
5 x 25 cm	25 - 500 mL/min	≤ 5 psig	200 g	125 g

Note: Faster flow rate can be used for the lab scale cartridges depending on the application or the scavenging difficulty (*1 cm up to 100 mL/min, 10 cm up to 500 mL/min and 25 cm up to 1 L/min*).

Pilot & Commercial Scale

E-PAK pilot scale cartridges provide rapid processing for volumes from 10 to hundreds of liters, and can establish the parameters upon moving to larger scales, since E-PAK achieve true linear scalability.

E-PAK commercial scale cartridges provide rapid processing for manufacturing operations needing to process batch sizes of > 10,000 liters or can be adapted for continuous operation using a duplex design.

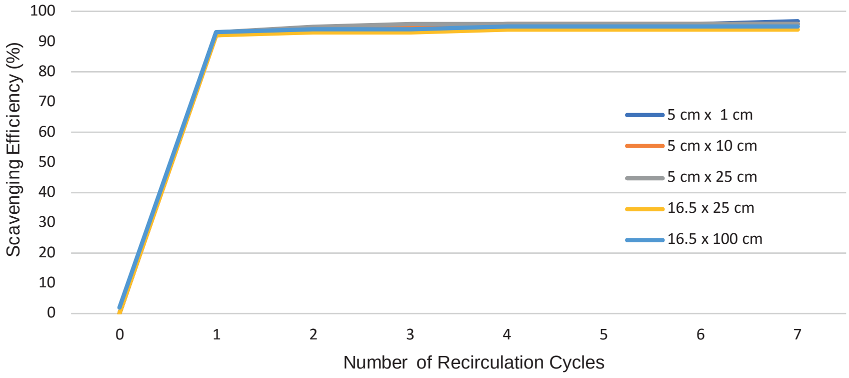
Pilot & Commercial Scale Cartridges

Cartridge Size Diameter x Height	Flow Rate Range	Pressure Drop ΔP (Psig) with w/1 cps Fluid	Media Weight	
			Silia*MetS* & Silia*Bond*	Silia*Flash* & Activated Carbons
Pilot Scale				
16.5 x 12.5 cm	0.10 - 2.5 L/min	≤ 10 psig	875 g	850 g
16.5 x 25 cm	0.25 - 5 L/min	≤ 10 psig	1.75 kg	1.7 kg
Commercial Scale				
16.5 x 50 cm	0.50 - 10 L/min	≤ 10 psig	3.5 kg	3.4 kg
16.5 x 100 cm	1 - 20 L/min	≤ 10 psig	7 kg	6.8 kg

All cartridges are provided with a Code 8 (*closed top & open bottom endcaps-bottom with double 2-222 Teflon® encapsulated Viton® o-ring*) cartridge sealing configuration. To meet commercial processing requirements, E-PAK cartridges can be operated in parallel for increased capacity.

Scale-Up Linearity Demonstration

Using the same typical Suzuki-Miyaura reaction shown at page 19, with ~ 12 molar equiv., scale-up reactions were performed from lab to commercial scale. As you can see below, each format behaved similarly in terms of efficiency and kinetics.



Scale-Up Calculation

Scale-up projections based on a linear extrapolation of adsorbent mass have proven to be quite accurate when test conditions including contact time, temperature, solvent type and contaminant and compound levels are held constant. The following table shows the scale-up/relative change in mass between lab, pilot and commercial size E-PAK cartridges.

Scale-Up calculation for Silica-Based Adsorbents

Cartridge Sizes	5 x 1 cm	5 x 10 cm	5 x 25 cm	16.5 x 12.5 cm	16.5 x 25 cm	16.5 x 50 cm	16.5 x 100 cm
Scale-up Factor	-	10	25	80	220	440	875
Mass of Silica (*g*)	8	75	200	875	1,750	3,500	7,000
# mmol Silia*MetS* Thiol (*1.20 mmol/g*)	9.6	90	240	1,050	2,100	4,200	8,400
# mmol Silia*MetS* DMT (*0.50 mmol/g*)	4.0	38	100	438	875	1,750	3,500
# mmol Silia*MetS* Imidazole (*0.96 mmol/g*)	7.7	72	192	840	1,680	3,360	6,720
# mmol Silia*Bond* Amine (*1.20 mmol/g*)	9.6	90	240	1,050	2,100	4,200	8,400
# mmol Silia*MetS* Diamine (*1.28 mmol/g*)	10.2	96	256	1,120	2,240	4,480	8,960
# mmol Silia*MetS* Triamine (*1.11 mmol/g*)	8.9	83	222	971	1,942	3,885	7,770
Bed volume (*cm*^{3})	18.8	188	470	2,375	4,750	9,500	19,000
Recommended Flow Rate (*mL/min*)	7.5	75	190	950	1,900	3,800	7,600
Typical Flow Rate Range (*mL/min*)	1 - 20	10 - 200	25 - 500	100 - 2,500	250 - 5,000	500 - 10,000	1,000 - 20,000
Approximated Tank Volume	50 mL	200 mL	450 mL	2.5 L	5 L	11.6 L	23.3 L
Conditionning	150 mL	600 mL	1.35 L	7.5 L	15 L	35 L	70 L

Measurement Methodology:

- Scale-up Factor: mass of silica / 8 g (*smallest size*)
- Mass of Silica (*g*): upon packing of cartridge
- # mmol Silia*MetS* / Silia*Bond* XXX (*X.X mmol/g*): silica mass x typical loading of Silia*MetS* / Silia*Bond*
- Bed volume (*cm*^{3}): cake total volume, excluding cap
- Recommended Flow Rate (*mL/min*): for residence times of 2.5 minutes
- Recommended Flow Rate Range (*mL/min*): for residence times from 1 to 20 minutes. Faster flow rate can be used for some applications.
- Conditionning: 3 x Tank volume including cartridge

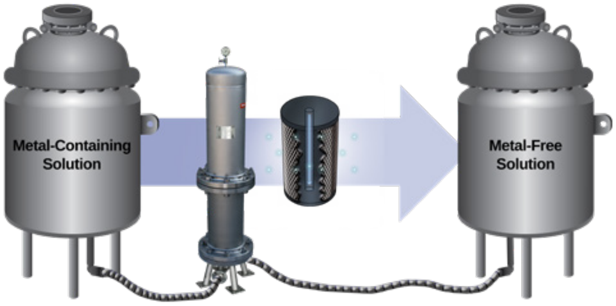
Cartridge Housings

Lab Scale

- Various housing length available
  (*for 1 cm, 10 cm & 25 cm cartridges*)
- Operated with standard pump
- Typical Pressure rating: 150 psi
- Easy housing conversion for all lengths by simply changing the bowl

Pilot & Commercial Scale

- A series of cartridge housings for operation of 1 to 12 cartridges
- Made in stainless steel or Hastelloy
- Pressure rating: 150 psi
- Can be operated in parallel to process batch sizes of ≥ 10,000 L



Experimental Optimization for Scavengers

If the scavenging is incomplete or if you wish to optimize the reaction, you can try the steps below. Various parameters can be changed one at a time or simultaneously to improve removal efficiency.

Note: you can mix multiple scavengers to get superior efficiency for example when multiple species are suspected.

• Number of Silia*MetS* or Silia*Bond* Equivalents

For initial screening experiments we suggest using 4 - 8 molar equivalents of scavengers relative to the concentration of the residual impurities. Once the preferred scavenger is identified, further optimization can be done to reduce the number of equivalents used.

• Subsequent Treatments

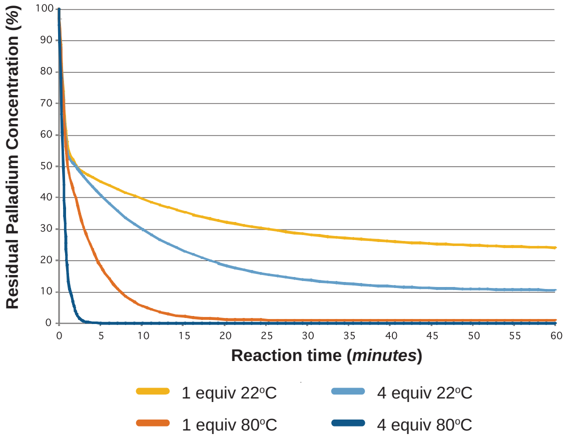
In some cases (*equilibrium process or the presence of multiple species*), multiple treatments with our scavengers are desirable over a single treatment with a larger amount.
For optimal results, filtration between each treatment can enable higher scavenging efficiency.

• Temperature

In initial screening, we suggest the scavenging experiments to be run at room temperature. Usually, scavenging is completed after one to four hours.

However, when shorter scavenging times are required, higher scavenging rates can be achieved by increasing the temperature. Silia*MetS* and Silia*Bond* can be safely used at elevated temperature without degradation and can be added either at room temperature or directly to a warm solution.

Residual Concentration (%) of Pd(OAc)$_2$ with Silia*MetS* Thiol in DMF

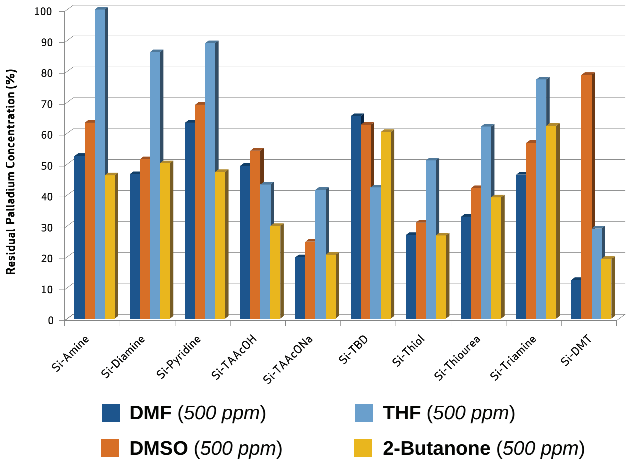


• Solvent

Silia*MetS* and Silia*Bond* can safely be used in a wide range of organic and aqueous solvents commonly used in laboratory and in process, such as DMF, DMSO, THF, 2-butanone, alcohols, ethers, chlorinated solvent, etc.

As demonstrated in the figure, the nature of the solvent does sometimes influence scavenging efficiency. If scavenging or kinetics are too slow, changing solvent or adding a co-solvent should be considered.

Pd(PPh$_3$)$_4$



- **Mixing Rate**

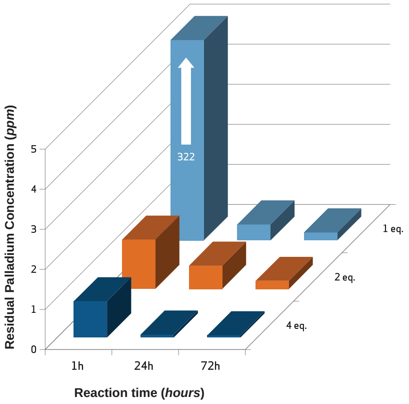
  Our scavengers are mechanically stable and offer excellent scavenging efficiency in batch processes agitated by overhead stirrers as well as orbital shaking under low to moderate agitation rates.
  If required, mixing rates can be increased to get better scavenging results. With faster stirring, scavenger dispersion in solution is improved.

- **pH of the Aqueous Solution**

  When the scavenging is done in aqueous solutions, it is possible to use our scavengers in a pH range of 2 to 12. Depending on the nature of the scavenging agent, pH can modify the functional groups present on the scavengers by charging them, scavenging might be affected (*e.g.: amine groups in acidic conditions*).

- **Reaction Time**

  In some cases, where increasing the temperature is impossible, longer contact time with the scavenger can allow higher scavenging efficiency.



Conditions: $Pd(OAc)_2$, THF, Silia*MetS* Thiol, r.t.
Initial concentration: 1,000 ppm

Typical Experimental Procedures

In Batch Mode Reactor (*Bulk*)

	For Silia*MetS* Metal Scavengers	For Silia*Bond* Organic Scavengers
STEP	For initial screening, start with 4 - 8 molar equivalents of Silia*MetS* in respect to the residual metal concentration.	For initial test, start with 4 - 8 molar equivalents of Silia*Bond* in respect to the impurity.
1	Dissolve the crude product to be treated in a suitable solvent (*or directly use the crude reaction mixture*) and prepare vials containing the same solution volume. Directly add your chosen Silia*MetS* / Silia*Bond* to these vials. **Note**: no pre-wetting / pre-activation is required.	
2	For initial tests, stir the solution for at least one hour at room temperature.	
3	Scavenging progress can be followed by normal analytical techniques. The scavenging progress can also be estimated by looking at the color of the solution, as depicted herein:  When the scavenging is almost complete, the solution is less colored and Silia*MetS* becomes colored. In some occasional cases, if all the samples are still colored, try one or all of the following: let them react for a longer period of time; add more equivalents of the Silia*MetS*; increase the temperature of the reaction. Keep in mind that colors can come from other factors unrelated to the impurities.	Scavenging progress can be followed by normal analytical techniques. If scavenging seems incomplete or very slow, reaction time or temperature can be increased, or more equivalents of the scavenger can be added.
4	At the end of the scavenging, filter off the scavenger using a fritted funnel or filtration device.	
5	Wash the Silia*MetS* with additional solvent for total recovery of the API (*or compound of interest*) and concentrate the solution under vacuum.	Wash thoroughly with solvent to afford impurity-free solution. Concentrate under vaccum.
6	Analyze the residual metal or organic impurity concentration of each vial to identify the most efficient scavenger.	
7	Direct scale-up is now possible. Otherwise, scavenging optimization can be examined.	

Please keep in mind that the above procedures are standard and introductory, but optimization of conditions is key to optimal scavenging efficiency.

In SPE or Flash cartridges

Fixed-bed formats are a great alternative for metal or organic removal and are directly scalable.
We suggest initial screening investigations to be done using Silia*Prep* 2 g / 6 mL SPE cartridges.

	Typical Experimental Procecures
STEP	Description
1	Condition the cartridge with 3 - 4 column volumes using the same solvent as the solution to be treated.
2	Add the solution containing the API and the metal or organic impurity to the top of the cartridge and let it pass through the cartridge under gravity. **Note**: if needed, a slight positive pressure on the top of the cartridge or a light vacuum at the bottom can be applied to speed up the flow rate.
3	For most Silia*MetS* metal scavengers, a dark colored band will be observed on the top of the silica bed (*right*). **Note**: if the residual solution is still colored, multiple passes through the same cartridge can be done.
4	Once the scavenging is completed, wash the cartridge using at least three column volumes of solvent to ensure total API recovery.

Contact us for E-PAK® Typical Experimental Procedures Guide.

Determining the Optimal Amount of Scavenger to be Used

From Residual Metal Concentration

Example: knowing that the Palladium (*Pd*) concentration in 800 g of material is 500 ppm (*the oxidation state does not affect the calculation*)

Data needed

- Loading of the scavenger: e.g.: Silia*MetS* Thiol = 1.2 mmol/g
- Metal molecular weight: e.g.: Pd = 106.42 g/mol
- Amount of product to be treated: e.g.: 800 g
- Residual concentration of metal: e.g.: 500 ppm of Pd

If you have any doubt, please go to our online calculator to have all the work automatically done for you !
www.silicycle.com/web-tools

1. Determine the amount of palladium to be scavenged

$$\text{Amount of Pd in mg} = \frac{\text{Residual metal concentration x Qty of product to be treated}}{\text{1,000}}$$

$$\text{Amount of Pd in mg} = \frac{\text{500 ppm x 800 g of product}}{\text{1,000}} = \text{400 mg of Pd in 800 g of product}$$

$$\text{Conversion in mmol of Pd} = \frac{\text{Amount of Pd in mg}}{\text{Metal molecular weight}}$$

$$\text{Conversion in mmol of Pd} = \frac{\text{400 mg}}{\text{106.42 g/mol}} = \text{3.76 mmol of Pd}$$

2. Calculate the amount of scavenger to use (*1 equivalent*)

$$\text{Amount of Silia}\textit{MetS}\text{ to use} = \frac{\text{Number of mmol of metal concentration}}{\text{Silia}\textit{MetS}\text{ Thiol loading}}$$

$$\text{Amount of Silia}\textit{MetS}\text{ to use} = \frac{\text{3.76 mmol of Pd}}{\text{1.2 mmol/g}} = \text{3.13 g of Silia}\textit{MetS}\text{ Thiol for 1 equiv}$$

To scavenge 400 mg of palladium, 3.13 g of Silia*MetS* Thiol are needed if using only one equivalent.

However, it is highly recommended that a minimum of four equivalents be used at first. In this case, the amount of Silia*MetS* Thiol will be four times higher (*4 x 3.13 g = 12.52 g*).

Sometimes, the metal residual concentration is unknown. In such case, the amount (*g*) of palladium to be scavenged can be replaced by the amount of metal catalyst used for the reaction.

From Amount of Metal Catalyst Used

Data needed

- Amount of metal catalyst used: e.g.: 10 g of $Pd(PPh_3)_4$
- Metal catalyst molecular weight: $Pd(PPh_3)_4$ = 1,155.56 g/mol

Determine the amount of Palladium to be scavenged

$$\text{Amount of Pd in mmol} = \frac{\text{Quantity of catalyst used for the reaction x 1,000}}{\text{Metal catalyst molecular weight}}$$

$$\text{Amount of Pd in mmol} = \frac{\text{10 g of } Pd(PPh_3)_4 \text{ x 1,000}}{\text{1,155.56 g/mol}} = \text{8.65 mmol of Pd (}\textit{max to be scavenged}\text{)}$$

The amount of Silia*MetS* Thiol to be used can then be determined as stated above (*see point 2. above*).

In this particular case, one equivalent of Silia*MetS* Thiol corresponds to 7.20 g.

From Residual Organic Residue Concentration

Data needed

- Loading of organic scavenger: e.g.: Silia*Bond* Guanidine = 0.74 mmol/g
- Estimated amount of impurity to be removed (*in mmol*): e.g.: 5 mmol

Calculate the amount of scavenger to use (*1 equivalent*)

$$\text{Amount of Silia}\textit{Bond}\text{ Guanidine to use} = \frac{\text{Number of mmol of impurity}}{\text{Silia}\textit{Bond}\text{ Guanidine loading}}$$

$$\text{Amount of Silia}\textit{Bond}\text{ Guanidine to use} = \frac{\text{5 mmol}}{\text{0.74 mmol/g}} = \text{6.76 g of Silia}\textit{Bond}\text{ Guanidine for 1 equiv}$$

To scavenge 5 mmol of impurity, 6.76 g of Silia*Bond* Guanidine are needed if using only one equivalent.

However, keep in mind that it is highly recommended that a minimum of two equivalents be used at first.

In this case, the amount (*g*) of Silia*Bond* Guanidine will be two times higher (*2 x 6.76 g = 13.52 g*).

Silia*MetS* Thiol & DMT Stability & Leaching Studies

Since our Metal and Organic Scavengers are being used by many pharmaceutical companies, each Silia*MetS* and Silia*Bond* manufactured by SiliCycle is submitted to an extensive washing procedure to ensure the product exhibits extremely low levels of extractables and leachables.

SiliCycle has implemented a quality control procedure that includes loading and reactivity determination, as well as leachables and extractables analysis. The solution must be free of contaminants for the product to successfully pass the quality control tests.

Chemical Resistance In Acidic Medium

Silia*MetS* Thiol or DMT (*0.4 g*) was added to several acidic solutions for chemical resistance testing (*4 mL*). Methanol (*0.4 mL*) was added to each vial in order to ensure the silica was well impregnated with the aqueous medium. The solution was stirred mechanically for 1 to 16 hours at 22°C, and 1 hour at 60°C. Si-Thiol or Si-DMT was then filtered and rinsed thoroughly with water and methanol, dried and subjected to CNS analysis.

Chemical Resistance of Silia*MetS* Thiol in Acidic Media

Experimental Conditions	1 M, 1h 22°C	5 M, 1h 22°C	5 M, 16h 22°C	5 M, 1h 60°C	5 M, 16h 60°C
H_3PO_4 (*phosphoric acid*)	🟩	🟩	🟩	🟩	🟩
H_2SO_4 (*sulfuric acid*)	🟩	🟩	🟩	🟩	🟩
HCl (*hydrochloric acid*)	🟩	🟩	🟩	🟩 [1]	🟩
HNO_3 (*nitric acid*)	🟩	🟩	🟩	🟩	🟨
AcOH (*acetic acid*)	🟩	🟩	🟩	🟩	🟩
TFA (*trifluoroacetic acid*)	🟩	🟩	🟩	🟩	🟩
HCO_2H (*formic acid*)	N/A	N/A	🟩	🟩	🟩

[1]: reaction was stirred at 40°C.

Chemical Resistance of Silia*MetS* DMT in Acidic Media

Experimental Conditions	1 M, 1h 22°C	5 M, 1h 22°C	5 M, 16h 22°C	5 M, 1h 60°C	5 M, 16h 60°C
H_3PO_4 (*phosphoric acid*)	🟩	🟩	🟩	🟩	🟩
H_2SO_4 (*sulfuric acid*)	🟩	🟩	🟩	🟩	🟩
HCl (*hydrochloric acid*)	🟩	🟩	🟩	🟩 [1]	🟩
HNO_3 (*nitric acid*)	🟩	🟨	🟨	🟨	🟨
AcOH (*acetic acid*)	🟩	🟩	🟩	🟩	🟩
TFA (*trifluoroacetic acid*)	🟩	🟩	🟩	🟩	🟩
HCO_2H (*formic acid*)	N/A	N/A	🟩	🟩	🟩

[1]: reaction was stirred at 40°C.

🟩 No Significant Change (*0 - 0.7 % difference*)
🟧 Fair Loss (*1.0 - 1.5 % difference*)
🟦 Silica was dissolved
🟨 Light Loss (*0.8 - 1.0 % difference*)
🟥 Substantial Loss (> *1.5 % difference*)

No change in color was observed in the supernatant after filtration and washing steps.
Silia*MetS* Thiol & DMT are resistant to most acidic conditions.

Chemical Resistance In Basic Medium

Silia*MetS* Thiol or DMT (*0.4 g*) was added to several basic media in water, methanol or dichloromethane (*4 mL*). In the case where water was the solvent, methanol (*0.4 mL*) was added to each vial in order to ensure the silica was well impregnated with the aqueous medium. The solution was stirred mechanically for 1 to 16 hours at 22°C. Si-Thiol or Si-DMT was then filtered and rinsed thoroughly with water and methanol, dried and subjected to CNS analysis.

Chemical Resistance of Silia*MetS* Thiol in Basic Media

Experimental Conditions	1 M, 1h, 22°C	5 M, 1h, 22°C	5 M, 16h, 22°C	5 M, 1h, 22°C
	in protic solvent (*water*)		in protic solvent (*methanol*)	in aprotic solvent (*dichloromethane*)
NaOH (*sodium hydroxide*)	🟥	🟦	N/A	
NH_4OH (*ammonium hydroxide*)	🟩	🟩		
Na_2CO_3 (*sodium carbonate*)	🟩	🟩		
$NaHCO_3$ (*sodium bicarbonate*)	🟩	🟩		
TEA (*triethylamine*)	🟩	🟩	🟩	🟩
DEA (*diethanolamine*)	🟩	🟩	🟩	🟩
Pyridine	🟩	🟩	🟩	🟩
NH_3 (*ammonia*)	N/A		🟩	🟩

Chemical Resistance of Silia*MetS* DMT in Basic Media

Experimental Conditions	1 M, 1h, 22°C	5 M, 1h, 22°C	5 M, 16h, 22°C	5 M, 1h, 22°C
	in protic solvent (*water*)		in protic solvent (*methanol*)	in aprotic solvent (*dichloromethane*)
NaOH (*sodium hydroxide*)	🟥	🟦	N/A	
NH_4OH (*ammonium hydroxide*)	🟩	🟩		
Na_2CO_3 (*sodium carbonate*)	🟩	🟩		
$NaHCO_3$ (*sodium bicarbonate*)	🟩	🟩		
TEA (*triethylamine*)	🟩	🟨	🟩	🟩
DEA (*diethanolamine*)	🟩	🟨	🟩	🟩
Pyridine	🟩	🟩	🟩	🟩
NH_3 (*ammonia*)	N/A		🟩	🟩

🟩 No Significant Change (*0 - 0.7 % difference*)
🟧 Fair Loss (*1.0 - 1.5 % difference*)
🟦 Silica was dissolved
🟨 Light Loss (*0.8 - 1.0 % difference*)
🟥 Substantial Loss (> *1.5 % difference*)

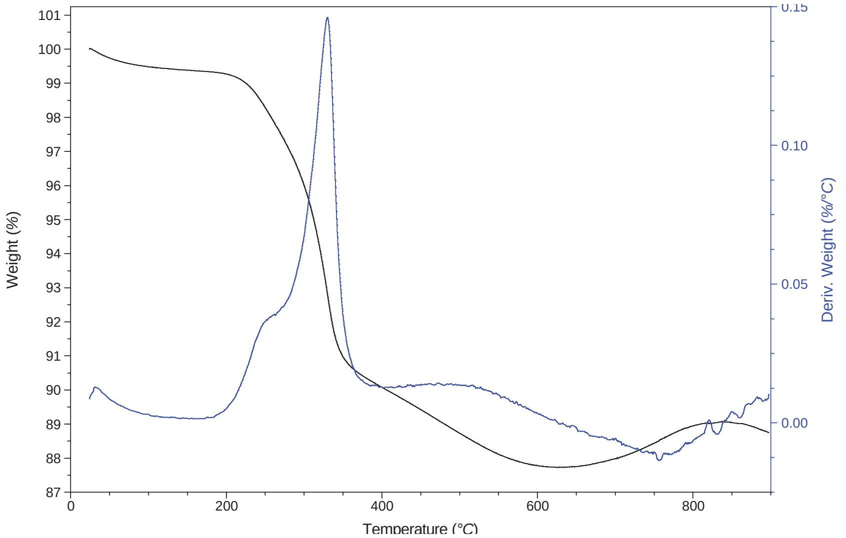
No change in color was observed in the supernatant after filtration and washing steps.
Silia*MetS* Thiol & DMT are resistant to most basic conditions.

Thermal Stability

Thermogravimetric analysis, or TGA, is our method to determine any mass loss on Si-Thiol due to decomposition, oxidation, or loss of volatiles (*such as moisture*).

Based on TGA Analysis, Silia*MetS* Thiol is considered to be stable up to 220°C, but we suggest not to go over 150°C.

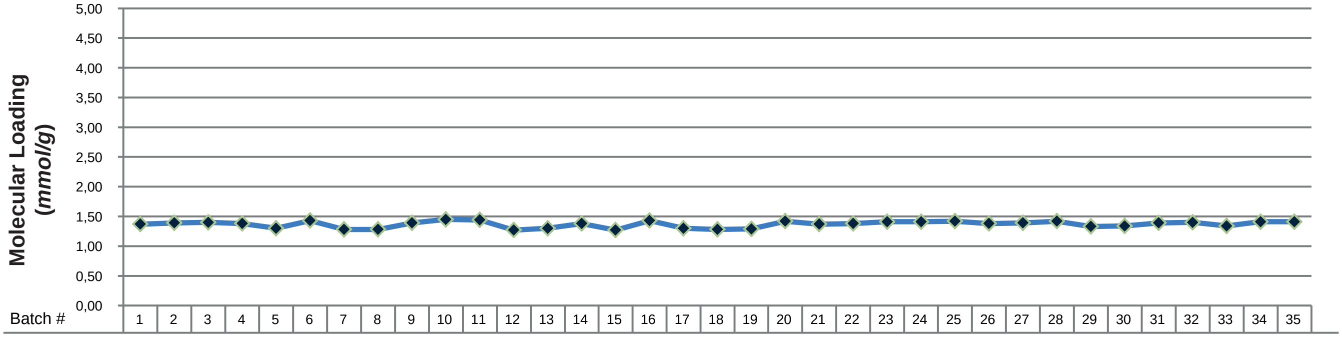
Zoom on important mass loss (*TGA from 0 to 400°C*)

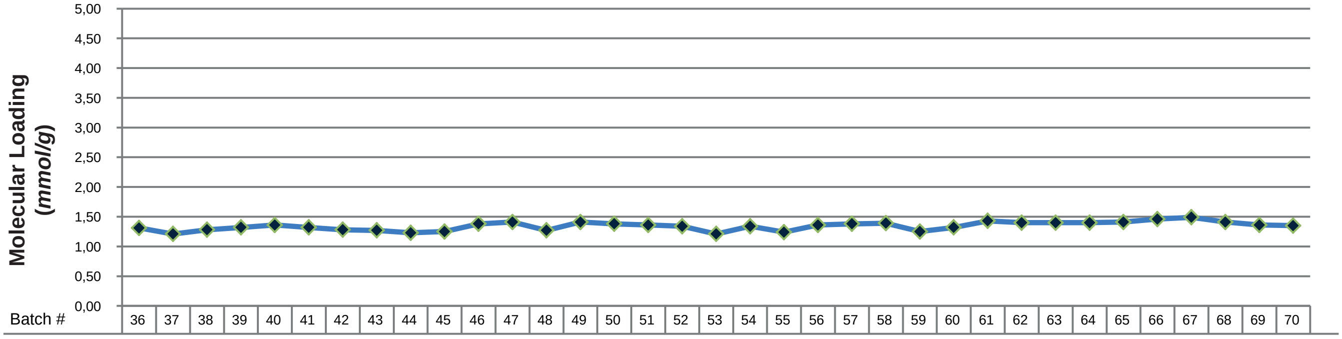


Silia*MetS* Thiol Batch History − Lot-to-lot Reproducibility

The manufacture of functionalized silica gels is both a complex and controlled process. SiliCycle maintains extensive records of each batch manufactured, and retains these for a minimum of 7 years. Such records contain the production history of finished and released products. They provide objective evidence that the functionalized gels were manufactured in accordance to our quality standards and minimal requirements, and act as a record of traceability information for all units or lots.

SiliCycle’s loadings of functionalized gels are always extremely constant from batch-to-batch. As an example, here is an overview of lot-to-lot reproducibility over seventy consecutive lots of Silia*MetS* Thiol of same batch size manufactured.

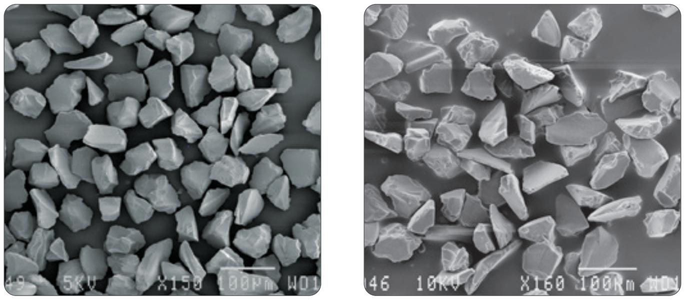




Mechanical Stability

The mechanical resistance of silica gel is roughly 10,000 psi. This value depends on pore diameter and particle size.
In the following experiment, a comparison of mechanical resistance between silica gel and polymer was conducted:

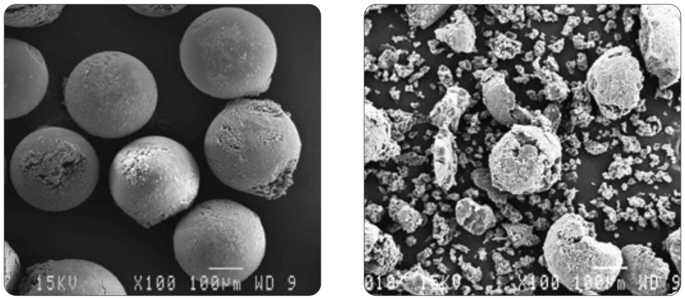
SEM of Silia*MetS* Thiol



After 4 hours
under mechanical stirring

After 16 hours
under mechanical stirring

SEM of Polymer Support



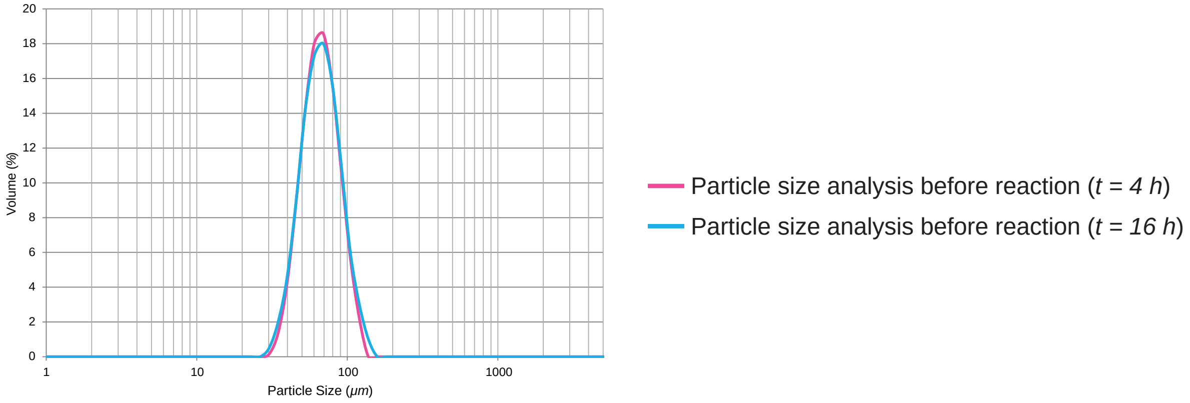
After 4 hours
under mechanical stirring

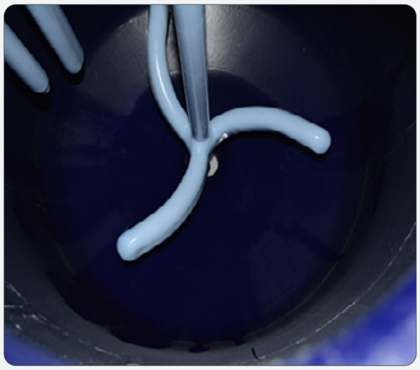
After 16 hours
under mechanical stirring

- Stirring speed: 500 RPM (*overhead*)
- Solvent: DMF
- Temperature: 22°C

After 16 hours, there was hardly no difference in the silica particles on which our scavengers are functionalized. In comparison, the polymer support was completely destroyed.

SEM & Malvern Analysis are a safe and clear demonstration that almost no mechanical grinding nor crushing of the silica occurs after stirring, which is not the case for polymeric support, for which drastic grinding appears.





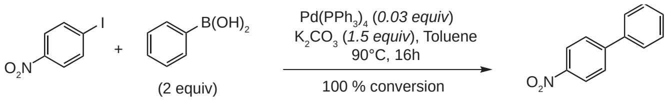
Mechanical Stirrer in Reactor

This picture was taken in one of SiliCycle's medium-sized reactors.

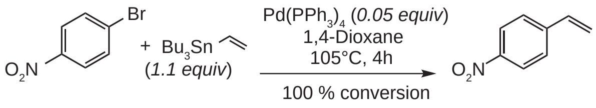
Silia*MetS* Thiol has been produced for more than 20 years in SiliCycle's reactors without any damage.

Leaching and Extractable Studies

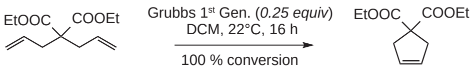
To address the concerns for potential leaching of impurities into reaction mixtures using Silia*MetS* Thiol & DMT, four typical metal-containing reactions were performed. Detection, identification and quantification of possible impurities resulting from the scavenging action was then performed.



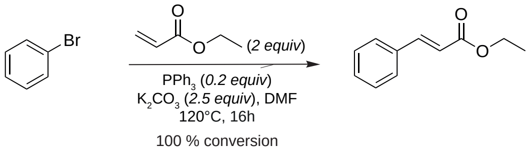
Suzuki Coupling



Stille Coupling



Grubbs Ring-Closing Metathesis



Heck Coupling

Experimental Procedure

Crude reaction mixtures (*8 mL*) were placed in a standard polypropylene tube equipped with a 20 µm frit, loaded with 1 g of the appropriate Silia*MetS* Metal Scavenger, and mixed for 4 h at either room temperature or 80°C. Solutions were then filtered through a 0.2 µm filter prior to analysis.

Leaching Analysis

Silane leaching was analyzed by Inductively-Coupled Plasma-Optical Emission Spectroscopy (*ICP-OES*) which has proven to be very sensitive for silicon quantification (*detection limit in solution is 0.125 ppm*).

Traces of non-silicon containing impurities were also analyzed by Gas Chromatography-Mass Spectrometry (*GC-MS*), Liquid chromatography-tandem mass spectrometry (*LC-MS*) and ^{1}H NMR Analysis.

Gel Purity Calculation

Here is an example of how gel purity can be calculated:

$$\textbf{Impurity \%} = \frac{\text{2 mg of silicon x 100}}{\text{1,000,000 mg of SiliaMetS}} \Rightarrow \text{0.0002 \% impurity}$$

Gel purity = 100 - (Impurity %) => 99.9998 % purity

Silane Leaching Analysis by ICP-OES

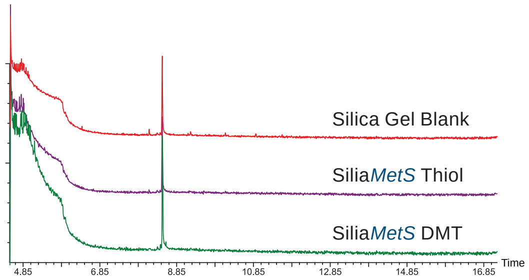
Results shown in the table below for Silia*MetS* Thiol & DMT confirm that minimal leaching occurs with our scavengers.

Stability of Silia*MetS* in Suzuki, Stille, Heck and Grubbs Ring-Closing Metathesis Reactions

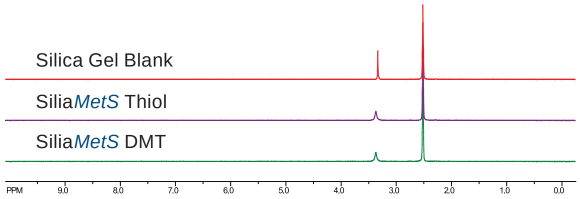
Reaction (*solvent*)	Temperature	Silia***MetS*** Thiol		Silia***MetS*** DMT	
		[Silicon]	Gel Purity (%)	[Silicon]	Gel Purity (%)
Suzuki (*Toluene*)	22°C	2 ppm	99.9998	1 ppm	99.9999
	80°C	2 ppm	99.9998	2 ppm	99.9998
Stille (*1,4-Dioxane*)	22°C	2 ppm	99.9998	1 ppm	99.9999
	80°C	1 ppm	99.9999	3 ppm	99.9997
Heck (*DMF*)	22°C	2 ppm	99.9998	1 ppm	99.9999
	80°C	1 ppm	99.9999	2 ppm	99.9998
Grubbs Ring-Closing Met. (*DCM*)	22°C	2 ppm	99.9998	2 ppm	99.9998

Non-Silicon Leaching Analysis

Each experiment was run on a 1 g aliquote of Silia*MetS* and was shaken for 1 hour at room temperature. Leaching examination was performed through both GC-MS and 1H NMR analysis, comparing leaching profiles of bare silica, Silia*MetS* Thiol and Silia*MetS* DMT.



Gas Chromatography-Mass Spectrometry (*GC-MS*)



^{1}H NMR Analysis (d_6-*DMSO*)

Compared to the silica blank spectrum, neither experiment showed evidence of any impurities for either Silia*MetS* Thiol or DMT.

Note: in GC-MS spectrum, peak at 8.5 minutes is the internal standard (*1-fluoronaphthalene, 100 ppm*).
In NMR spectrum, peaks at 2.4 and 3.4 ppm are, respectively, d6-DMSO and water contained in deuterated solvent.

Stability Study (*Shelf Life*)

SiliCycle certifies that Silia*MetS* Metal Scavengers stored under recommended conditions in an undamaged container are guaranteed to perform for two years from the manufacturing date without significant loss of performance.

Silia*MetS* Thiol Efficiency within Shelflife of 2 years

Lot #	QC Date	Scavenging (%)
11577	Year 0	> 99.9
	Year 1	99.5
	Year 2	99.6
12218	Year 0	99.9
	Year 1	99.5
	Year 2	99.1
64215	Year 0	99.2
	Year 1	99.3
	Year 2	99.5

Scavenging: 1,000 ppm of $Pd(OAc)_2$ in DMF.
Conditions: 2 equiv of Silia*MetS* Thiol, 1 h, 22°C.

Application Notes & Case Studies

Silia*MetS* Metal Scavengers

Antimony (*Sb*)

Cesium (*Cs*)

Copper (*Cu*)

Iridium (*Ir*)

Manganese (*Mn*)

Osmium (*Os*)

Palladium (*Pd*)

Platinum (*Pt*)

Ruthenium (*Ru*)

Tin (*Sn*)

Uranium (*U*)

Multiple Metals

Silia*Bond* Organic Scavengers

Removal of Sb

In situ speciation of dissolved inorganic antimony in surface waters & sediment porewaters

Antimony is a priority environmental contaminant, yet very little research on the behavior and fate of Sb in the environment has been reported. The primary source is mining and processing of Sb for industrial applications. To properly understand the processes controlling the movement of Sb through the environment, there is a need for tools to accurately measure the speciation of Sb, not just total concentration.

Both toxicity & mobility of Sb are affected by oxidation state, thus the accurate measurement of Sb speciation is essential for investigating the behavior of this contaminant in aquatic systems.

The authors present herein a diffusive gradients in thin films (*DGT*) technique, which utilizes a binding layer containing Silia*MetS* Thiol, for the selective measurement of Sb^{III} in surface waters and sediment porewaters.

The mercapto-silica showed a high affinity for Sb^{III}, with uptake efficiencies > 97 % and elution efficiencies of 86.9 +/- 2.6 %

The Silia*MetS* Thiol based DGT technique was also applied to measure porewater concentrations of Sb^{III} and As^{III} in a contaminated freshwater sediment at high resolution.

Initial and/or residual metal content was not disclosed.

Bennet, W. W. *et al. Environ. Sci.: Processes Impacts*, **2016**, *18*, 992-998
Griffith University, South East Queensland, Australia

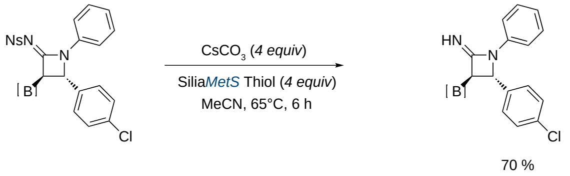
Removal of Cs

Amphoteric borylketenimines: versatile intermediates in the synthesis of borylated heterocycles

Reported herein was the 1st synthesis of amphoteric borylketenimines from ethynyl N-methyliminodiacetic acid (*MIDA*) boronate and sulfonyl azides via copper catalysis.

This work highlights the unexplored utility of borylketenimines in the synthesis of potentially bioactive molecules.

In situ Silia*MetS* Thiol (*4 equiv*) successfully removed the remaining Cs in deprotection reaction, which resulted in complete conversion and high selectivity.



Initial and/or residual metal content was not disclosed.

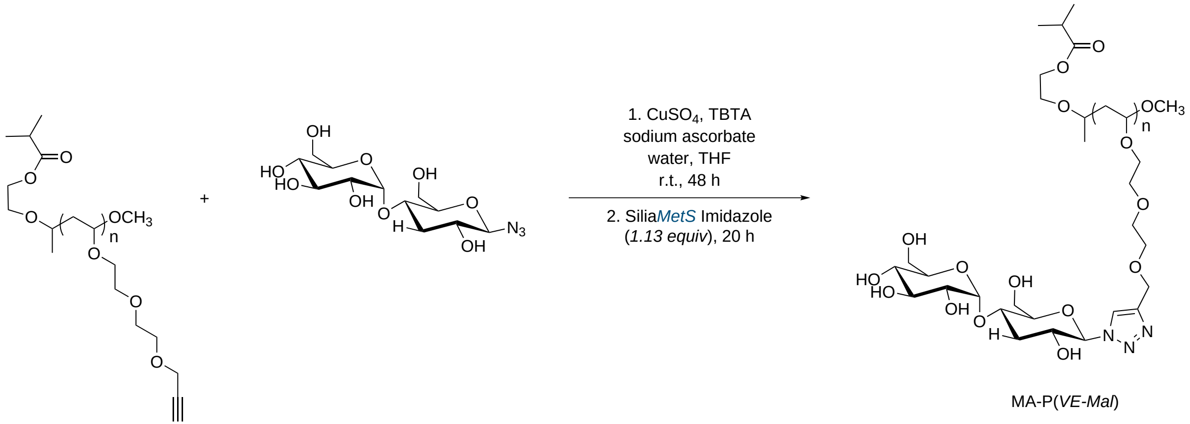
Yudin, A. K. *et al. Chem. Eur. J.*, **2017**, *23*, 9711-9715
University of Toronto, Ontario, Canada

Removal of Cu

Silia*MetS* Imidazole in the synthesis of polymer films for measurement of optical properties

An asymmetric bifunctional monomer having both an unprotected alkynyl group and a vinyl ether (*VE*) polymerization of VEEP smoothly proceeded in a controlled manner under a living cationic polymerization condition to give alkyne-substituted polyVE (*poly-VEEP*) without any protection of the pendant alkynyl function.

In the click reaction of precursor macromonomer MA-PVEEP, the resultant polymer MA-P(*VE-Mal*) was purified from contaminating copper with Silia*MetS* Imidazole (*0.192 mmol, 1.13 equiv*).



MA-P(*VE-Mal*)

49 %

Initial and/or residual metal content was not disclosed.

Minoda, M. *et al. J. Polym Sc. Part A. Polym. Chem.*, **2018**, 1
Kyoto Institute of Technology, Sakyo-Ku, Japan

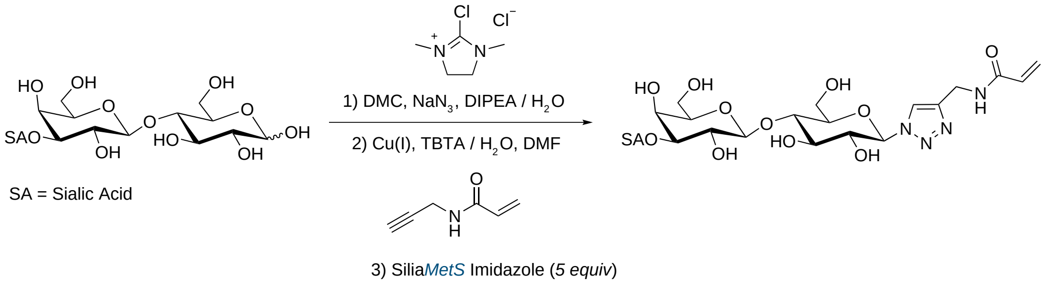
Removal of Cu

Synthesis of a multivalent glycoligand against avian and human influenza viruses

A glycopolymer bearing α2,3-linked sialyltrisaccharides was synthesized by living radical polymerization using a glycomonomer prepared by a protecting-group-free process, direct azidation of the free sialyllactose, and subsequent azide-alkyne cycloaddition.

The prepared glycopolymer with pendant 3’-sialyllactose moieties strongly interacted with both avian & human influenza viruses.

Silia*MetS* Imidazole (*5 equiv for Cu*) was successful in removing contaminating Cu, with only 5 equiv, O.N. at r.t.



Initial and/or residual metal content was not disclosed.

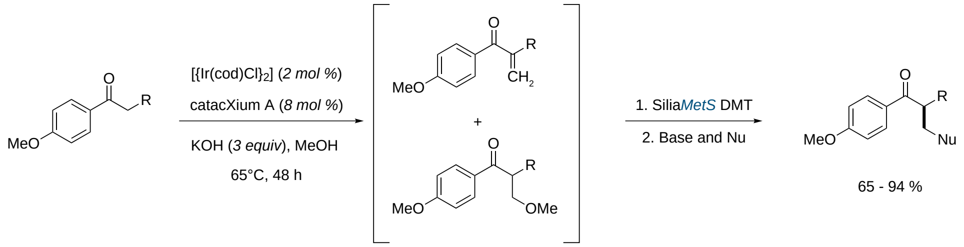
Tanaka, T. *et al. J. Appl. Glycosci.*, **2017**, *64*, 43-48

Removal of Ir

Hydrogen-borrowing and interrupted-hydrogen-borrowing reactions of ketones and methanol catalyzed by iridium

The use of catalytic [{Ir(cod)Cl}$_2$] was shown to facilitate hydrogen-borrowing reactions of ketone enolates with methanol at 65°C. An oxygen atmosphere accelerated the process, and when combined to a bulky monodentatephosphine ligand, the catalytic cycle could be interrupted by preventing the enone reduction.

Subsequent addition of pronucleophiles to the reaction mixture allowed a one-pot methylenation/conjugate addition protocol to be developed: the enone and methoxy adduct were not isolated but reacted *in situ* with an external nucleophile and extra base. In most cases they found to be beneficial to treat the crude reaction mixture with the Ir scavenger Silia*MetS* DMT while stirring the solution, open to the atmosphere, for 1 hour, before the addition of base and nucleophile. The team suggested that the removal of most of the metal catalyst from solution and prevented complications caused by methanol oxidation during the second phase of the reaction.



Initial and/or residual metal content was not disclosed.

Donohoe, J. *et al. Angew. Chem. Int. Ed.*, **2014**, *126*, 1-5
Donohoe, J *et al., Angew. Chem. Int. Ed.*, **2015**, *54*, 1642-1645
University of Oxford, Oxford, United Kingdom
Novartis Institute for Biomedical Research, Cambridge, United States

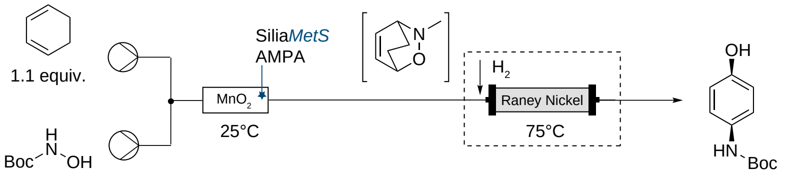
Removal of Mn

Diastereoselective synthesis of cis-N-Boc-4-aminocyclohexanol with reductive ring opening method using continuous flow

N-protected cis-4-aminocyclohexanol derivatives are valuable intermediates in the syntheses of APIs.

Compared with previously reported batch processes, the present multistep flow process is much more efficient in synthetizing valuable 4-aminocyclohexanol derivatives, and avoids some isolation and purification steps.

In this procedure, a nitroso hetero-Diels-Alder cycloaddition step using MnO$_2$ as the oxidant was fully integrated to a novel continuous flow process for the hydrogenation and ring opening of cycloadducts to the corresponding cis-4-aminocyclohexanols using H-Cube Pro.



It was shown that Raney Nickel was a significantly more performant catalyst compared to 10 % Pd/C and 5 % Ru/C in this last cleavage, and highly selective (≥ *99 % toward final cis-4-aminocyclohexanol*). Yet, the Raney Nickel cartridge lost its activity after a few measurements. A possible manganese leaching into the reaction mixture was presumed as the cause for catalyst deactivation. Based on the atom absorption measurements the average extent of manganese was 15 ppm in the reaction mixture. Filling the end of the MnO$_2$ column with Silia*MetS* AMPA as a Mn scavenger allowed the Raney nickel catalyst activity to be kept constant for longer time.

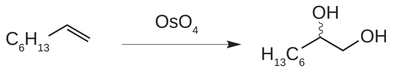
Initial and/or residual metal content was not disclosed.

Szabó, B. *et al. J. Flow Chem.*, **2019**, *9*, 13-17
University of Technology and Economics, Budapest, Hungary

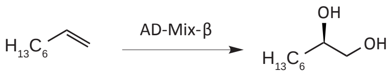
Osmium scavenging with Silia*MetS*

Osmium tetroxide (*OsO_4*), is a very reliable and powerful reagent for the cis-dihydroxylation of alkenes. However, osmium compounds, in particular OsO_4, are highly poisonous, even at low exposure levels, and must be handled with appropriate precautions.

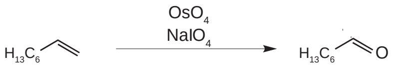
Therefore, it is important to efficiently remove residual osmium from products of interest. A scavenging study on three organic reactions involving osmium reactants were performed. The metal scavenging efficiency of Silia*MetS* is highlighted in the following table.



Dihydroxylation Reaction
[*OsO_4*]



Sharpless Dihydroxylation
[*Potassium osmate ($K_2OsO_2(OH)_4$)*]



Lemieux-Johnson Oxidation
[*$NaIO_4$, OsO_4*]

Osmium Scavenging using Silia*MetS* (*in %*) at 22°C

Silia*MetS*	**Dihydroxylation**	**Sharpless Dihydroxylation**		**Lemieux-Johnson Oxidation**	
	4 equiv, 4 h	**8 equiv, 4 h**	**8 equiv, 16 h**	**8 equiv, 4 h**	**8 equiv, 16 h**
Silia*MetS* Thiol	87	**> 98**	**> 98**	87	92
Silia*MetS* Cysteine	89	**> 98**	**> 98**	87	91
Silia*MetS* DMT	92	**97**	**> 98**	87	91
Silia*MetS* Imidazole	87	**> 98**	**> 98**	89	91
Initial Os Concentration (*in EtOAc*)	132 ppm	25 ppm		21 ppm	

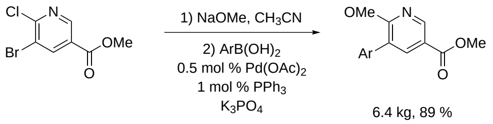
Note: > 98 % of scavenging means < 0.5 ppm of osmium.

All scavengers were equally effective for Sharpless dihydroxylation or Lemieux-Johnson oxidation.
As for simple dihydroxylation, Silia*MetS* DMT was slightly more efficient.

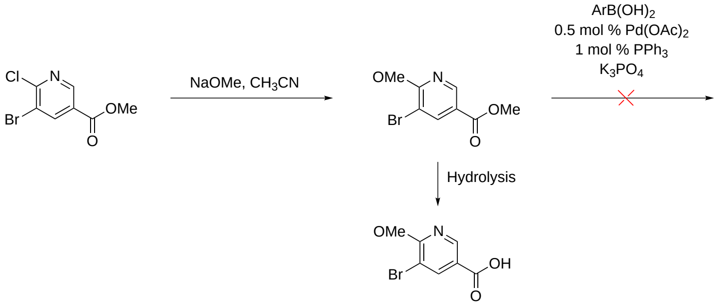
Removal of Pd

Circumventing an unexpected catalyst poisoning in a Suzuki coupling

In one project, ring methoxylation of a chloronicotinate was achieved by scientists at Dart NeuroScience and Accela ChemBio, followed by a one-pot Suzuki-coupling to yield a biaryl intermediate, one that was needed on a KG scale in further synthetic steps.



Consistent and excellent results were first obtained from R&D (*mg-scale*) up to a first cGMP process-scale tryout (*6.4 kg*). Yet, subsequent couplings on other batches gave practically no expected birayl compound. Instead, the first methoxylation product simply hydrolyzed from its ester form to the corresponding carboxylic acid!



After investigation, the only time the team could reproduce the non-reactive behavior of the reaction was upon intentionally omitting the $Pd(OAc)_2$ catalyst – hence the idea of catalyst poisoning – but the reaction could still be conducted by adding some more palladium in the reaction mixture (*up to 5 %*). This also leads to downstream issues, as higher palladium loading also implies higher residual palladium, which can greatly impair subsequent reactions.

Among all metal removal strategies, it was the use of Silia*MetS* Thiol that proved to be the best protocol for a simple, fast and efficient removal of palladium. The Pd levels were thus lowered below 200 ppm. The team concluded that "*The subsequent Pd removal step was carried out as planned, and the remainder of the GMP synthesis proceeded well to provide final API in the desired quantity and purity*", as the expected biaryl intermediate was isolated in 73 % yield and 98 % purity.

Initial and/or residual metal content was not disclosed.

Liu, J. *et al. Org. Process Res. Dev.*, **2018**, *22*, 111-116
Dart NeuroSciemce L.L.C., California, United States
Accela ChemBio Ltd, Shanghai, China

Removal of Pd

Development and scale-up to improve an API's physiochemical and bulk powder properties

Purification process for TAK-117, a selective PI3Kα inhibitor currently in Phase 1b of clinical trials, was developed and greatly improved the overall purity, recovery, physiochemical and bulk powder properties of the isolated product, which was obtained after a Suzuki coupling.

TAK-117
87.2 - 91.7 %

A purification process is required to control the Pd levels within International Conference on Harmonisation (*ICH*) guidelines.

The revised process was found to produce purified material across a total of 6 batches at 15 and 30 kg scales.
Original protocol subjected TAK-117 to 2 treatments with decreasing quantities of GCB and Silia*MetS* Thiol scavenger (*20 wt % each then 10 wt % each*). New protocol uses Silia*MetS* Diamine (*80 wt %*) and GCB (*20 wt %*).

Initial and/or residual metal content was not disclosed.

Papageorgiou, C. D. *et al. Org. Process Res. Dev.*, **2018**, *22*, 296-305
Takeda Pharmaceuticals International Co., Process Chemistry, Cambridge, United States

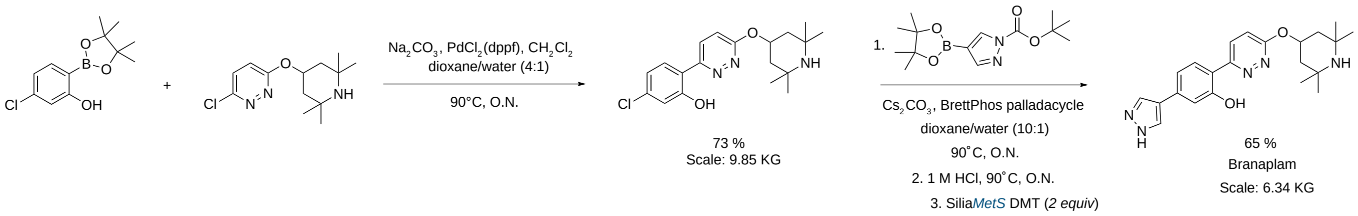
Removal of Pd

Discovery of small molecule splicing modulators of survival motor neuron-2 (*SMN2*) for the treatment of Spinal Muscular Atrophy (*SMA*)

Spinal muscular atrophy (*SMA*), a rare neuromuscular disorder, is the leading genetic cause of death in infants and toddlers. SMA is caused by the deletion or a loss of function mutation of the survival motor neuron 1 (*SMN1*) gene. SMN2 (*survival of motor neuron 2*) is a closely related gene which can partially compensate for the loss of SMN1, however coding for a less stable SMN protein.

In recent years, modulating SMN2 pre-mRNA splicing has greatly improved SMA treatments by means of the discovery of LMI070 / Branaplam, a small molecule stabilizing interaction between the spliceosome and SMN2 pre-mRNA.

An efficient two-step synthesis of Branaplam (*from an advanced intermediate S2*) was developed to avoid late stage demethylation which proved challenging upon scaling. Suzuki coupling occurred between pinacol ester of (4-chloro-2-hydroxyphenyl)boronic acid and pyridazine intermediate S2 in the presence of $PdCl_2$(dppf), CH_2Cl_2 and sodium carbonate, followed by a second Suzuki coupling catalyzed by BrettPhos palladacycle with 1-Boc-pyrazole pinacol boronate to form the Boc protected intermediate. After stirring overnight in the presence of 1M HCl, and then treated with Silia*MetS* DMT (*5 mmol, 2 equiv*) for 20 h, Branaplam was obtained in good overall yield (*65 %*).



Initial and/or residual metal content was not disclosed.

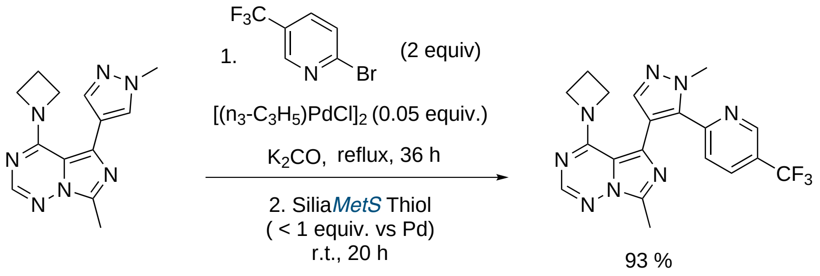
Cheung, A. K. *et al. J. Med. Chem.*, **2018**, *61*, 11021-11036
Novartis Institutes for Biomedical Research & Novartis Pharmaceuticals, Cambridge, United States

Removal of Pd

Identification of a potent, highly selective, and brain penetrant phosphodiesterase 2A inhibitor clinical candidate

Computational modeling was used to direct the synthesis of analogs of previously reported phosphodiesterase 2A (*PDE2A*) inhibitor with an imidazotriazine core to yield compounds of significantly enhanced potency.

The analog PF-05180999 was subsequently identified as a preclinical candidate targeting cognitive impairment associated with schizophrenia.



Silia*MetS* Thiol was used to remove Pd from the palladium-catalyzed C−H arylation on the pyrazole C-5 position with heteroaryl halide to synthesize the PF-05180999. It was found that C−H arylation chemistry was superior to Suzuki coupling for heteroaromatic derivatives, likely due to instability of the required heteroaryl boronates.

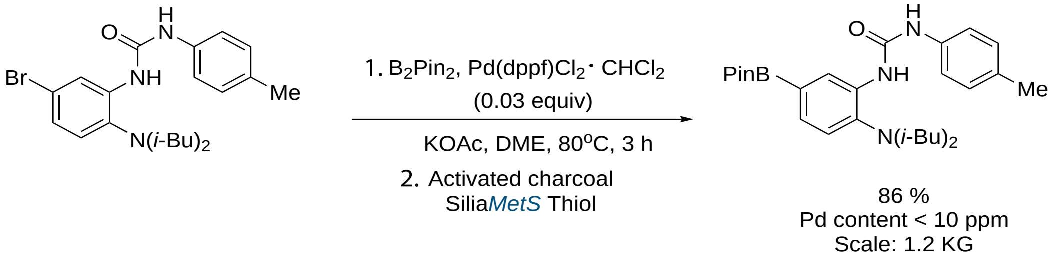
Initial and/or residual metal content was not disclosed.

Helal, C. *et al. J. Med. Chem.*, **2018**, *61*, 1001-1018
Research API, Pfizer Global Research & Development, Connecticut, United States

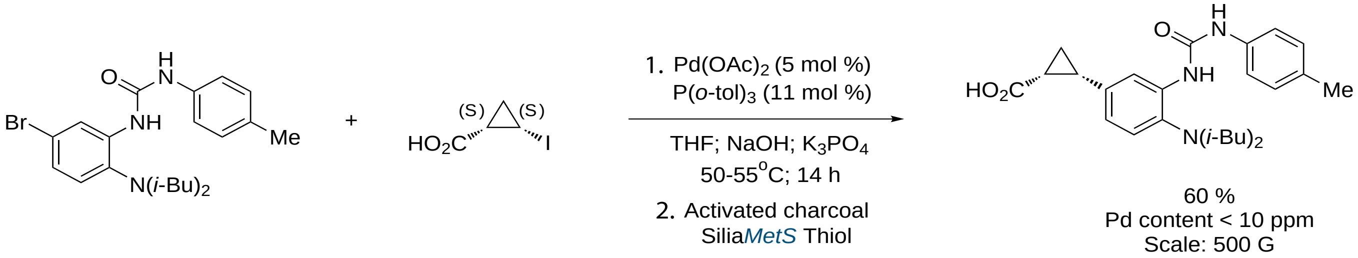
Development of a scalable synthesis of an IDO[1] inhibitor featuring a stereospecific Suzuki coupling of a cyclopropane carboxylic acid

A modified synthetic route to an IDO inhibitor was developed, which synthetic steps comprised a chemoselective nitro reduction, a Miyaura coupling (*Scheme 1*) followed by a key stereospecific Suzuki coupling (*Scheme 2*). A systematic evaluation of the Suzuki conditions led to the identification of a robust catalyst/ligand/base combination to reproducibly duplicate the coupling reaction on large scale, without recourse to chromatography given optimized purification methodology.

Post-reaction treatment included activated charcoal (*for pigments, inorganics...*) and Silia*MetS* Thiol (*for residual Pd*): following the reaction work-up, the organic layer was stirred over activated charcoal (*125 g*) at 20 - 30°C for 2 h. Silia*MetS* Thiol (*1.3 kg*) was charged to the mixture, and the slurry was stirred for 16 h at ambient temperature and filtered through Celite.



Scheme 1



Scheme 2

Purification of final IDO inhibitor was done by treatment with activated charcoal and Silia*MetS* Thiol for removal of pigments, inorganics and residual palladium. After the work-up, the organic layer was distilled under reduced pressure, and the resultant brown viscous liquid was dissolved in MTBE (*8 L*).

Activated charcoal (*40 g*), silica gel (*300 g*), and Silia*MetS* Thiol (*300 g*) were added into this solution and stirred at 20 - 30°C for 18 h. The slurry was filtered through Celite.

Overall, the API was delivered in high quality (*> 99 %*) and good yield (*42 %, less than 10 ppm of Pd*) for a 5-step synthesis.

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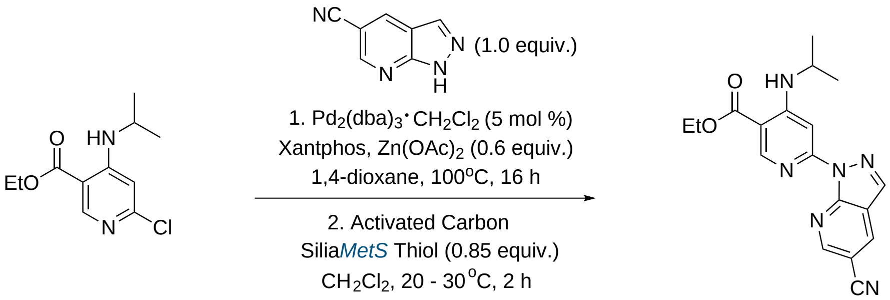
[1] Indoleamine-2,3-dioxygenase is a heme-containing intracellular enzyme

Vaidyanathan, R. *et al. Org. Process Res. Dev.*, **2018**, *22*, 888-897
Chemical Development and API Supply, Bristol Myers Squibb Research and Development Center, India

Removal of Pd

Scalable Zn-catalyzed regioselective allylation of 1 methyl-1-α-rhamnopyranoside

The construction of C−N bonds by Pd-catalyzed cross coupling of amines with aryl halides, pseudohalides, and aryl ethers is an uncontested tool for the synthesis of functionalized diaryl amines (*widely found in pharmaceuticals, natural products and so on*).



Zinc salts have been shown to promote the Buchwald-Hartwig coupling of azaindoles and azaindazoles with heteroaryl chlorides to provide the corresponding 1-aryl-1H-azaindoles and 1-aryl-1H-azaindazoles.

The optimal Zinc salt was shown to be $Zn(OAc)_2$, because of high conversion, availability, low molecular weight and cost. Silia*MetS* Thiol successfully removed traces of palladium.

Initial and/or residual metal content was not disclosed.

Vaidyanathan, R. *et al. J. Org. Chem.*, **2017**, *82*, 7420-7427
Chemical Development and API Supply, Bristol Myers Squibb Research and Development Center, India

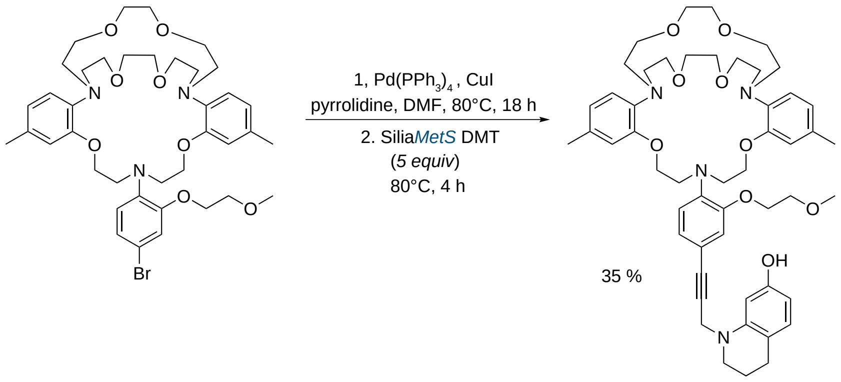
Removal of Pd

Palladium-mediated synthesis of a near-infrared fluorescent K+ sensor

Potassium (K+) exits electrically excitable cells during normal and pathophysiological activity.

Currently, K+-sensitive electrodes and electrical measurements are the primary tools to detect K+ fluxes. A near-IR, oxazine fluorescent K+ sensor (*KNIR-1*) with a dissociation constant suited for detecting changes in intracellular and extracellular K+ concentrations were synthetized, via a Sonogashira coupling between a halogenated triazacryptand (*TAC*) and a tetrahydroquinoline. The reaction proceeded smoothly.

Remaining palladium in the resultant alkyne was removed using Silia*MetS* DMT, as failure to remove all of the palladium impurities in the following reduction reaction resulted in cleavage of the tetrahydroquinoline from the TAC K+ binding domain during reduction.



Initial and/or residual metal content was not disclosed.

Robertz, W. R. *et al. J. Org. Chem.*, **2017**, *82*, 8199-8205
University of Massachusetts Medical School, Massachusetts, United States
& Assumption College, Massachusetts, United States

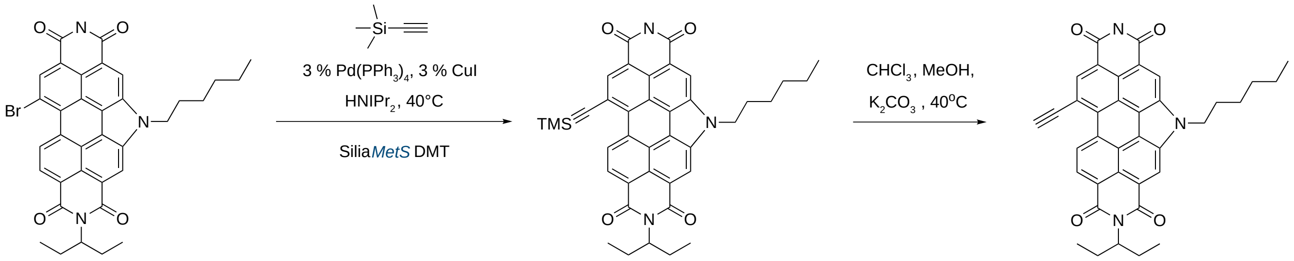
N-annulated perylene diimide dimers: controlling structural conformation & impact on physical, electronic, optical & photovoltaic properties

The geometry of organic π-conjugated small molecules can impact the morphology of blended-thin films and subsequent performance in opto-electronic devices.

The role of molecular conformation of perylene diimide (*PDI*) dimers designed to act as non-fullerene acceptors in organic solar cells was studied.

Silia*MetS* DMT removed all traces of Pd to generate Sonogashira product in near quantitative yield.

This was mandatory in the synthesis as it was found that the subsequent deprotection to form PDI-Ac was found to be sensitive to the amount of Pd remaining in the sample.



PDI-Br

94 %

PDI-AC

99 %

Initial and/or residual metal content was not disclosed.

Welch, G. *et al., J. Mater. Chem. C*, **2017**, *5*, 2074-2083
University of Calgary, Alberta, Canada
Dalhousie University, Nova Scotia, Canada

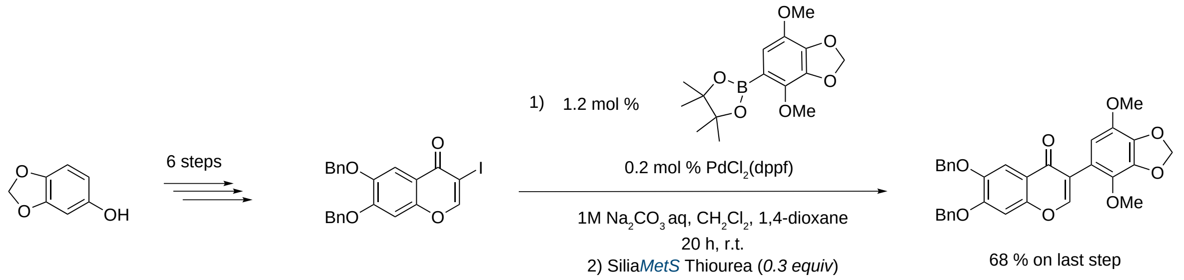
Removal of **Pd**

Suzuki-Miyaura cross-coupling synthesis of O^6-benzyl glaziovianin A

O^6-benzyl glaziovianin A is a potent cytotoxic substance & a potent inhibitor of α,β-tubulin polymerization. Following a Suzuki-Miyaura cross-coupling, Pd-containing O^6-benzyl glaziovianin A was purified using Silia*MetS* Thiourea.

Purification was done stirring the API with Silia*MetS* Thiourea at r.t. in $CHCl_3$ for 12 h.

Less than 1 equiv. of Silia*MetS* (*0.3 equiv*) was needed for scavenging!



Initial and/or residual metal content was not disclosed.

Hayakawa, I. *et al. Bioorg. Med. Chem.*, **2016**, *24*, 5639-5645
Okayama University, Okayama, Japan
University of Tsukuba, Tsukuba, Japan

Removal of **Pd**

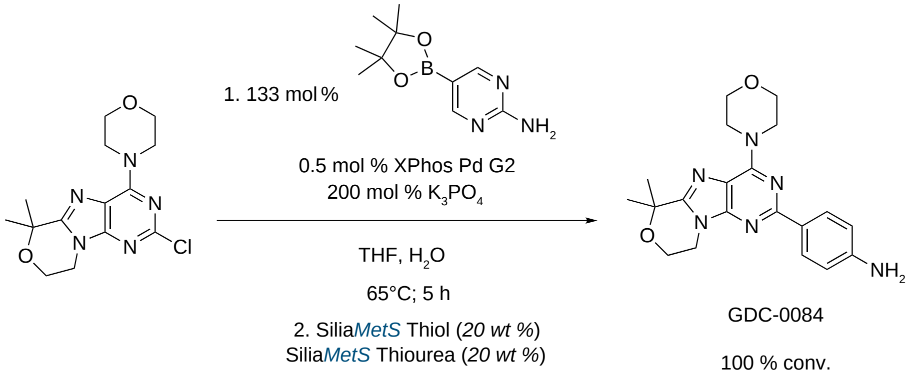
Suzuki-Miyaura cross-coupling synthesis of GDC-0084, a glioblastoma multiforme cancer inhibitor

GDC-0084 is a BBB (*Blood-Brain Barrier*)-inhibitor of the PI3K pathway, where GBM cancer cells reside.

In order to remove residual palladium from the API, a scavenging study using 40 functionalized resins, silicas & activated carbon was performed. Representative samples containing 2,400 ppm Pd were exposed to Silia*MetS* Scavengers (*20 wt % loading, 14 h*) in a solvent mixture of THF and HOAc (*67:33*).

Both Silia*MetS* Thiol & Thiourea were chosen for lowering residual Pd to ≤16 ppm in G-scale experiments.

On KG-scale, a mixture of the two scavengers was used.



GDC-0084

100 % conv.
Pd content: < 16 ppm

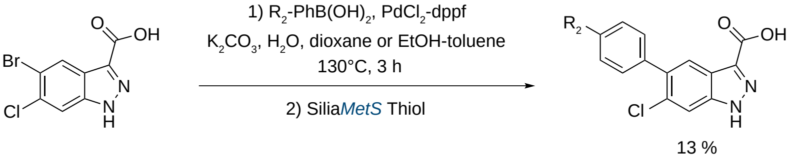
Stumpf, A. *et al.*, *ACS Symp. Series*, **2016**, *6*, 147-173
Genentech Inc., San Francisco, United States

Removal of Pd

Discovery and synthesis of a direct activator of AMP-Kinase PF-06409577 against diabetic nephropathy

Adenosine monophosphate-activated protein kinase (*AMPK*) is a protein kinase involved in maintaining energy homeostasis within cells. PF-06409577 has been discovered as an indole acid with excellent balance of properties and has now been advanced to first-in-human trials for the treatment of diabetic nephropathy. Key indazoles in the synthesis were prepared by Suzuki coupling to some commercially available 5-bromoindazoles.

Silia*MetS* Thiol was used to remove remaining Pd after only 30 min of stirring.



Initial and/or residual metal content was not disclosed.

Cameron, K. *et al. J. Med. Chem.*, **2016**, *59*, 8068-8081
Pfizer Worldwide Research & Development, Massachusetts & Connecticut, United States

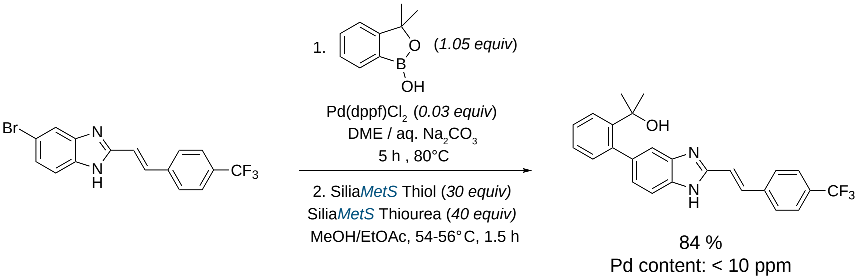
Removal of Pd

Synthesis of Mavatrep: a potent antagonist of transient receptor potential vanilloid-1

Mavatrep, a potent transient receptor potential vanilloid-1 (*TRPV1*) antagonist, was prepared in four steps in 63% overall yield. One of the two key synthetic transformations was the last step Suzuki coupling of an imidazole with an oxaborolole moiety.

Repeated attempts to carry out the Suzuki coupling reaction under the original conditions in presence of Pd(dppf)Cl$_2$ as a catalyst resulted in very poor yields (*5-35 %*) and formation of high levels of impurities requiring tedious purification. This poor outcome was even worse on larger scale.

After screening various experimental conditions, the best result was obtained by the use of Pd(d*t*bpf)Cl$_2$ in DME in the presence of aqueous Na_2CO_3 which led to a remarkable improvement in both reaction rate and yield. The crude salt was obtained in 80-90% as a brownish solid that typically contained about 1400-1600 ppm of residual palladium. Out of the six screened Silia*MetS* (*Diamine, TAAcOH, TAAcOH, Thiol, Thiourea and Triamine*), Thiourea proved to be the most effective palladium scavenger.



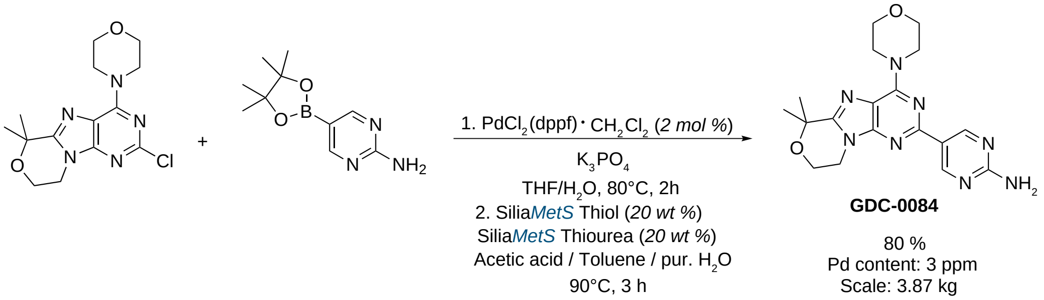
However, an unexpected result was found by the synergistic effect of a combination of two Silia*MetS*, Thiol and Thiourea when used in concert, which was not apparent from the screening array. Their use in combination left the API with less than 10 ppm of Pd.

Wells, K. M. *et al. Org. Process Res. Dev.*, **2015**, *19*, 1774-1783
Janssen Research and Development, Pennsylvania, United States

Development of an efficient, safe, and environmentally friendly process for the manufacture of GDC-0084

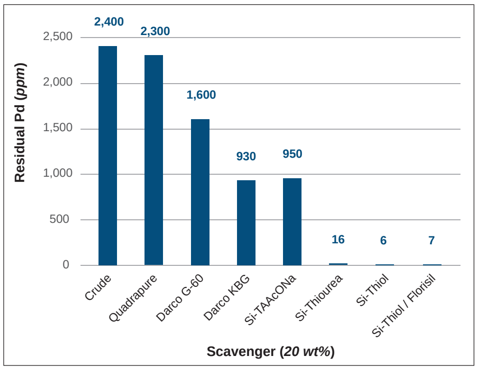
GDC-0084 is a potent and selective dual inhibitor of PI3K/mTOR with the ability to penetrate the blood−brain barrier, as it was discovered in Genentech laboratories (*Roche group*) for the treatment of various brain cancers. Highlights of the synthesis include a phase transfer catalyzed annulation in water, and the last step of the API is the Suzuki-Miyaura cross-coupling of a chloropyrimidine with an arylboronic acid using a palladium catalyst.

In this cross-coupling reaction, an initial catalyst screen found $PdCl_2(dppf){\bullet}CH_2Cl_2$ to be superior to $PdCl_2(PPh_3)_2$, $PdCl_2$(AmPhos), and $Pd(OAc)_2$/SPhos in terms of conversion. A brief solvent screen using 2 mol % catalyst showed that aqueous THF was the best system, affording more than 98 % conversion after 2 h.



GDC-0084

80 %
Pd content: 3 ppm
Scale: 3.87 kg



The crude GDC-0084 contained a large amount of residual palladium (≈ *2400 ppm*) was exposed to a variety of scavengers (*20 wt % loading*) in an effort to reduce the level of metal.

Both Silia*MetS* Thiol and Silia*MetS* Thiourea were found to lower the residual Pd the most efficiently (*lowered down to 3 ppm*).

The main issues in the stage 2 of this process were the high catalyst loading (*2 mol %,* $PdCl_2(dppf){\bullet}CH_2Cl_2$) for the Suzuki coupling and the large total of solvent volume (*58 vol*). The optimized Suzuki coupling was successfully demonstrated to provide 7.49 kg of crude GDC-0084 (*94 % yield*).

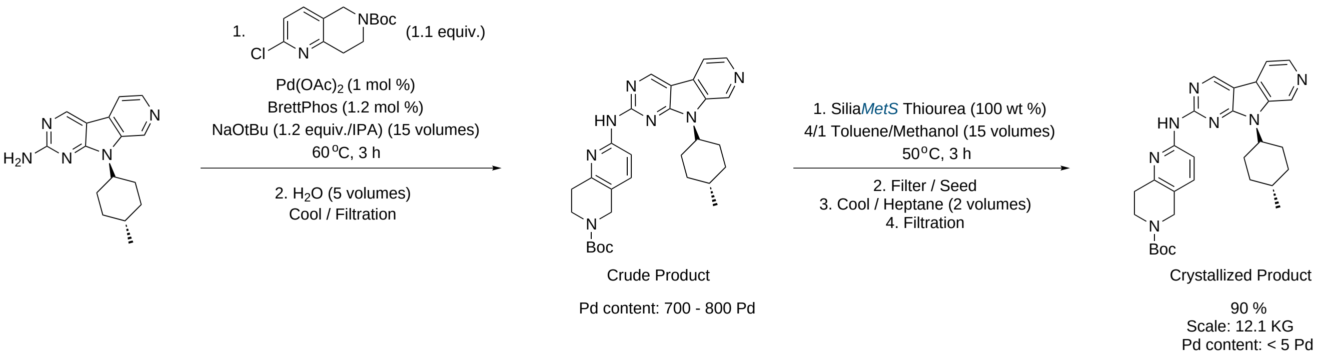
Overall, replacing $PdCl_2(dppf){\bullet}CH_2Cl_2$ with Buchwald's second generation XPhos Pd G_2 catalyst enabled the catalyst loading to be lowered from 2 to 0.5 mol %, and the scavenging procedure to be limited to one single Silia*MetS*, aka Silia*MetS* Thiol (*instead of both Si-Thiol and Si-Thiourea*), and only 10 wt % was sufficient to lower residual Pd to below 10 ppm.

Stumpf, A. et al. Org. Process Res. Dev., **2016**, *20*, 751-759
Stumpf, A. et al. ACS Symp. Series, **2016**, *6*, 147-173
Small Molecule Process Chemistry
Genentech Inc., A member of the Roche Group, California, United States

Multi-kilo delivery of AMG 925 featuring a Buchwald-Hartwig amination and processing with insoluble synthetic intermediates

Amgen describes the development of a synthetic route to manufacture the drug candidate AMG 925 on kilogram scale. The synthetic route features a Buchwald-Hartwig amination using BrettPhos as ligand and conducted to afford 12 kg of product in a single batch.

Yet, the target levels of heavy metal in the drug substance AMG 925 were < 100 ppm, much lower than that found in the crude Buchwald-Hartwig product (*700 - 800 ppm*).



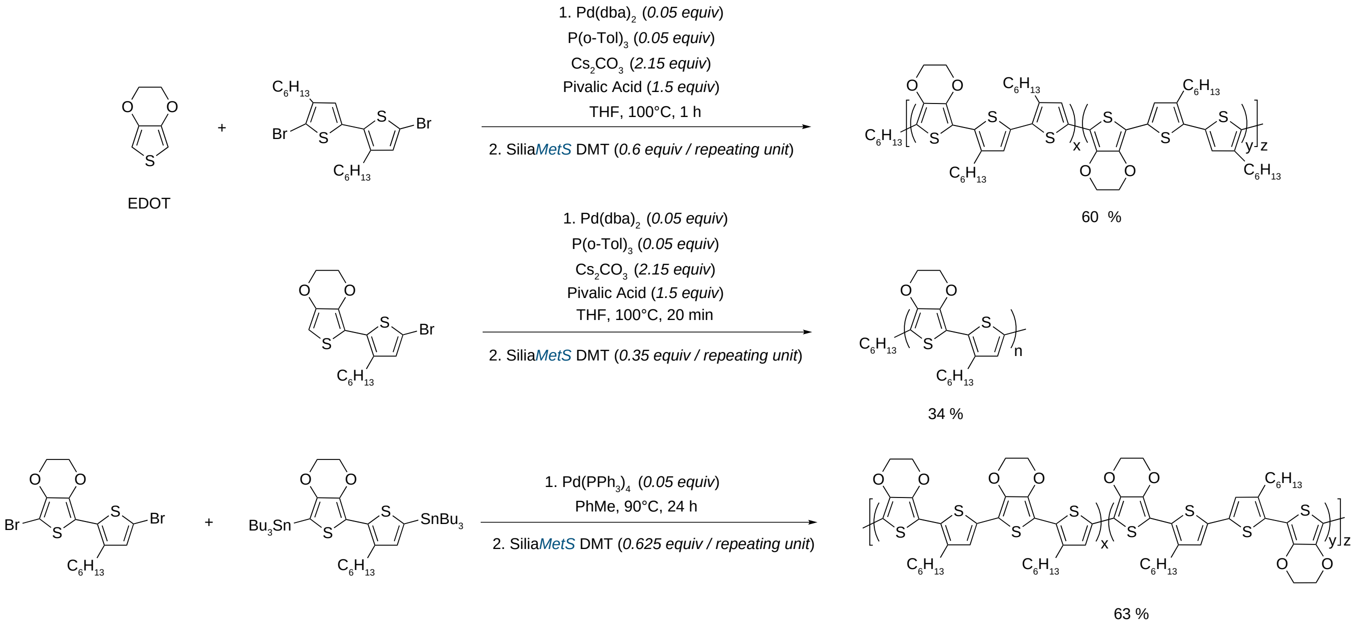
After the screening of potential scavengers, Silia*MetS* Thiourea was selected as the scavenger of choice since it was the most effective. At 100 wt % relative to crude product, in 80 % (*v/v*) toluene/MeOH and a total of 15 volumes of solvent, it afforded product in 90 % with less than 2 ppm of residual Pd.

Caille, S. *et al. Org. Process Res. Dev.*, **2015**, *19*, 476-485
Amgen Inc., Thousands Oaks, California

Synthesis of EDOT-containing polythiophenes and their properties in relation to the composition ratio of EDOT

Polythiophenes composed of 3,4-ethylenedioxythiophene (*EDOT*) and 3-hexylthiophene (*3HT*) with different composition ratios of EDOT in the repeat unit of the polymer backbone were synthesized by polycondensation reactions. The optical, electrochemical and charge transport properties of the polymers were compared and found to be well correlated with the EDOT composition ratio.

Three kinds of polythiophenes containing 3HT and different EDOT composition ratios were synthesized by polycondensation reactions using direct C–H arylation and Stille coupling, from which Pd residues was removed with Silia*MetS* DMT.



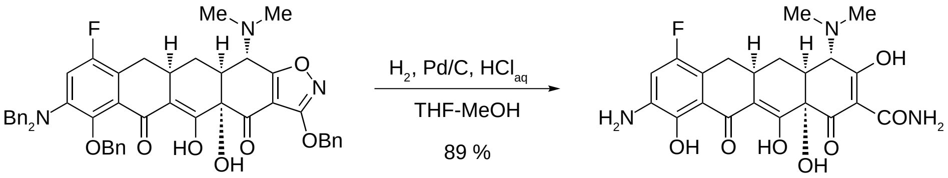
Initial and/or residual metal content was not disclosed.

Imae, I. *et al. RSC Adv.*, **2015**, *5*, 84694-84702
Hiroshima University, Hiroshima, Japan

A Tetraphase case study: palladium scavenging in the development of the first fully synthetic fluorocycline using Silia*MetS* DMT

Process research and development of the first fully synthetic broad spectrum fluorotetracycline in clinical development was reported by Tetraphase Pharmaceuticals. The key reaction was a Dieckmann condensation between a suitable substituted aromatic moiety and a cyclohexanone derivative. Subsequent hydrogenolysis was extensively studied, using a Pd/C catalyst. **Without any treatment, residual palladium levels as high as 2,000 ppm were detected**.

Silia*MetS* DMT was found to be an excellent metal scavenger to reduce the residual Pd content to more than acceptable levels.



Scale-Up of Hydrogenation and Pd Scavenging Results

Entry[1]	Hydrogenation Time (*h*)	Time for Slurry in EtOH / H_2O (*h*)	Yield (%)	Pd Content (*ppm*) (*after treatment*)
1	12	2	82	0.4
2	4	17	73	2
3	7	2	77	0.39
4	10	2.5	79	1.11
5	11	4	85	**< 0.2**

[1] 6.2 to 10 wt % Pd/C was used

Conclusion

The reaction was run in THF / MeOH (*3.3/10 v/v*) under nitrogen with 10 wt % Pd/C. Without any treatment, residual palladium levels were as high as 2,000 ppm, but after stirring with 50 or 100 wt % Silia*MetS* DMT in MeOH for 2 - 3 h, residual levels were consistently below 1.5 ppm.

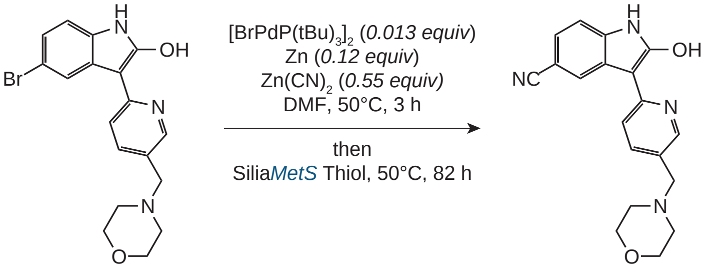
M. Ronn *et al.*, *Org. Proc. Res. Dev.*, **2013**, *17*, 838-845
Tetraphase Pharmaceuticals Inc., Massachusetts, United States

Removal of Pd

An AstraZeneca case study: palladium removal using Silia*MetS* Thiol

AstraZeneca published a paper on removal of palladium impurities in a pilot-scale process.

The work-up method found to work the best was a treatment with Silia*MetS* Thiol (*25 % w/w or ~1.4 kg*) at 50°C to purify more than 6.7 kg of material. Final residual palladium concentration was as low as 1 - 2 ppm.



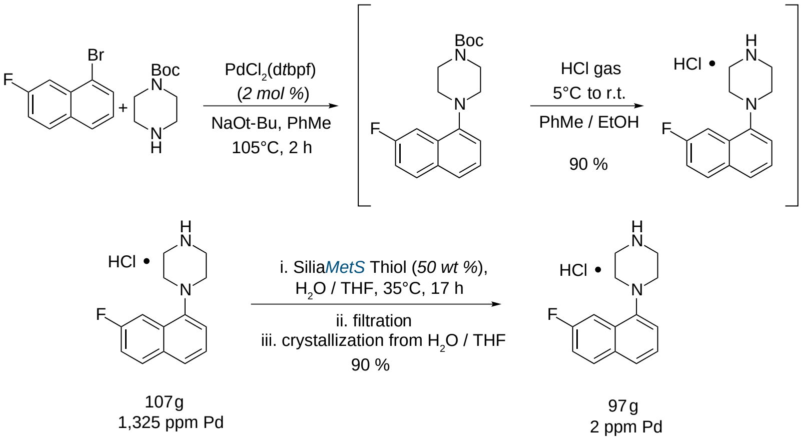
P. Ryberg *et al.*, *Org. Proc. Res. Dev.*, **2008**, *12*, 540-543
Process Chemistry, AstraZeneca PR&D, Sweden

Removal of Pd

A Pfizer case study: palladium removal using Silia*MetS* Thiol after a Buchwald-Hartwig amination

Silia*MetS* Thiol was employed by researchers at Pfizer for Pd removal during the preparation of a naphthalenopiperazine HCl salt. The product from the Buchwald-Hartwig amination of naphthyl bromide with Boc-piperazine was telescoped as a toluene solution and the Boc protecting group was subsequently cleaved with HCl gas to afford the HCl salt containing over 1,300 ppm Pd.

A water / THF solution of this material was then treated with Silia*MetS* Thiol (*50 wt %*) at 35°C for 17 h and, following crystallization from water / THF.



Conclusion

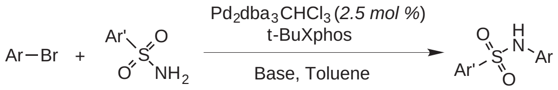
The HCl salt was obtained with a 90 % yield with only 2 ppm Pd. This chemistry was demonstrated on a kilogram scale.

J. Magano *et al.*, *J. Synth. Commun.*, **2008**, *38*, 3631-3639
Research API, Pfizer Global Research and Development, Connecticut, United States
Separation Sciences, Pfizer Global Research and Development, Connecticut, United States
Research API, Pfizer Global Research and Development, Michigan, United States
Supply Chain API, Pfizer Global Research and Development, Michigan, United States

An Amgen case study: Palladium removal using various resins

Amgen published a chapter in *"Catalysis of Organic Reactions"* related to the use of scavengers for the removal of palladium in small to multi-kilogram production scales.

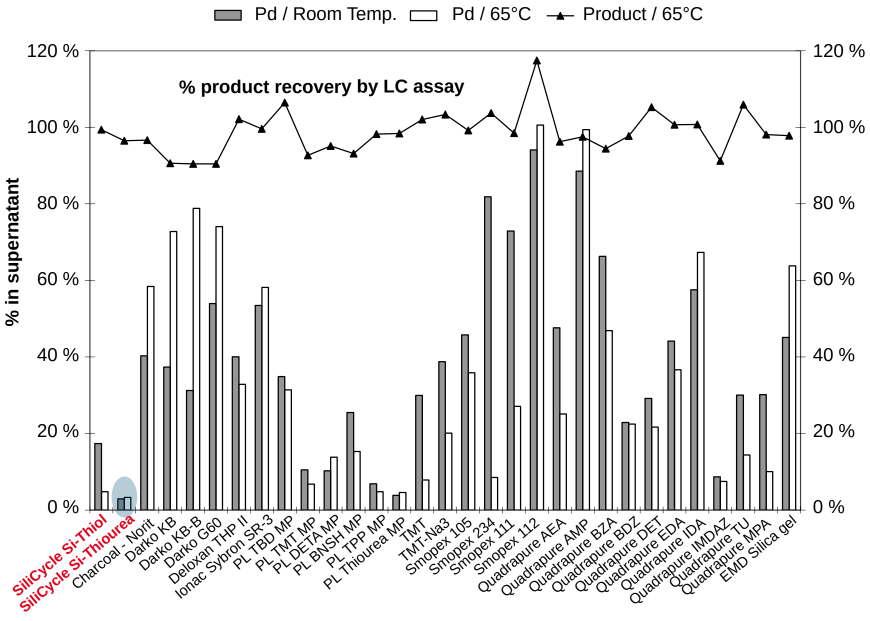
In this study, several parameters were evaluated, such as scavenging efficiency, influence of the scavenger loading and loss of product to adsorption (*recovery*). The study was based on a palladium-catalyzed sulfonamide coupling and scavenger screening was performed at both room temperature and 65°C using 31 different scavengers.



Amgen Scavenger Screening Results

Conditions: 20 mg of each scavenger (*20 % w/w*) were placed in 2 mL HPLC vials each containing 1 mL of crude reaction mixture containing 100 mg of product. Each vial was sealed and agitated overnight. Initial palladium concentration was 423 ppm.

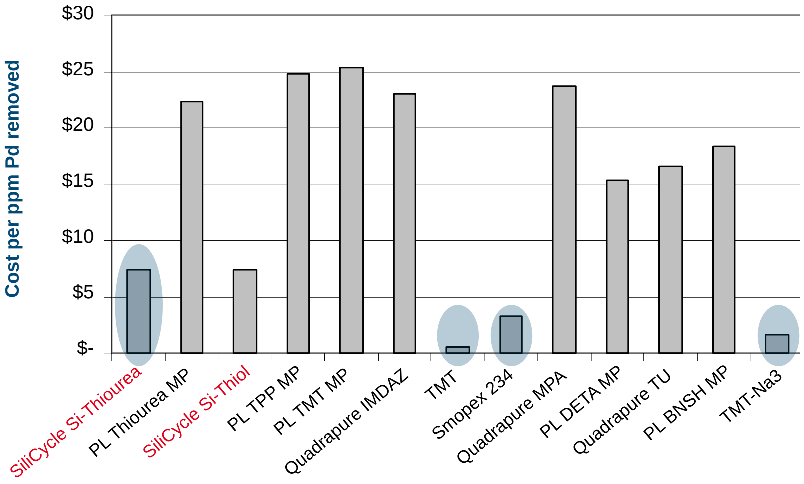
The best scavenger identified during their study was the Silia*MetS* Thiourea providing the lowest Pd content (*residual palladium concentration: 3 % or < 14 ppm*) without product sequestration. They mentioned that Silia*MetS* Thiourea was used extensively in early process development work.



Cost Comparison for Most Efficient Scavengers (≥ *80 %*)

At pilot-plant scale, the optimal compromise between the cost per ppm removed and the scavenging efficiency is crucial.

Results highlighted by the graph reduced the number of options to only four candidates for further evaluation: in pole position Silia*MetS* Thiourea, followed by TMT, TMT-Na_3 and Smopex 234.



Note: Silia*MetS* DMT does not appear in this study because it had not been commercialized yet at the time of the study.

Top Four Scavengers Overview

A screening validation was conducted on 1-g scale purification (*10 mL of solution*) with 20 % w/w of the four best scavengers at 65°C overnight. After filtration, residual metal concentration was analyzed by ICP-MS and product recovery was determined by HPLC. Silia*MetS* Thiourea was chosen for the large scale purification.

Screening Validation Results on Top 4 Scavengers

Scavengers	Residual Metal Concentration (*ppm*)			Product Recovery	Commentary from Amgen
	Screening Exp. in Solution	Validation Exp. in Solution	Validation Exp. in Solid Product		
SiliCycle Thiourea	14	11	158	102 %	Best performance
TMT	33	15	264	104 %	Fine in suspension, filterability concerns on scale
Smopex 234	36	38	496	84 %	Favorable cost but product recovery inadequate
TMT-Na3	85	81	1 555	78 %	Very basic compounds (*not effective with base-sensitive groups*) and low recovery
Initial Concentration	423 ppm	381 ppm	3,577 ppm	-	-
Purification Scale	100 mg	1 g	1 g	1 g	-

Please see Amgen’s chapter for further details (*see reference below*).

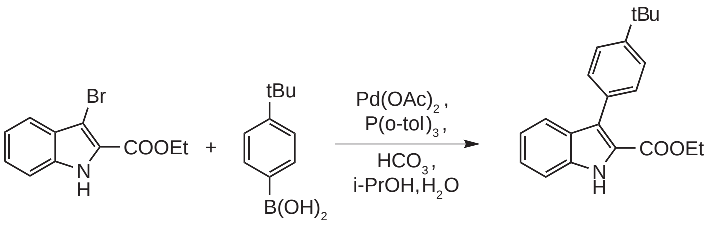
Amgen’s Conclusion

“Scavengers offer a practical and expedient option for removal of palladium from process streams to ensure quality of organic products... The screening protocol involves treatment of a candidate process stream with 20 % w/w scavenger on product at both room temperature and 65°C followed by analysis of Pd and product adsorption. High-temperature treatment increased the efficiency of Pd removal... Evaluation of process costs is key to identifying Pd removal solutions. While scavengers add cost to a process, their use is often justified by the speed to production in early phase development.”

J. Allgeier *et al.*, « Application of Scavengers for the Removal of Palladiumin Small Lot Manufacturing », *Catalysis of Organic Reactions*, Chapter 5., Amgen Inc., Thousand Oaks, California

Pd scavenging after a Suzuki-Miyaura coupling using a GlaxoSmithKline published reaction

A metal scavenging study was performed following the synthesis of a key synthetic intermediate obtained by the Suzuki-Miyaura coupling presented in scheme below. Various parameters were investigated including the efficiency of Silia*MetS* in different formats, scavenging kinetics, intermediate recovery and purity.



Small-Scale Scavenging (*Synthesis Scale ~ 5 g*)

The table below shows the most efficient Silia*MetS* Metal Scavenger products for the treatment of the reaction mixture after work-up in both bulk and fixed-bed mode bed (*pre-packed SPE cartridges*).

Silia*MetS* Scavenging Efficiency & Intermediate Recovery Results (*in %*)

Scavengers	Batch Reactor Mode (*Bulk*)		Fixed-Bed Mode (*SPE*)	Intermediate Recovery
	5 equiv, 4 h, 22°C	5 equiv, 4 h, 40°C	6 mL / 1 g	
Silia*MetS* Thiol	**95**	**> 99**	**98**	**> 99**
Silia*MetS* Thiourea	83	93	**99**	**98**
Silia*MetS* Cysteine	84	91	**97**	**> 99**
Silia*MetS* DMT	**97**	**> 99**	**> 99**	**98**
Initial Pd Concentration	179 ppm in MTBE		76 ppm in Toluene	-

Scavenging Conclusion

Addition of 5 equivalents of Silia*MetS* products for 4 h at the end of the reaction reduces the residual metal concentration to single digit ppm.

Recovery & Purity Conclusion

Palladium was completely removed, while the organic compound was not sequestrated by Silia*MetS* products.
No impurities were released.

Larger Scale Scavenging (*Synthesis Scale ~ 55 g*)

Silia*MetS* Metal Scavengers in pre-packed Silia*Sep* Flash Cartridges are a great alternative for metal removal at process development scale. These cartridges offer excellent scavenging efficiency as shown by the results in associated table.

After the first run, almost all the palladium was captured.

After three runs, less than 1 ppm remained in solution.

Results

Silia*Sep* Scavenging Results (*in %*)

Run #	Scavenging
1	**97**
2	**99**
3	**> 99**

Initial Pd Concentration: 700 ppm in AcOEt

Experimental Conditions

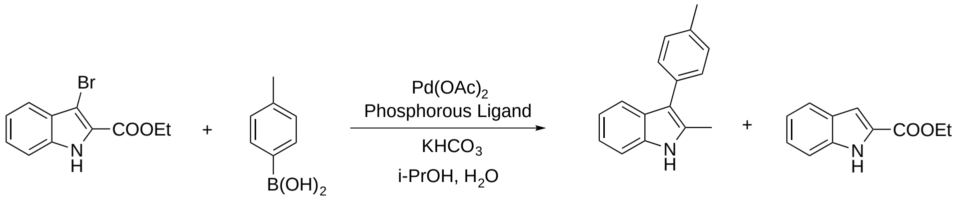
Scavenger Used	Silia*MetS* Thiol
Cartridge Size	120 g
Nb. Equivalent	25 equiv
Solution Volume	1 L
Flow Rate	40 mL/min

J. F. Toczko *et al.*, *Org. Proc. Res. Dev.*, **2008**, *12*, 896-899
Chemical Development, GlaxoSmithKline, North Carolina, United States

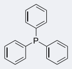
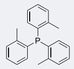
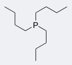
The effect of variation of phosphorous ligand nature on scavenging

Even for the same metal, a variation in the scavenging efficiency can be observed depending on the nature of the products present in the solution to be treated. For example, steric hindrance and the electronic effects of the phosphorous ligands are factors influencing the removal of the metal.

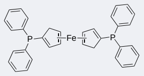
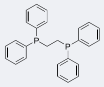
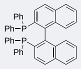
The same Suzuki coupling was performed using different phosphorous ligands: three monodentate and three bidentate. For comparison purposes, scavenging screening was done by using the same two sets of conditions. No optimization was done to increase Silia*MetS* performance. By experience, using longer reaction times or higher temperatures will allow better results.



Silia*MetS* Scavenging Results with Monodentate Ligands (*in* %) with 4 equiv, 4 h

Silia***MetS***	Triphenylphosphine [PPh$_3$] 		Tri(o-tolyl)phosphine [P(otol)$_3$] 		Tri-n-butylphosphine [PnBu$_3$] 	
	22°C	60°C	22°C	60°C	22°C	60°C
Silia*MetS* Thiol	70	97	87	96	26	85
Silia*MetS* DMT	95	97	95	> 99	36	87
Initial Pd Concentration:	27 ppm in EtOAc		84 ppm in EtOAc		90 ppm in EtOAc	

Silia*MetS* Scavenging Results with Bidentate Ligands (*in* %) with 4 equiv, 4 h

Silia***MetS***	1,1'-bis(diphenylphosphino)ferrocene [dppf] 		1,3-bis(diphenylphosphino)propane [dppp] 		(+/-) BINAP 	
	22°C	60°C	22°C	60°C	22°C	60°C
Silia*MetS* Thiol	50	69	75	90	31	56
Silia*MetS* DMT	14	22	95	98	41	64
Initial Pd Concentration:	63 ppm in EtOAc		93 ppm in EtOAc		16 ppm in EtOAc	

Conclusion

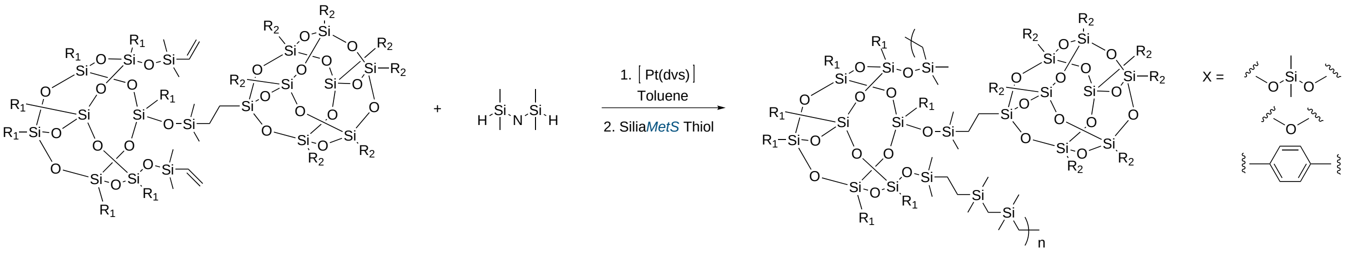
In all cases, Silia*MetS* DMT and Thiol remained the best scavengers throughout the study, even though there is a variation in the nature of the ligand.
As expected, scavenging was more difficult with bidentate phosphine ligands.
The best conditions were using 4 equiv for 4 h, at 60°C.

Polyhedral oligomeric silsesquioxanes (*POSSs*) are promising building blocks for organic-inorganic hybrid materials

Polyhedral oligomeric silsesquioxanes (*POSSs*) are promising building blocks for organic-inorganic hybrid materials, yet they have rarely been studied because the synthesis of bifunctional POSS monomers is a very difficult one in general.

In this work, a novel molecular design of a POSS monomer has been proposed and it was shown that substituents on the completely-condensed or incompletely-condensed POSSs can be widely varied. Furthermore, the resulting polymers are suitable for optically transparent materials because of their high thermal stability and transparency. The properties were controlled by the substituents on the silicon atoms of the POSSs and comonomers. The platinum-catalyzed hydrosilylation polymerization of the bifunctional POSS monomers was performed with siloxane comonomers.

For the measurement of optical properties, the obtained polymers films were fabricated according to the solution-casting method (*refer to experimental protocol*), and were approximately 50 µm thick, measured with a thickness gauge. They showed high transparency in the 380 - 400 nm range.



Experimental Protocol: A polymer (*0.1 g*) was dissolved in $CHCl_3$ (*1 mL*) in the presence of Silia*MetS* Thiol, and the solution was filtered and cast onto a glass substrate.

Initial and/or residual metal content was not disclosed.

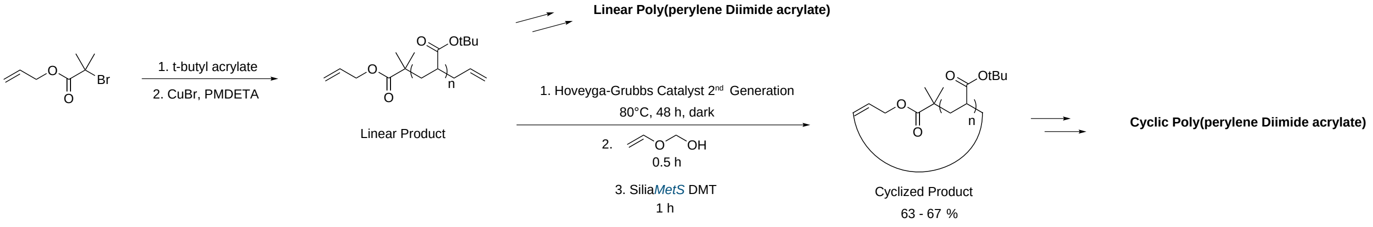
Naka, K. et al. J. Polymer Sci. Part A: Polymer Chem., **2018**, *9*, 4108-4112
Kyoto Institute of Technology, Sakyo-Ku, Japan

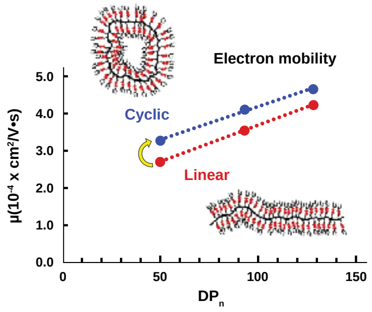
Electrostatic self-assembly and covalent fixation (*ESA-CF*) process for the synthesis of linear and cyclic polymers and their topology effects on thin-film electron mobility

A pair of topologically contrastive, linear and cyclic polymers having densely appended perylene diimide (*PDI*) units have been prepared by means of an electrostatic self-assembly and covalent fixation (*ESA-CF*) process.

As a first step, a pair of linear and cyclic poly(sodium acrylate) of different segment lengths were prepared through an atom transfer radical polymerization, followed by the end-capping reaction and subsequent ring-closing metathesis in the presence of Hoveyda-Grubbs catalyst second generation.

Unreacted precursor as well as unassigned side products were removed by flash chromatography and Ru removal with Silia*MetS* DMT.





The electron-only device (*EOD*) measurement by using thin-film samples of a series of the Cyclic Poly(perylene Diimide acrylates), revealed consistently higher electron carrier mobilities in comparison with the corresponding linear counterparts, the linear Poly(perylene Diimide acrylates).

Initial and/or residual metal content was not disclosed.

Tenuka, Y. *et al. Macromolecules*, **2016**, *49*, 5831-5840
University of Calgary, Alberta, Canada
Dalhousie University, Nova Scotia, Canada

Removal of Ru

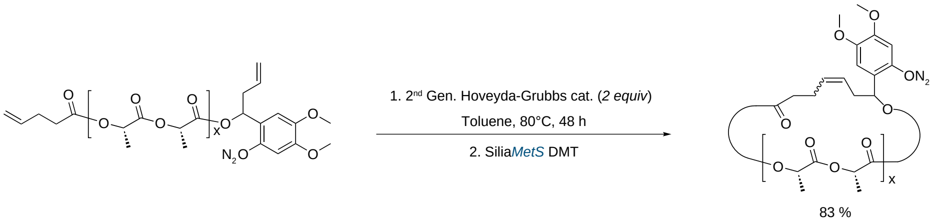
Photoinduced topological transformation of cyclized polylactides for switching the properties of homocrystals and stereocomplexes

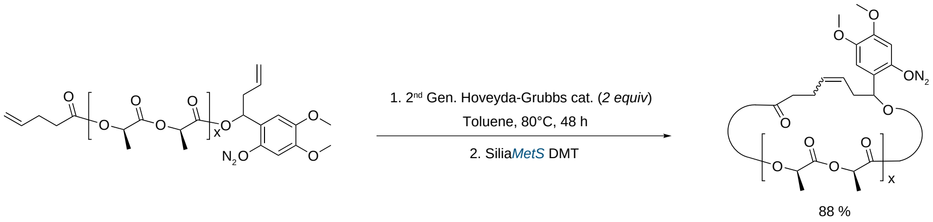
Cyclized poly(L-lactide) (*PLLA*) and poly(D-lactide) (*PDLA*) incorporating an o-nitrobenzyl group as a photocleavable linker were synthesized and photoirradiated for topological transformation to form photocleaved linear polylactides.

The o-nitrobenzyl group was chosen as it is one of the most widely used photolabile protecting groups due to its prompt removal.

Two cyclic PLLA and PDLA with this photocleavable linker were prepared via a Hoveyda-Grubbs catalyzed olefin metathesis, a polymerization known to form highly optically pure polylactides without degradation in the stereochemistry. Silia*MetS* DMT was used to remove residues of ruthenium.

It was shown that the enthalpy of the photocleaved cyclized polylactides was much lower than that of the linear prepolylactides, hence the crystalline-amorphous interface is more stable for the cyclized polylactides arising from the topology.





Initial and/or residual metal content was not disclosed.

Yamamoto, T. *et al.* *Polym. Chem.*, **2015**, *6*, 3591-3600

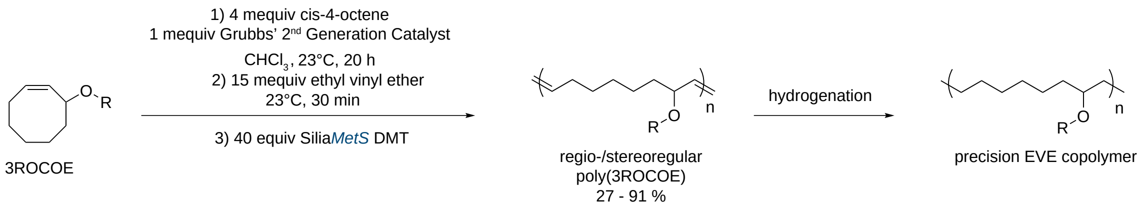
Removal of Ru

Regioselective ring-opening metathesis polymerization of 3-substituted cyclooctenes

Allyl-substituted cyclooctenes with various sidechains [amides, methoxy, methoxy-terminated oligo(ethylene glycol)s, and tetrahydrofurfuryloxy groups] were prepared as monomers and polymerized by ring-opening metathesis polymerization (*ROMP*) using Grubbs second-generation catalyst.

In all cases, the ROMP of allyl-substituted monomers proceeded in a regio- and stereoselective manner to afford polymers with remarkably high head-to-tail regioregularity with high trans-stereoregularity.

Poly(3ROCOE) were purified from contaminating Ru with Silia*MetS* DMT (*O.N. at 40°C*)

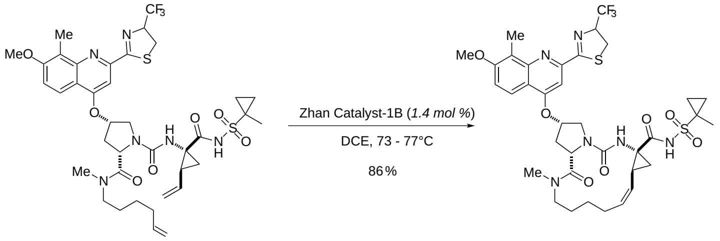


Initial and/or residual metal content was not disclosed.

Kobayashi, S. *et al.* *Macromolecules*, **2016**, *49*, 2493-2501
Macromolecules, **2016**, 49, 8154 - 8161
Kyushu University, Fukuoka, Japan
Yamagata University, Yamagata, Japan

An Idenix case study: ruthenium removal in the macrocyclization of dienyl-ureas via RCM, using Silia*MetS* DMT

A novel assembly of two structurally related 14-membered ring macrocyclic hepatitis C virus protease inhibitors was reported by Idenix Pharmaceuticals. Key to their successful construction was an ultimate ring-closing metathesis step on the highly functionalized dienyl-urea via Zhan Catalyst-1B (*Ru-based catalyst*).



Several methods have been reported to remove Ru by-products, and were investigated in this study with some variations, including the use of tris(hydroxymethyl)phosphine, lead tetraacetate, TPPO, DMSO followed by silica gel filtration, adsorption onto silica gel, activated carbon and silica gel chromatography, treatment with mercaptonicotinic acid (*MNA*) and washing with aqueous $NaHCO_3$, and the use of supercritical fluid extraction. Resulting Ru levels of those methods vs Silia*MetS* DMT treatment were analyzed by ICP-OES and are listed below.

Effect of Reaction Conditions and Purification on Ru Content and Yield of Protease Inhibitor

Entry	Reaction Conditions	Ru Reduction Operation	Ru content (*ppm*)	Yield (%)
1	250 mL/g diene 4.9 mM 1.5 wt % catalyst	MNA / $NaHCO_3$ wash ; charcoal ; silica gel filtration	14 (*initial*)	-
		1st MeOH trituration	12	63
		2nd MeOH trituration	7.5	58
2	250 mL/g diene 4.9 mM 1.5 wt % catalyst	Charcoal ; silica gel filtration	120 (*initial*)	-
		1st MeOH trituration	34	81
		2nd MeOH trituration	20	75
3	250 mL/g diene 4.9 mM 1.5 wt % catalyst	Charcoal ; silica gel filtration	120 (*initial*)	-
		1st MeOH trituration	48	79
		5/4 v/v DCE / MeOH crystallization	4.6	61
4	80 mL/g diene 15.2 mM 1.1 wt % catalyst	Charcoal ; silica gel filtration	880 (*initial*)	-
		1st MeOH trituration	300	84
		Toluene crystallization	22	45
5	80 mL/g diene 15.2 mM 1.1 wt % catalyst	Charcoal ; silica gel filtration	880 (*initial*)	-
		1st MeOH trituration 2:1 v/v	300	84
		EtOAc / n-heptane crystallization	19	51
6	80 mL/g diene 15.2 mM 1.25 wt % catalyst	Silia*MetS* DMT 16 h treatment + filtration	380 (*initial*)	-
			66	75
7	160 mL/g diene 7.6 mM 1.25 wt % catalyst		200 (*initial*)	-
			3.6	86
8	250 mL/g diene 4.9 mM 1.25 wt % catalyst		180 (*initial*)	-
			7.7	89

Conclusion

As one can easily note, treatment with Silia*MetS* DMT gave a much lower Ru residual content conjointly with the highest final yields. Hence, low yield losses *(11 - 14 %)* and high purities (*98 %*) were achieved, together with excellent Ru levels observed (*as low as 3.6 ppm*), indicating the strong utility of this approach in Ru removal in the synthesis of macrocycle HCV PIs IDX316.

B. A. Mayes *et al.*, *Org. Proc. Res. Dev.*, **2013**, *17*, 811-828
Idenix Pharmaceuticals Inc., Massachusetts, United States

Removal of **Ru**

Ruthenium scavenging

Ruthenium-based catalysts are commonly used in organic synthesis, mainly in olefin metathesis reactions [*ROM(P) and RCM*]. Grubbs and Hoveyda-Grubbs catalysts are the most popular ruthenium-based complexes in this field of application. Complete ruthenium removal can be tedious using conventional methods.

Under various conditions, several Silia*MetS* are known to be excellent scavengers to obtain minimal tolerated concentrations of residual ruthenium.

A ruthenium scavenging study was conducted and various parameters were investigated in order to learn more about their influence on the scavengers' robustness as well as to establish the best experimental conditions.

Ruthenium Scavenging Results using Silia*MetS* (*in %*)

Silia*MetS*	Grubbs 1st Gen.		Grubbs 2nd Gen.		Hoveyda-Grubbs 1st Gen.		Hoveyda-Grubbs 2nd Gen.	
	Toluene[1]	DMF[2]	Toluene[1]	DMF[2]	Toluene[1]	DMF[2]	Toluene[1]	DMF[2]
Silia*MetS* Thiol	90	96	-	99	97	93	-	-
Silia*MetS* Thiourea	-	98	-	96	97	98	-	-
Silia*MetS* DMT	95	99	> 99	99	> 99	98	98	99
Silia*MetS* Diamine	99	99	91	94	> 99	98	-	90

Notes: Silia*MetS* Cysteine and Imidazole were not screened in this study.
Only Silia*MetS* results higher than 90 % are presented in this table.

Experimental Conditions

Nb. Equivalent: [1] 8 equiv of Silia*MetS*, 16 h, 80°C

[2] 4 equiv of Silia*MetS*, 16 h, 80°C

Initial Concentration: 500 ppm for all ruthenium-based catalysts

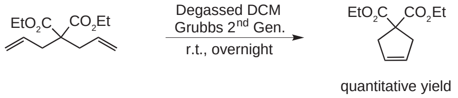
Conclusion

For all Ru-catalyzed reactions, the best scavenging was achieved using Silia*MetS* DMT. For most experiments, little or no difference was observed when using toluene or DMF.

Removal of **Ru**

Silia*MetS* vs other purification methods for ruthenium scavenging

The use of Silia*MetS* to remove ruthenium catalysts after a ring-closing metathesis (*RCM*) reaction is a very effective purification method. One of its main advantages is that no product is lost during the purification step.



Scavenging Results for Various Purification Methods* (*in %*)

Scavenging	Scavenger	Filtration over packed bed of ...[2]			Flash Purification	
	Silia***MetS*** DMT[1]	Act. Carbon	Celite	Silica	Manual	Silia*Sep* Cart.
Ruthenium captation	93	73	24	58	70	73

[1] Using 4 equiv, 16 h, 22°C.

[2] Solution is passed directly on a packed bed of various adsorbents, which was then washed with the same quantity of solvent.

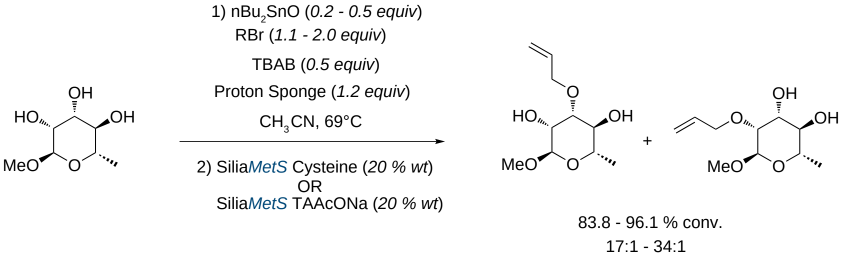
* Quantitative yield obtained for each purification method (*adjusted in function of the residual concentration of catalyst*). No impurities were generated in all cases using the different methods (*determined by NMR*).

Removal of Sn

Tin acetate-promoted Buchwald-Hartwig couplings of heteroaromatic amines

Regioselective manipulation of hydroxyl groups in polyols has been critical to carbohydrate chemistry.

A robust selective allylation of 1-methyl-L-α-rhamnose was developed using n-Bu$_2$SnO as the catalyst and proton sponge as optimal base for high regioselective control. The optimized condition afforded the 3-O-allylated rhamnose in excellent regioselectivity (> *20:1*) and 82 % isolated yield on a 50 g scale.



A scalable isolation/purification process was developed which afforded the desired product in 72 % yield with 1530 ppm of Sn.

The residual Sn level can be further reduced to < 20 ppm by treatment with Silia*MetS* Cysteine & TAAcONa.

Residual Sn (*ppm*)

Experimental Step	Starting Level	End Level	Recovery (%)
Extractive Work Up	-	1,530	72
1st treatment 20 wt % with Silia*MetS* Cysteine	1,530	273	92
2nd treatment 20 wt % with Silia*MetS* Cysteine	273	31.9	93
1st treatment 20 wt % with Silia*MetS* TAAcONa	1,530	267	91
2nd treatment 20 wt % with Silia*MetS* TAAcONa	267	19.5	95

This catalytic system also showed outstanding potential in the selective benzylation of the same substrate.

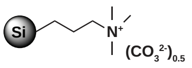
The isomeric purity remained unchanged after the scavenger treatment.

Li, X. *et al. Org. Process Res. Dev.*, **2017**, *21*, 1653-1658
Process Development & Process Chemistry, DOW AgroSciences, Michigan & Indiana, United States

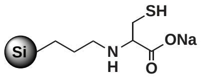
Removal of Sn

Tin scavenging using Silia*Bond* Carbonate vs Silia*MetS* Cysteine

SiliCycle also provides a quaternary ammonium salt grafted on silica to which a carbonate group is ionically bounded. The latter has shown to be an excellent alternative for tin retrieval from organic mixtures.



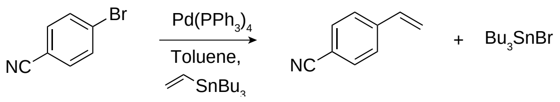
Silia*Bond* Carbonate



Silia*MetS* Cysteine

Stille Reaction

Tin scavenging was demonstrated on a Stille coupling in which Bu$_3$SnBr is the major tin by-product. In each test, residual Pd was scavenged in its entirety (*from 24 mg/L to < 0.1 mg/L*).



Tin Scavenging (*in %*)

Scavenger	4 h, 8 equiv, 22°C	4 h, 16 equiv, 22°C
Silia*Bond* Carbonate	91	**99**
Silia*MetS* Cysteine	77	**99**

Conclusion

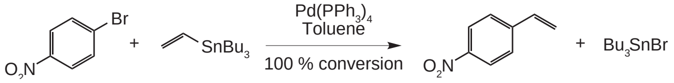
Scavenging yields were excellent with both scavengers. Hence, Silia*Bond* Carbonate was found to be of the same high efficiency as Silia*MetS* Cysteine to scavenge tin compounds of R$_3$SnX type.

Removal of Sn

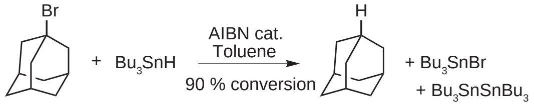
Tin scavenging using Silia*MetS* Cysteine & TAAcONa

The removal of tin residues can often be an issue due to the high toxicity of this metal. Traditional removal methods for this impurity are treatment with an aqueous solution of KF, NH_4OH or NaOH, or with bases such as DBU. However, the efficiency of these methods can vary and may be inapplicable for some particular compounds.

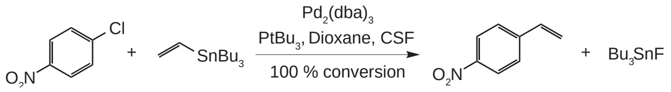
Both Silia*MetS* Cysteine & TAAcONa can be used to efficiently remove tin residues from organic mixtures, as demonstrated below.



Stille Coupling #1



Radical Reduction



Stille Coupling #2

Tin Scavenging using Silia*MetS* Cysteine & TAAcONa (*in %*)

Reactions	Initial Concentration	Silia*MetS* Cysteine		Silia*MetS* TAAcONa		
		4 equiv, 4 h, 22°C [*2 treatments*]	8 equiv, 4 h, 22°C	4 equiv, 4 h, 22°C [*2 treatments*]	8 equiv, 4 h, 22°C	4 equiv, 16 h, 22°C
Stille coupling #1[1]	3,385 ppm	**99**	64	**96**	62	-
Stille coupling #2[1]	981 ppm	90	66	66	50	-
Radical Reduction	4,090 ppm	92	88	90	90	90

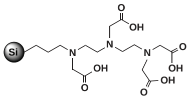
[1] Pd residues were completely removed after only one treatment with Silia*MetS* Cysteine.

Removal of U

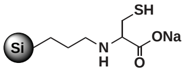
Uranium XAFS analysis of kidney from rats exposed to uranium

The kidney is the critical target of uranium exposure because uranium accumulates in the proximal tubules and causes tubular damage, but the chemical nature of uranium in kidney, such as its chemical status in the toxic target site, is poorly understood. In this study, micro-X-ray absorption fine-structure (*mXAFS*) analysis was used to examine renal thin sections of rats exposed to uranyl acetate.

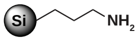
In the preparation of uranium standards for XAFS analyses, uranium adsorbed on 6 different metal scavengers were prepared: Silia*MetS* TAAcOH, Silia*MetS* Cysteine, Silia*MetS* Amine, Silia*MetS* DMT, Silia*MetS* Imidazole & Silia*MetS* Thiol.



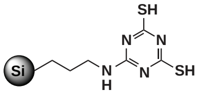
Silia*MetS* TAAcOH



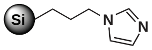
Silia*MetS* Cysteine



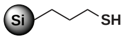
Silia*MetS* Amine



Silia*MetS* DMT



Silia*MetS* Imidazole



Silia*MetS* Thiol

Uranium Concentrations

Scavenger	Uranium concentration (*µg/g*)
Silia*MetS* TAAcOH	149,000
Silia*MetS* Cysteine	77,640
Silia*MetS* Amine	37,400
Silia*MetS* DMT	87,530
Silia*MetS* Imidazole	74,400
Silia*MetS* Thiol	22,500

The concentrations of uranium bound to the functionalized resin were above 15,000 µg/g.

Homma-Takeda, S. *et al.*, *J. Synchrotron Rad.*, **2017**, *24*, 456-462
National Institute for Quantum and Radiological Science and Technology, Chiba, Japan
Japan Synchrotron Radiation Research Institute, Hyogo, Japan

A Genentech case study: palladium and ruthenium removal in the synthesis of AKT inhibitor Ipatasertib using Silia*MetS* Thiol (*multi-kilogram scale*)

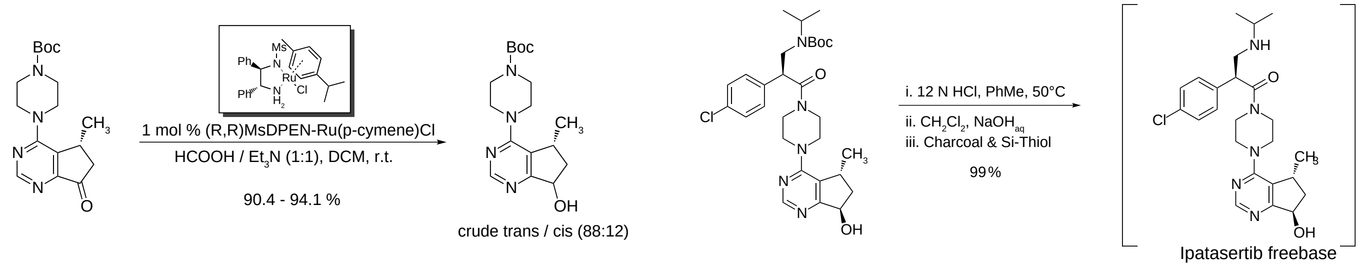
The first-generation process to manufacture Akt inhibitor Ipatasertib through a late-stage convergent coupling of two challenging chiral components on a multi-kilogram scale was reported by Array BioPharma.

A carbonylative esterification and subsequent Dieckmann cyclization was developed to forge a cyclopentane ring in the target. A second key chiral component, a β2-amino acid, was produced using an asymmetric aminomethylation (*Mannich*) reaction.

Upon scale-up, the deprotection of the Boc-API for the preparation of the Ipatasertib mono-HCl salt was easily completed in toluene in 12 N HCl.

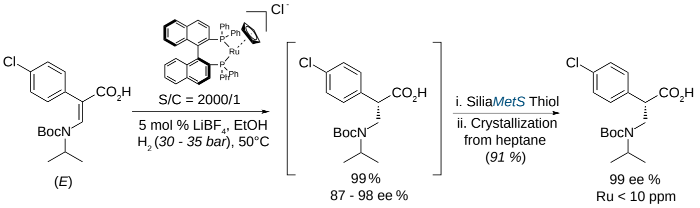
The aqueous layer was then basified to pH ≥ 12 with aqueous NaOH in order to extract the Ipatasertib free-base with DCM. The DCM solution was subsequently treated with charcoal and Silia*MetS* Thiol to remove colored impurities and trace heavy metals resulting from previous synthetic steps.

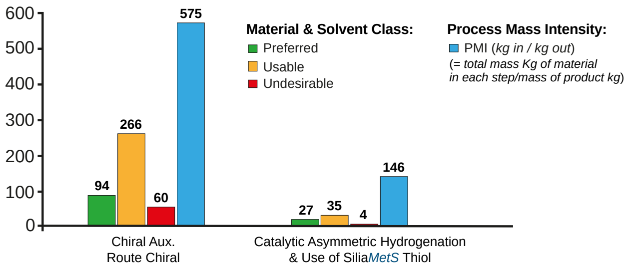
These metals consisted in Palladium (*Pd/C catalyst in a Noyori Asymetric Transfer Hydrogenation of ketone*), Ruthenium [(R,R) MsDPEN-Ru(p-cymene)Cl) catalyst for asymmetric ketone reduction] and Titanium (*$TiCl_4$ catalyst in asymmetric Aldol addition*).



In Akt inhibitor synthesis, Genentech describes a scalable catalytic asymmetric hydrogenation process for the multi-kilogram scale production of a β2-amino acid, the last building block. An extensive catalysis screening and optimization study was done and identified a simple Ru-BINAP catalyst system to directly afford the S product in high enantiomeric excess and yield was reported.

The final process enabled the multi-kilogram production in > 99 % ee to be used as a key component for one of their clinical candidates.




Process Mass Intensity & Kg Solvents Input / Kg of β2-amino acid

Conclusion

For 138 kg of the crude amino acid, 8.3 kg of Silia*MetS* Thiol were necessary. Filtration of the DCM solution over Celite® resulted in a 99 % yield of Ipatasertib free-base with a ruthenium content of less than 5 ppm (*ICP-OES*).

J. Lane, T. Remarchuk *et al.*, *Org. Proc. Res. Dev.*, **2014**, *18*, 1641-1651
Small Molecule Process Chemistry, Genentech, Inc., a member of the Roche Group, California, United States
Array BioPharma Inc., Colorado, United States

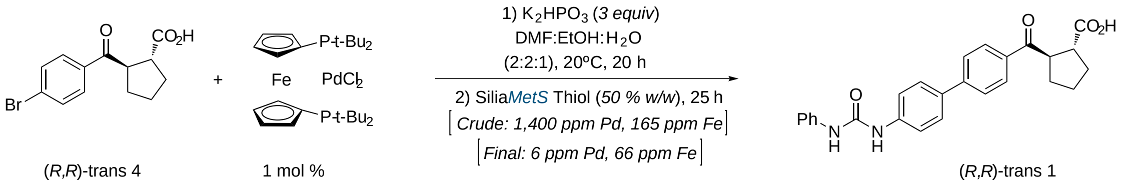
T. Remarchuk *et al.*, *Org. Proc. Res. Dev.*, **2014**, *18*, 1652-1666
Small Molecule Process Chemistry, Genentech, Inc., a member of the Roche Group, California, United States
Array BioPharma Inc., Colorado, United States

T. Remarchuk *et al.*, *Org. Proc. Res. Dev.*, **2014**, 18, 135-141
Small Molecule Process Chemistry, Genentech Inc., A member of the Roche Group, California, United States
Catalysis and Chiral Technologies, Johnson Matthey, Cambridge United Kingdom
WuXi AppTec Co., Ltd., Shanghai, China

Removal of Pd Fe

An Abbott Laboratories case study: palladium and iron removal using Silia*MetS* Thiol

Abbott Laboratories published a paper on removal of palladium and iron impurities using Silia*MetS* Thiol (*50 % w/w*). Thus, palladium and iron levels were 6 ppm and 66 ppm respectively. Although this final iron concentration was sufficient for the herein study, a much lower residual iron concentration can ben achieved by optimizing the purification experimental conditions.



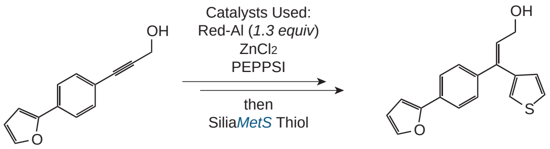
(*R*,*R*)-trans 4 1 mol % (*R*,*R*)-trans 1

M. M. Ravn *et al.*, *P., Org. Proc. Res. Dev.*, **2010**, *14*, 417-424
Global Pharmaceutical R&D, Process Research & Development and Discovery, Abbott Laboratories, Chicago, Illinois, United States

Removal of Al Cu Pd

A Johnson & Johnson case study: Sonogashira reaction & metal scavenging of various metals

Johnson & Johnson, in collaboration with Solvias, published a paper in which a mild Sonogashira reaction was developed using various metal catalysts. Treatment with Silia*MetS* Thiol simultaneously removed Pd, Cu & Al. Residual concentrations were below 50, 10 and 3 ppm respectively, in the isolated product 3.



[Final: < 50 ppm Pd, 10 ppm Cu & 3 ppm Al]

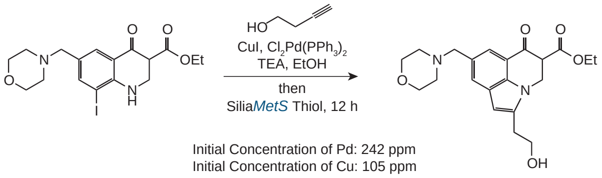
Note: copper comes from a previous synthesis step.

I. N. Houpis *et al.*, *Org. Proc. Res. Dev.*, **2009**, *13*, 598-606
Johnson & Johnson PRD, API Development, Belgium, and Solvias A.G., Synthesis and Catalysis, Switzerland

Removal of Cu Pd

A Pfizer Global R&D case study: palladium and copper removal on a large scale batch using Silia*MetS* Thiol

Pfizer published a paper on removal of palladium & copper impurities from a 20 kg pilot-plant batch. They made two subsequent treatments using Silia*MetS* Thiol (*20 % + 7 % w/w*) at room temperature for 12 hours. After scavenging with Silia*MetS* Thiol, the desired product was obtained with a yield of 76 %, containing only 17 ppm Pd and 1 ppm Cu.



Initial Concentration of Pd: 242 ppm
Initial Concentration of Cu: 105 ppm

An alternative method was also tried using 80 % w/w of Deloxan THP (*Degussa AG*) overnight followed by basification with Na_2CO_3. Residual metal concentration with this method was higher compared to that of Silia*MetS* and the yield was lower.

Screening Validation Results on Top 4 Scavengers

Scavengers	Residual Metal Concentration (*ppm*)		Yield (%)
	Pd	Cu	
Degussa Deloxan THP	20	2	60 - 70
SiliCycle SIlia*MetS* Thiol	**17**	**1**	**76**

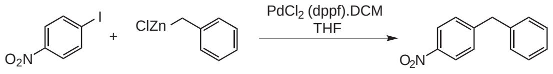
Silia*MetS* allows lower residual metal concentration & higher yield with fewer manipulations!

R. L. Dorow *et al.*, *Org. Proc. Res. Dev.*, **2006**, *10*, 493-499
Pfizer Global Research and Development, Michigan, United States

Removal of Pd Fe Zn

Multiple metal scavenging

Silia*MetS* can be used to remove multiple metals in the same reaction with excellent efficiency.



The Negishi coupling presented in scheme above was performed to show that Silia*MetS* can be used to simultaneously remove residual palladium, iron and zinc present after the reaction.

Multiple Removal Scavenging Results (*in %*)

Silia*MetS*	Pd	Fe	Zn
Silia*MetS* Cysteine	95	> 99	98
Silia*MetS* DMT	83	93	99
Silia*MetS* Imidazole	84	91	97
Silia*MetS* TAAcONa	97	> 99	> 99
Initial Concentration (*in THF*)	188 ppm	110 ppm	6 ppm

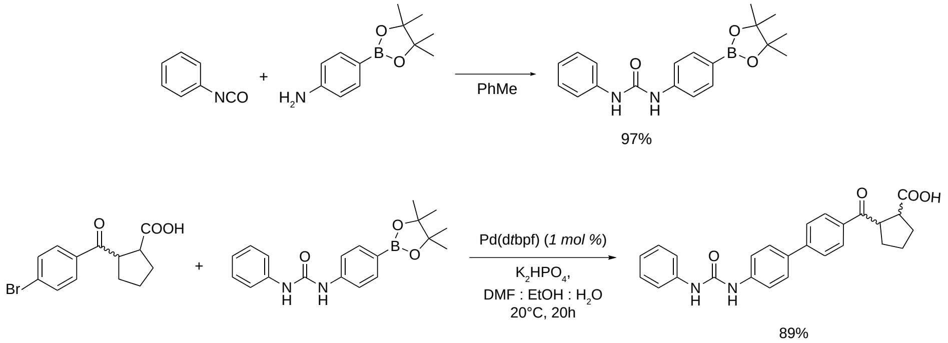
Conditions: 4 equiv of Silia*MetS* (*relative to palladium*), 4 h, 22°C.

For Zinc removal, all tested scavengers gave excellent results. Overall, for multiple removal scavenging results, Silia*MetS* Cysteine and TAAcONa showed to be the most versatile scavengers.

Scavenging of Pd(d*t*bpf) in Suzuki coupling for the synthesis of a DGAT-1 inhibitor

Diacyl glycerolacyltransferase-1 (*DGAT-1*) is one of two known isoforms that catalyse the final step of triglyceride biosynthesis and hence could play a role in the development of obesity and insulin resistance.
In a DGAT-1 inhibitor synthesis project, a kilogram-scale Suzuki-Miyaura reaction was described by Abbott researchers in 2010.

This synthesis was reproduced in SiliCycle's labs and the resulting contaminated mixtures were treated with our most promising scavengers.



Effect of Time in the Scavenging Efficiency with 4 equiv. at 22°C (*in %*)

Scavengers / Conditions	1 h		4 h		16 h	
	Pd	Fe	Pd	Fe	Pd	Fe
Silia*MetS* Thiol	53	19	72	31	**90**	67
Silia*Bond* Tosic Acid	11	54	24	**92**	22	**95**

Effect of Time in the Scavenging Efficiency with 8 equiv. at 22°C (*in %*)

Scavengers / Conditions	1 h		4 h		16 h	
	Pd	Fe	Pd	Fe	Pd	Fe
Silia*MetS* Thiol	69	12	**86**	37	**96**	69
Silia*Bond* Tosic Acid	24	**91**	33	**91**	17	**92**

Effect of Time in the Scavenging Efficiency with 4 equiv. at 45°C (*in %*)
Treatment with 2 Scavengers Simultaneously: Silia*MetS* Thiol & Silia*Bond* Tosic Acid

Scavengers / Conditions	1 h		4 h		16 h	
	Pd	Fe	Pd	Fe	Pd	Fe
Silia*MetS* Thiol & Silia*Bond* Tosic Acid	78	81	91	81	**96**	81

Conclusion

In this case again, it was Silia*MetS* Thiol that proved to be the preferred scavenger for palladium under any conditions.
As for iron, Silia*Bond* Tosic Acid was, again and by far, the most effective.

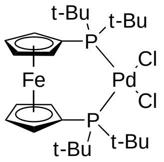
Scavenger combinations can achieve, in some cases, even higher removal of both metals.
The best conditions were using 4 or 8 equiv at 22°C for 16h.

M. Ravn *et al.*, *Org. Proc. Res. Dev.*, **2010**, *14*, 417-424
D. Barnes *et al.*, *Org. Proc. Res. Dev.*, **2009**, *13*, 225-229
Abbott Laboratories, North Chicago, Illinois, United States

Scavenging of Pd-118 using Silia*MetS* metal scavengers

Some of Silia*MetS* Metal Scavengers have a particularly powerful scavenging behavior toward reagent Pd-118.

Pd-118, or Pd(d*t*bpf)Cl_2 is a strong, homogeneous catalyst that has been shown to be very stable and active for all coupling reactions, especially aminations, reductive carbonylations and Suzuki couplings. Nevertheless, metals from this active catalyst can act as severe contaminants and be tricky to get rid of.



Pd-118 Complex

Behavior of Silia*MetS* Metal Scavengers Toward this Specific Complex (*catalyst only in solvent*)

Scavenging Efficiency of Preliminary Screening (*in %*)

Scavengers	DMF, 22°C		DMF, 60°C		Methyl-THF, 22°C		Methyl-THF, 60°C		DCM, 22°C	
	Pd	Fe	Pd	Fe	Pd	Fe	Pd	Fe	Pd	Fe
Silia*MetS* DMT	76	45	**97**	51	85	63	**97**	47	**96**	83
Silia*MetS* Thiol	51	28	72	34	50	50	88	64	36	48
Silia*MetS* Cysteine	59	49	67	49	70	60	**93**	52	53	50
Silia*Bond* Tosic Acid	25	47	8	54	70	69	85	**83**	80	**78**

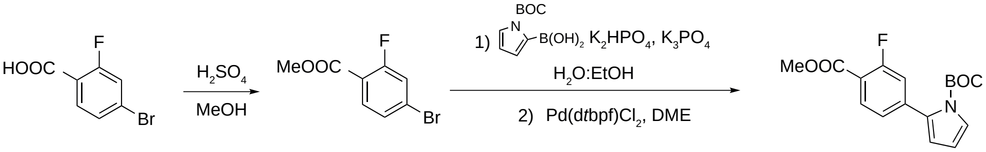
Conditions: Palladium complex solutions were made in DMF, methyl-THF and dichloromethane, and shaken with 4 equiv. of metal scavengers for 4 hours, at room temperature or 60°C.

Scavenging Conclusion

Silia*MetS* DMT and Cysteine proved to be the preferred scavengers for Palladium (*Pd*) in this application.
As for Iron (*Fe*), Silia*Bond* Tosic Acid (*SCX*) was the best scavenger.
Furthermore, very good removal of both metals could be achieved through a combination of both scavengers.

Scavenging of Pd(d*t*bpf)Cl_2 in Suzuki coupling for the preparation of arylpyrrolidines

Abbott Laboratories has used Pd(d*t*bpf)Cl_2 for the preparation of arylpyrrolidines resulting in a final mixture contaminated with Pd and Fe.



SiliCycle has used this latter synthesis as a control reaction to study the effect of our Metal Scavengers on such contamination. The final crude mixtures were treated with the most promising metal scavengers and further optimization was carried out.

Overview of Metal Residues Scavenging Efficiency (*in %*) in Various Experimental Conditions of a Suzuki Coupling for the Preparation of Arylpyrrolidines

Effect of Time in the Scavenging Efficiency with 4 equiv at 22°C (*in %*)

Scavengers / Conditions	1 h		4 h		16 h	
	Pd	Fe	Pd	Fe	Pd	Fe
Silia*MetS* DMT	78	44	89	51	**98**	35
Silia*Bond* Tosic Acid	34	65	34	70	36	86

Effect of Time in the Scavenging Efficiency with 8 equiv at 22°C (*in %*)

Scavengers / Conditions	1 h		4 h		16 h	
	Pd	Fe	Pd	Fe	Pd	Fe
Silia*MetS* DMT	**90**	53	94	56	**96**	47
Silia*Bond* Tosic Acid	31	85	32	89	33	**91**

Effect of Time in the Scavenging Efficiency with 4 equiv at 45°C (*in %*)

Scavengers / Conditions	1 h		4 h		16 h	
	Pd	Fe	Pd	Fe	Pd	Fe
Silia*MetS* DMT	81	57	**90**	58	**95**	34
Silia*Bond* Tosic Acid	27	81	28	85	29	89

Scavenging Conclusion

Clearly, Silia*MetS* DMT proves to be the preferred scavenger for palladium. As for iron, Silia*Bond* Tosic Acid was by far the best reagent. A combination of scavengers can achieve, in some cases, stronger removal of both metals.
The best results were obtained using 8 equiv of each scavenger at 22°C for 16 h.

M. Ravn *et al.*, *Org. Proc. Res. Dev.*, **2010**, *14*, 417-424
D. Barnes *et al.*, *Org. Proc. Res. Dev.*, **2009**, *13*, 225-229
Abbott Laboratories, North Chicago, Illinois, United States

Silia*MetS* in aqueous conditions

Along with growing importance of sustainable chemistry and catalysis, Silia*MetS* compatibility in aqueous conditions needed to be evaluated. As a preliminary exploration, palladium nitrate scavenging was tested at four different pH in various acidic medias. In purely aqueous conditions, Silia*MetS* TAAcOH was the most compatible and efficient scavenger. However, in acidic conditions, apart from Silia*Bond* Tosic Acid, all scavengers showed good to excellent removal capability.
Scavenging activity can either be driven by H_3O+ concentration (*pH*), or its counter-ion.

Scavenging (*in %*) of $Pd(NO_3)_2$ in Various Aqueous Conditions, 4 equiv at 22°C, 4 h

Scavengers	H_2SO_4 (*1 M*)	HNO_3 (*1 M*)	AcOH (*1 M*)	H_2O
Silia*MetS* Diamine	43	23	**> 99**	5
Silia*MetS* DMT	**> 99**	**> 99**	**> 99**	15
Silia*MetS* Imidazole	**> 99**	**> 99**	**> 99**	36
Silia*MetS* TAAcOH	**98**	**98**	**98**	**98**
Silia*MetS* Thiol	**> 99**	**> 99**	**> 99**	77
Silia*MetS* Thiourea	**> 99**	**> 99**	**> 99**	35
Silia*Bond* Tosic Acid	19	6	76	28
Silia*MetS* Triamine	55	49	**96**	10

Results illustrate well that the counter-anion (*and counter-cation*) plays a determinant role in the affinity of the resin toward palladium.

Experimental Conditions: an aqueous 250 ppm solution of $Pd(NO_3)_3$ was prepared in a volumetric flask. 8 mL of this solution was introduced in 10 mL polypropylene tube charged with four molar equivalents of a metal scavenger. All scavengers were treated identically. The tubes were shaken on the SiliCycle MiniBlock® orbital shaker for four hours. All solutions were filtered on separate tubes, and the remaining palladium was measured.

Other complexes were tested using the same method described as above for scavenging of $Pd(NO_3)_3$.

Various Metallic Complexes Scavenging (*in %*) & Concentrations in Aqueous Conditions, 4 Equiv at 22°C, 4 h

Scavenger	$RuCl_3$ [*150 ppm*]	K_3PtCl_6 [*250 ppm*]	$FeCl_3$ [*250 ppm*]	$RhCl_3$ [*250 ppm*]	$Pd(NO_3)_2$ [*250 ppm*]
Silia*MetS* Diamine	11	71	25	94	5
Silia*MetS* DMT	0	**97**	6	68	15
Silia*MetS* Imidazole	0	91	6	59	36
Silia*MetS* TAAcOH	63	0	**> 99**	5	**98**
Silia*MetS* TAAcONa	47	87	**98**	7	77
Silia*MetS* Thiol	0	57	7	0	35
Silia*MetS* Thiourea	0	92	9	34	28
Silia*Bond* Tosic Acid	52	87	**> 99**	**98**	**99**
Silia*MetS* Triamine	14	61	13	92	10

Various Metallic Complexes Scavenging (*in %*) & Concentrations in Aqueous Conditions, 4 Equiv at 22°C, 4 h

Scavenger	$AgNO_3$ [*250 ppm*]	$Ni(NO_3)_2$ [*250 ppm*]	$Sn(OTf)_2$ [*250 ppm*]	$CuSO_4$ [*250 ppm*]	$ZnSO_4$ [*250 ppm*]
Silia*MetS* Diamine	74	43	47	93	58
Silia*MetS* DMT	**> 99**	40	60	86	51
Silia*MetS* Imidazole	90	25	39	64	39
Silia*MetS* TAAcOH	**> 99**	84	93	**99**	86
Silia*MetS* TAAcONa	**97**	**96**	73	94	**95**
Silia*MetS* Thiol	**96**	6	6	0	0
Silia*MetS* Thiourea	79	1	17	14	3
Silia*Bond* Tosic Acid	86	90	**95**	88	81
Silia*MetS* Triamine	76	33	58	44	58

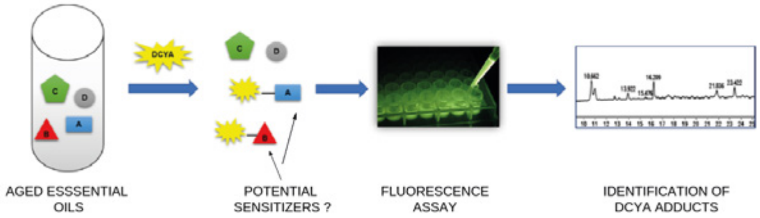
Conclusion

Silia*MetS* TAAcONa has shown to have very good scavenging efficiency in aqueous media. Silia*MetS* TAAcOH and Silia*Bond* Tosic Acid were also efficient. Generally speaking, many metal scavengers have demonstrated excellent performance in aqueous environment, even when bearing hydrophobic moieties.

Silia*Bond* trapping agent in the evaluation of tea tree essential oils as skin sensitizers

Authentic Tea Tree Oils (*especially aged ones*) have been identified as potential skin sensitizers. Thiols were used a trapping agents (*DCYA*) for isolation, characterization and identification of several possible DCYA-adducts, which can be used to deduce the structure of the candidate reactive species.

Silia*Bond* Maleimide was used to quench excess of thiols. Both Silia*Bond* Maleimide and Tosyl Chloride were tested, but Silia*Bond* Maleimide was found to be more selective in their experimental procedures.



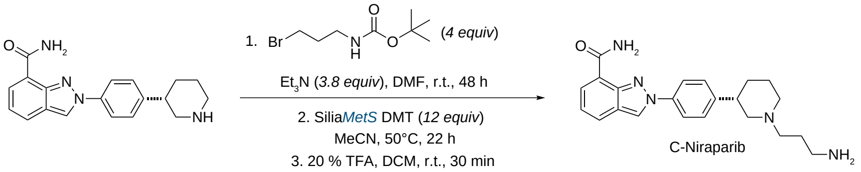
Further studies on detection and identification of potential ingredients of concern for skin sensitization were later conducted using Silia*Bond* Maleimide as a thio-scavenger in HTS-DCYA assays.

I. Khan, I. *et al. Chem. Res. Toxicol.*, **2016**, *29*, 1108-1117
II. Khan, I. *et al. Chem. Res. Toxicol.*, **2016**, *29*, 1488-1492
III. Khan, I. *et al. Toxicol. in Vitro*, **2018**, *46*, 237-245
University of Mississippi, Mississippi, United States

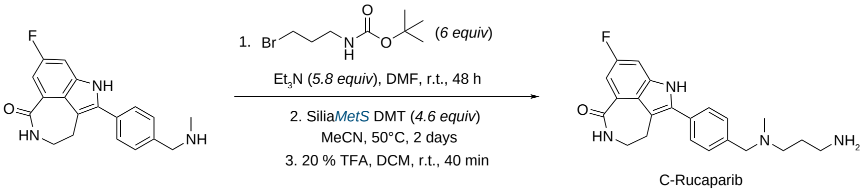
Proteome-wide profiling of clinical PARP inhibitors to reveal compound-specific secondary targets

Poly(ADP-ribose) polymerase (*PARP*) inhibitors (*PARPi*) are a promising class of targeted cancer drugs, but their individual target profiles beyond the PARP family, which could result in differential clinical use or toxicity, are unknown.

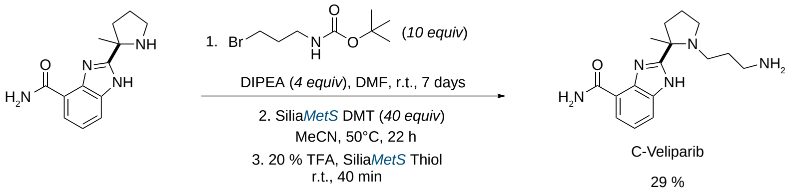
Using an unbiased, mass spectrometry-based chemical proteomics approach, a comparative proteome wide target map of four clinical PARPi was generated. Silia*MetS* DMT and Thiol were useful as organic scavengers for three out of the four PARPi: Niraparib (*scheme 1*), Rucaparib (*scheme 2*) and Veliparib (*scheme 3*).



Scheme 1



Scheme 2



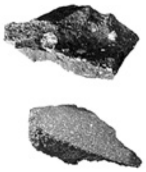
Scheme 3

Rix, U. *et al. Cell. Chem. Biol.*, **2016**, *23*, 1490-1503
H. Lee Moffitt Cancer Center & Research Institute, Tampa, United States
University of California, Los Angeles, United States
University of South Florida, Tampa, United States

Aliphatic amines in Antarctic CR2, CM2, and CM1/2 carbonaceous chondrites amines

Meteoritic water-soluble organic compounds provide a unique record of the processes that occurred during the formation of the solar system and the chemistry preceding the origins of life on Earth. Hence, molecular, isotopic, and enantiomeric compositions of amines in Antarctic carbonaceous chondrites were studied.

Silia*MetS* DMT & Silia*Bond* Amine were used to purify the organic compounds from carbonaceous chondrites.



1) Crushing of meteroites into fine powders; homogenization
2) Acid-aqueous extraction
3) Separation of supernatants by centrifugation
4) Re-dissolvation of residues in 0.1 M NaOH / DCM
5) Silia*Bond* Amine
6) Silia*MetS* DMT

Compositional and isotopic analyses
Processing and derivatization for amino acid analysis

Results provided information on the prebiotic synthesis of amines and amino acids and on the origins of homochirality on Earth.

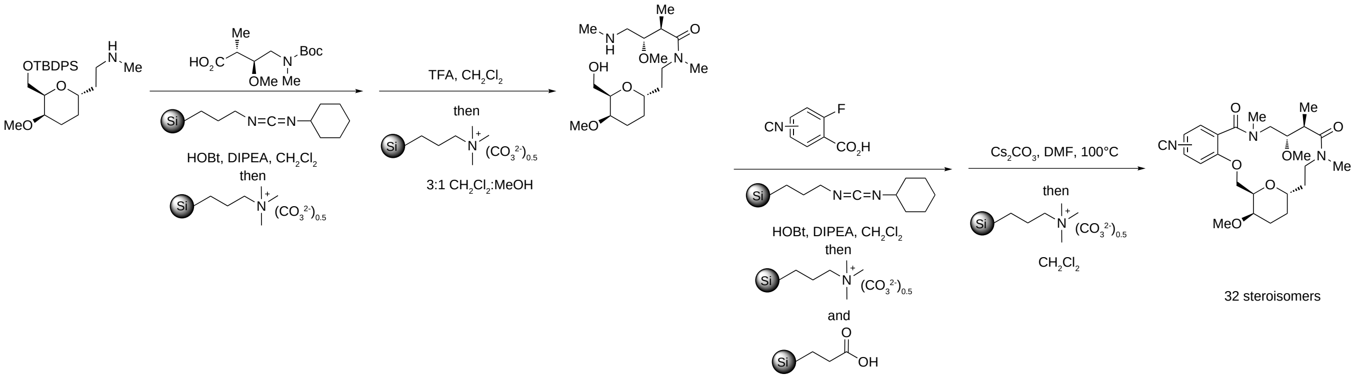
Aponte, J. C. *et al. Geochimica et Cosmochimica Acta*, **2016**, *189*, 296-311
Solar System Exploration Division, NASA Goddard Space Flight Center, Maryland, United States

A Broad Institute case study: ionic scavenging of acids with Silia*Bond* carbonate & scavenging of amines with Silia*Bond* carboxylic acid

In the context of the synthesis of a library of highly complex macrocycles with a pyran core, Silia*Bond* Carbonate (*Si-CO$_3$*) and Silia*Bond* Carboxylic Acid (*Si-WCX*) were used in the purification process.

In the reaction below, Silia*Bond* Carbonate was used to remove excess of the acidic acylating reagent, and used again in the next step to remove excess benzoic acid. Then, Silia*Bond* Carboxylic Acid was added to remove any excess N,N-Diisopropylethylamine or potential o-acylation by-products.

Purities of various macrocycles were between 70-92 %, with an average purity of 87 %.



32 steroisomers

General Procedures

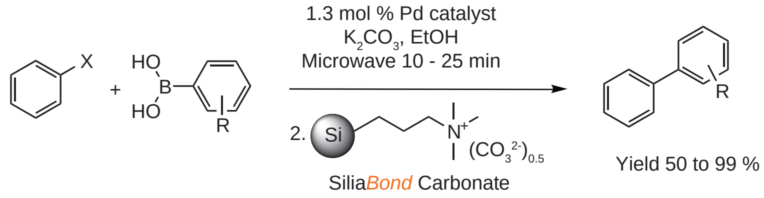
Acylation: The crude amino alcohols, cyano-fluorobenzoic acid 4-o or 4-p (*0.14 mmol; 1.0 equiv*), Silia*Bond* Carbodiimide (*Si-DCC*) (*0.19 mmol; 1.4 equiv*) and DIEA (*0.090 mmol; 0.7 equiv*) were combined in 2 % dimethylformamide (*DMF / DCM 3.0 mL*), and stirred at room temperature overnight. In cases where acylation is slow, additional Si-DCC (*0.19 mmol; 1.4 equiv*) and a solution of HOBt (*0.03 mmol; 0.2 equiv*) in DMF / DCM (*1.0 mL*) and DIEA base (*0.03 mmol; 0.2 equiv*) were added. After acylation was deemed complete, reactions were scavenged with Si-CO$_3$ (*0.18 mmol; 1.4 equiv*) and Si-WCX (*0.18 mmol; 1.4 equiv*) for 30 min and then filtered and evaporated for 4 h.

SNAr Macrocyclization: All crude products from above were dissolved in DMF (*4.0 mL*) and heated at 110°C with Cs$_2$CO$_3$ (*approximately 0.61 mmol; 4.5 equiv for 4 h*). Reaction mixtures were filtered through Celite, washed with DCM, and solvents evaporated. Crude products were dissolved in DCM and treated with Si-CO$_3$ (*0.18 mmol; 1.4 equiv*) and Si-WCX (*0.18 mmol; 1.4 equiv*) for 30 min, and then filtered through Celite and concentrated.

E. Comer *et al.*, *Proceedings of the National Academy of Sciences of the United States of America*, **2011**, *108*, 6751-6756
Chemical Biology Platform, Broad Institute, Cambridge, MA 02142

An Abbott case study: ionic scavenging of boronic acids with Silia*Bond* carbonate

An efficient Suzuki coupling protocol was developed and excess boronic acids were rapidly removed using solid-phase extraction and Silia*Bond* Carbonate to yield clean product.

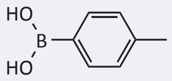
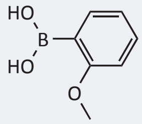
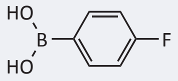
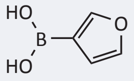


General Procedure

A Smith Process vial was charged with a stir bar, 4-bromobenzonitrile, p-tolylboronic acid and 2 mL of ethanol. A solution of 1 M K_2CO_3 was added followed by the Pd catalyst. The reaction vessel was sealed and heated to 110°C for 10 minutes under microwave irradiation.
After cooling, the reaction mixture was transferred to a pre-packed column of Silia*Bond* Carbonate which had been conditioned with MeOH / CH_2Cl_2 (*1:1*), and the eluent was collected via gravity filtration.
The column was then washed with MeOH / CH_2Cl_2 (*1:1*) (*3 × 3 mL*).

The eluents were combined, concentrated and purified by flash chromatography to yield a purified compound.

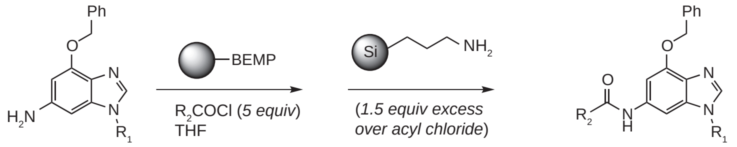
Scavenging Boronic Acids Results (*in %*)

# of Equiv				
10	**> 97**	**> 97**	**> 97**	**> 97**

Y. Wang, D. R. Sauer *et al.*, *Org. Lett.*, **2004**, *6*, 2793-2796
High-Throughput Organic Synthesis Group, Global Pharmaceutical R&D, Abbott Laboratories, Illinois, United States

A Roche case study: nucleophilic scavenging of acyl chlorides with Silia*Bond* Amine

The guanine synthesis started with the simple and direct acylation of O-benzyl-2-aminopurine with polymeric BEMP. This convenient acylation approach using polymeric base was attempted in order to avoid the laborious Mitsunobu reaction introducing N9 substituents and tedious aqueous work-up steps. Silia*Bond* Amine was used to sequester the excess acyl chloride instead of using polystyrene-based trisamine resins.



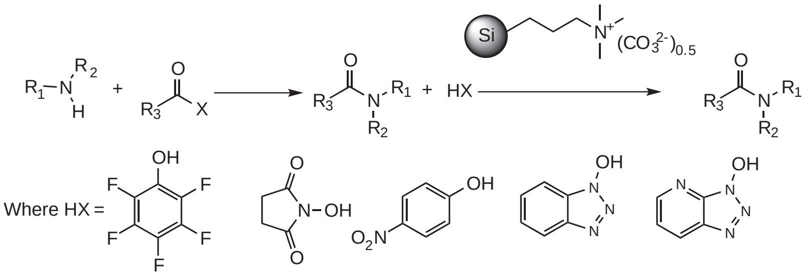
General Procedure

Silia*Bond* Amine (*1.5 equiv*) was added to the reaction mixture and stirred for 1 h at room temperature.
The Silia*Bond* Amine scavenger with bound acyl chloride was then filtered off and rinsed with solvent (*e.g.: MeOH*) to yield an acyl chloride-free solution.

K. Kim *et al.*, *Tett. Lett.*, **2000**, **41**, 3573-3576
Roche Research Center, Hoffmann La-Roche, Inc., Nutley, NJ, USA

Ionic scavenging of phenols and acids with Silia*Bond* carbonate

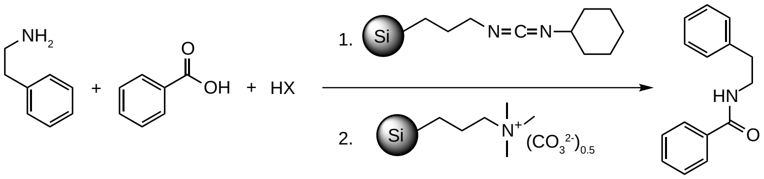
The efficiency of Silia*Bond* Carbonate as a scavenger of various coupling reagents (HX) - including pentafluorophenol, N-hydroxysuccinimide (*HOSu or NHS*), 4-nitrophenol, 1-hydroxybenzotriazole (*HOBt*) and 1-hydroxy-7-azabenzotriazole (*HOAt*) - was studied, as well as a comparison with two suppliers of polymer-supported carbonate.



Phenol Scavenging Results (*in %*)

HX	Silia*Bond* Carbonate		Polymer 1		Polymer 2	
	5 min	60 min	5 min	60 min	5 min	60 min
Pentafluorophenol[1]	**98**	**98**	92	**95**	85	94
N-Hydroxysuccinimide	93	**> 95**	41	64	40	42
4-Nitrophenol	94	**96**	89	**95**	77	88
1-Hydroxybenzotriazole[2]	88	**96**	68	92	26	**96**
1-Hydroxy-7-azabenzotriazole[2]	**97**	**97**	72	**96**	30	92

Initial concentration: 5,000 ppm - 3 equiv of Silia*Bond* Carbonate. Analyzed by UV. 1 Analyzed by GC-MS, 2 in THF.



Benzoic Acid Scavenging Results (*in %*)

HX	Yield	Purity
No Catalyst	35	**95**
N-Hydroxysuccinimide[1]	67	**98**
1-Hydroxybenzotriazole[2]	**99**	**98**
1-Hydroxy-7-azabenzotriazole[2]	**100**	**99**

Note: 1.0 equiv of amine, 1.5 equiv acid, 1.7 equiv catalyst (HX), 2.0 equiv Silia*Bond* Carbodiimide, 7.0 equiv Silia*Bond* Carbonate.
Yield refers to the mass of isolated product. Purity was determined by GC-FID. 1 in DCM, 2 in THF.

Conclusion

For each of the various experimental conditions / coupling reagents that were tested, Silia*Bond* Carbonate yielded better to much better scavenging results than its polymer-bound Carbonate equivalents.

Silia*Bond* Carbonate was also very useful in the scavenging of benzoic acid, in the following amide coupling, using Silia*Bond* DCC as a coupling reagent.

Nucleophilic scavenging of boronic acids with Silia*Bond* Diol, Silia*Bond* Carbonate and Silia*MetS* DEAM

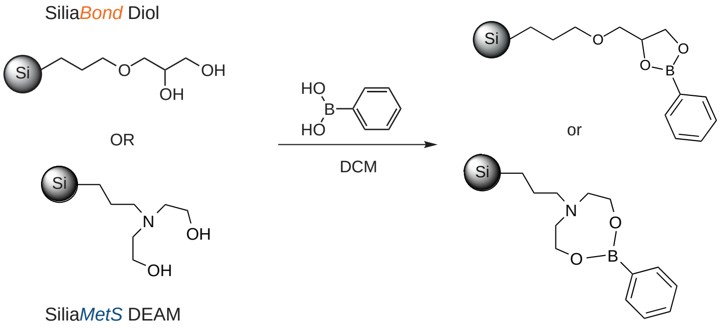
Boronic acids and their derivatives are one of the most widespread intermediates and reagents in organic and medicinal synthesis. On-the-market drugs have even been adding boron atoms to enhance compatibility, selectivity and potency to their target molecules.

Up to very recently, boronic acids had always been reported as lacking apparent toxicity, mutagenic activity or in vivo instability issues. New studies have raised objections about this safe toxicological profile, both based on experimental and clinical data.

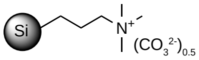
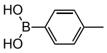
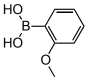
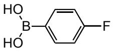
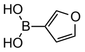
This is major in the chemical and pharmaceutical industry, as more and more studies denounce the genotoxicity of boronic acids. Today, in view of new data concerning boronic acids, there is pressure building on the ICH steering committee to assess boron compounds as potential genotoxic impurities (*PGIs*) per ICH M7.

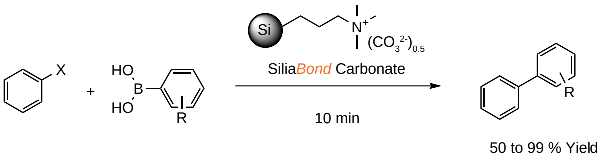
Scavenging Boronic Acids Results

Scavengers	# Equiv	Time	Efficiency (%)
Silia*MetS* DEAM	4	1 h	> 99
Silia*Bond* Diol	4	1 h	> 99



Scavenging Boronic Acids Results

Scavenger	# Equiv	Boronic Acid	Time	Efficiency (%)
 Silia*Bond* Carbonate	10		10 min	> 99
	10			> 99
	10			> 99
	10			> 99



All % of scavenging are determined by GC-MS

Depending on ones' needs, all three scavengers gave excellent scavenging results and showed to be an efficient and fast method for the removal of boronic acids.

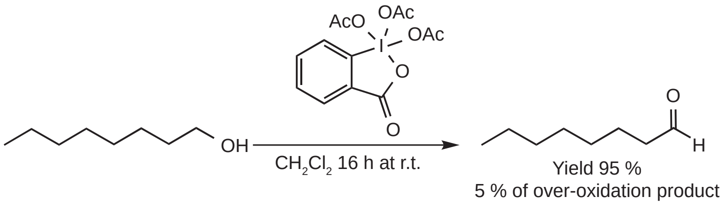
Silia*MetS* DEAM and Silia*Bond* Diol are both excellent scavengers for Catch & Release: i.e., when the molecule of interest is temporarily bound either ionically or covalently to a functionnalized silica and subsequently released, once all undesirable impurities were washed out.

Scavenging in two different formats: bulk vs SPE

Ionic scavenging of 2-iodobenzoic acid with Silia*Bond* TMA Acetate and Silia*Bond* Carbonate

Dess-Martin Periodinane (*DMP*) is a mild and chemoselective oxidant. It is readily accessible, environmentally benign and has a good shelf-life. Furthermore, the ease of handling, simple reaction work-up, product purification and good yields obtained with DMP make it a valuable reagent in organic synthesis.

2-Iodobenzoic acid is the degradation product from DMP formed during the work-up. Most of it can be removed with a basic work-up, but sometimes, it can be difficult to get rid of all this side product.



General Procedure

A solution of 1-octanol (*1.00 mmol; 1.0 equiv*) in CH_2Cl_2 (*6 mL*) at room temperature, was added to DMP (*1.10 mmol; 1.1 equiv*). The reaction mixture was stirred for 16 h, then diluted with 35 mL of MTBE and poured in 20 mL of an aqueous solution of $Na_2S_2O_3$ (*25 %*). The mixture was stirred for 10 min. Another portion of 35 mL of MTBE was added for the liquid-liquid extraction.

The MTBE phase was then washed with water and a saturated aqueous solution of NaCl (*10 mL*) and dried on $MgSO_4$.

Scavenging was done using Silia*Bond* TMA Acetate or Carbonate, both in bulk (*1 g*) and SPE cartridge (*6 mL / 1 g*) for comparison purposes. Each sample was washed or eluted with a fresh portion of MTBE (*8 mL*) and then the 2-iodobenzoic acid concentration was monitored by GC-MS against an internal standard. The over-oxidation product (*carboxylic acid*) was succesfully scavenged using all products and formats.

Scavenging of 2-Iodobenzoic Acid Results (*in %*)

Scavenger	Bulk	SPE
Silia*Bond* TMA Acetate	100	100
Silia*Bond* Carbonate	100	100

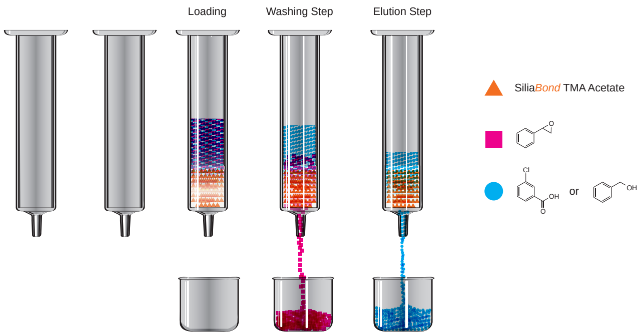
Carboxylic acids purification with Silia*Bond* TMA Acetate

Silia*Bond* TMA Acetate is an ion exchange media useful to extract organic anions from organic or inorganic matrices. It is less selective than Silia*Bond* TMA Chloride. The acetate anion being more labile than the chloride, it therefore retains more easily acidic compounds with pK_a in the range of 4 - 5, such as carboxylic acids.

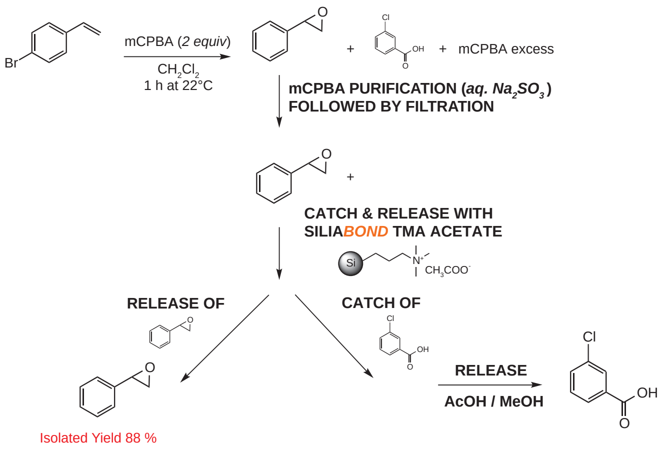
12 mL cartridges were filled with 2 or 4 g of Silia*Bond* TMA Acetate (*loading of 1 mmol/g, for an equivalent of about 4 mmol of active function*). They were tested with quantities of 1 and 2 mmol of each selected acid.

General Procedure for Catch & Release Purification

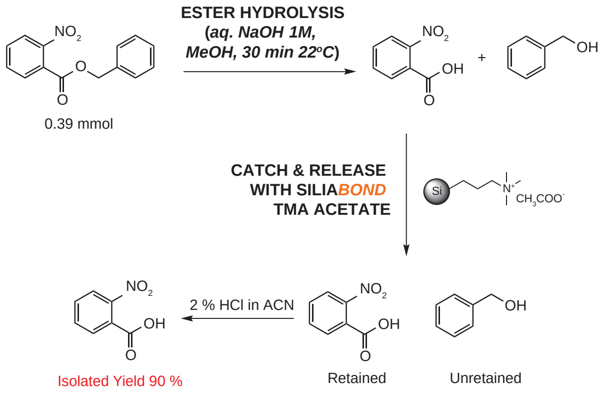
1. 12 mL cartridges (*2 or 4 g of SiliaBond TMA Acetate*) were conditionned with 6 mL of MeOH.
2. Compound was dissolved in 1 - 2 mL of MeOH and loaded onto the cartridge.
3. Column was washed with 15 mL of MeOH.
4. Compound was released with a solution of AcOH / MeOH : 2/98.
5. Solvents were evaporated and final compound weighted.



3-Chlorobenzoic Acid Purification Via Catch & Release



Ester Hydrolysis Purification Via Catch & Release



Conclusion

Epoxidation reactions with 3-chloroperbenzoic acid (*mCPBA*) often yield after treatment of the reaction a certain undesirable amount of 3-chlorobenzoic acid, which can sometimes be difficult to separate from the desired product.

In the present example, 4-bromostyrene was treated with mCPBA, and the reaction medium is then treated with an aqueous solution of sodium sulfite. The latter allows to destroy excess reagent and eliminates much of the 3-chlorobenzoic acid correspondent. After extraction with dichloromethane and evaporation, the product was loaded on a 12 mL TMA Acetate SPE cartridge of 2 or 4 g. A simple elution with methanol made it possible to isolate 88 % of the desired epoxide product. Similarly, the same strategy was applied for the purification of 2-nitrobenzoic acid after hydrolysis of benzyl-2-nitrobenzoate, to yield the former molecule in a 90 % final yield.

In conclusion, Silia*Bond* TMA Acetate is very useful for the purification of carboxylic acids. Conversely, it may free the reaction media from compounds having a pKa lower than 5.

Share your complete application with SiliCycle...

... and get a 5 g scavenger for free!

Send us:

- **The detailed method**
- **Pre- and Post-treatments**
- **Recoveries**
- **HPLC or GC analysis**

Contact us: **scavengers@silicycle.com**

Ordering Information

Batch Reactor Mode (*Bulk*)

All Scavengers are available in the following sizes: 5 g, 10 g, 25 g, 50 g, 100 g, 250 g, 500 g, 1 kg, 5 kg, 10 kg, 25 kg, etc.
Up to multi-ton scale!

Silia*MetS* Metal Scavengers

Scavenger Name	Scavenger PN
Silia*MetS* AMPA	R85130B
Silia*Bond* Amine (*WAX*)	R52030B
Silia*MetS* Cysteine	R80530B
Silia*MetS* DEAM	R54430B
Silia*MetS* DOTA	R91030B
Silia*MetS* DMT	R79030B
Silia*MetS* Diamine	R49030B
Silia*MetS* Imidazole	R79230B
Silia*MetS* TAAcOH *nec*	R69030B
Silia*MetS* TAAcONa *nec*	R69230B
Silia*MetS* Thiol	R51030B
Silia*MetS* Thiourea	R69530B
Silia*Bond* Tosic Acid (*SCX*)	R60530B
Silia*MetS* Triamine	R48030B

All Particle Size and Pore Size are respectively 40 - 63 µm and 60 Å.
Other matrices are available upon request.

Silia*Bond* Organic Scavengers

Scavenger Name	Scavenger PN
Silia*Bond* Amine (*WAX*)	R52030B
Silia*Bond* Carbonate	R66030B
Silia*Bond* Carboxylic Acid (*WCX*)	R70030B
Silia*MetS* DEAM	R54430B
Silia*Bond* DMAP	R75630B
Silia*MetS* Diamine	R49030B
Silia*Bond* Diol	R35030B
Silia*Bond* Guanidine	R68230B
Silia*Bond* Carbamate	R50130B
Silia*Bond* Maleimide	R71030B
Silia*Bond* Piperazine	R60030B
Silia*Bond* Propylsulfonic Acid (*SCX-2*)	R51230B
Silia*Bond* TMA Acetate *nec*	R66430B
Silia*Bond* Tosic Acid (*SCX*)	R60530B
Silia*Bond* Tosyl Chloride	R44030B
Silia*MetS* Triamine	R48030B

Available Kits

Because all matrices are unique, and that small differences can influence scavenging efficiency, we recommend first trying one of our Scavenger Kit for screening purposes, especially if you are new to this technology. Steric hindrance of the catalyst, electronic effects, solubility in solvents, all are factors that can influence the removal of your impurity.

How to order: simply note the Product Number which starts with “K”, add a dash mark and your choice of format.
Example: **K**30730B-10G to obtain 10 g of each one of the scavengers listed in the kit.

Silia*MetS* Metal Scavenger Kits

Kit Name	Kit PN	Composition
Silia*MetS* Tin Metal Scavenger Kit	K34730B	Carbonate, Cysteine, DEAM, DMT, TAAcOH, TAAcONa, Thiourea & Thiol
Silia*MetS* Universal Metal Scavenger Kit	K30730B	Cysteine, DMT, Imidazole, TAAcOH, TAAcONa, Thiol, Thiourea & Triamine
Silia*MetS* Palladium Metal Scavenger Kit	K34630B	DMT, Diamine, Thiol, Thiourea, Imidazole & Triamine

Silia*Bond* Scavenger Kits

Kit Name	Kit PN	Composition
Silia*Bond* Electrophile Complete Scavenger Kit	K35230B	Amine, DEAM, Diol, DMAP, TMA Acetate, Triamine, Diamine & Piperazine
Silia*Bond* Nucleophile Complete Scavenger Kit	K32630B	Carbonate, Carbamate, Maleimide & Tosyl Chloride

These kits are available in 5 g, 10 g, 25 g, 50 g and 100 g formats.

Silia*MetS*® E-PAK® Cartridges

E-PAK Cartridges							
Type	**Laboratory Scale - 5 cm diameter**			**Pilot Scale - 16.5 cm diameter**		**Commercial Scale - 16.5 cm diameter**	
	1 cm	**10 cm**	**25 cm**	**12.5 cm**	**25 cm**	**50 cm**	**100 cm**
Silia*Flash* Irregular Silica Gel							
40 - 63 µm	LS-R10030B-51	LS-R10030B-510	LS-R10030B-525	PS-R10030B-1612	PS-R10030B-1625	CS-R10030B-1650	CS-R10030B-16100
Silia*MetS* Metal Scavengers							
Thiol	LS-R51030B-51	LS-R51030B-510	LS-R51030B-525	PS-R51030B-1612	PS-R51030B-1625	CS-R51030B-1650	CS-R51030B-16100
DMT	LS-R79030B-51	LS-R79030B-510	LS-R79030B-525	PS-R79030B-1612	PS-R79030B-1625	CS-R79030B-1650	CS-R79030B-16100
Amine	LS-R52030B-51	LS-R52030B-510	LS-R52030B-525	PS-R52030B-1612	PS-R52030B-1625	CS-R52030B-1650	CS-R52030B-16100
Diamine	LS-R49030B-51	LS-R49030B-510	LS-R49030B-525	PS-R49030B-1612	PS-R49030B-1625	CS-R49030B-1650	CS-R49030B-16100
Triamine	LS-R48030B-51	LS-R48030B-510	LS-R48030B-525	PS-R48030B-1612	PS-R48030B-1625	CS-R48030B-1650	CS-R48030B-16100
Imidazole	LS-R79230B-51	LS-R79230B-510	LS-R79230B-525	PS-R79230B-1612	PS-R79230B-1625	CS-R79230B-1650	CS-R79230B-16100
Activated Carbon							
C-941	LS-C941-51	LS-C941-510	LS-C941-525	PS-C941-1612	PS-C941-1625	CS-C941-1650	CS-C941-16100
C-944	LS-C944-51	LS-C944-510	LS-C944-525	PS-C944-1612	PS-C944-1625	CS-C944-1650	CS-C944-16100
C-947	LS-C947-51	LS-C947-510	LS-C947-525	PS-C947-1612	PS-C947-1625	CS-C947-1650	CS-C947-16100
C-948	LS-C948-51	LS-C948-510	LS-C948-525	PS-C948-1612	PS-C948-1625	CS-C948-1650	CS-C948-16100

E-PAK Housings

Lab Scale

Housing Kits for Laboratory Scale E-PAK

Housing Size	316L	Hastelloy
5 x 1 cm	LSHK-1-S	LSHK-1-H
5 x 10 cm	LSHK-10-S	LSHK-10-H
5 x 25 cm	LSHK-25-S	LSHK-25-H
5 x 1 cm + 5 x 10 cm	LSHK-110-S	LSHK-110-H
5 x 1 cm + 5 x 25 cm	LSHK-125-S	LSHK-125-H
5 x 1 cm + 5 x 10 cm + 5 x 25 cm	LSHK-11025-S	LSHK-11025-H

Bowls for Laboratory Scale E-PAK Housing

Bowl Length	316L	Hastelloy
1 cm	LS-BOWL1-S	LS-BOWL1-H
5 cm	LS-BOWL10-S	LS-BOWL10-H
25 cm	LS-BOWL25-S	LS-BOWL25-H

Pilot Scale

Housing for Pilot Scale Fixed-Bed E-PAK

Housing Size	316L	Hastelloy
16.5 x 12.5 cm	PSHSR-12-S	PSHSR-12-H
16.5 x 25 cm	PSHSR-25-S	PSHSR-25-H

Commercial Scale

Housing for Commercial Scale Fixed-Bed E-PAK

Housing Type	316L	Hastelloy
Single Round, 16.5 x 50 cm Single Round, 16.5 x 100 cm	CSHSR-50100-S	CSHSR-50100-H
3-Round, 16.5 x 50 100 cm 3-Round, 16.5 x 100 cm	CSH3R-50100-S	CSH3R-50100-H
7-Round, 16.5 x 50 & 100 cm	CSH7R-50100-S	CSH7R-50100-H
12-Round, 16.5 x 50 cm 12-Round, 16.5 x 100 cm	CSH12R-50100-S	CSH12R-50100-H

Fixed-Bed Mode Formats (*SPE or Flash Cartridges*)

Silia*Prep*™ SPE Cartridges and Silia*Sep*™ Flash Cartridges

To build your SPE Cartridge Product Number, simply start with the code **SPE**, followed by the **Product Number of the scavenger** you wish your cartridge to be packed with (*see page 76*), followed by the **Format code**.

Example: Silia*Prep* Thiourea, 6 mL, 500 mg = SPE-R69530B-06P

Silia*Prep* SPE Cartridges

Formats available	Code	Units / Box
3 mL / 200 mg	03G	50
3 mL / 500 mg	03P	50
6 mL / 500 mg	06P	50
6 mL / 1 g	06S	50
6 mL / 2 g	06U	50

Silia*Sep*™ Flash Cartridges

To build your Flash Cartridge Product Number, simply start with the code **FLH**, followed by the **Product Number of the scavenger** you wish your cartridge to be packed with (*see page 76*), followed by the **Format code**.

Examples:
- Silia*Sep* Open-Top TAAcONa, 70 mL, 10 g = FLH-R69230B-70Y
- Silia*Sep* TAAcONa, 4 g = FLH-R69230B-ISO04

Silia*Sep* Flash Cartridges

Formats available	Code	Units / Box
4 g	ISO04	2
12 g	ISO12	1
25 g	ISO25	1
40 g	ISO40	1
80 g	ISO80	1
120 g	IS120	1
220 g	IS220	1
330 g	IS330	1
800 g	IS750	1
1,600 g	I1500	1

Silia*Sep* ISO04 to IS330 formats

Silia*Sep* OT Cartridges

Formats available	Code	Units / Box
12 mL / 200 g	12U	20
25 mL / 5 g	20X	20
70 mL / 10 g	70Y	16
70 mL / 15 g	70i	16
70 mL / 20 g	70Z	16
150 mL / 25 g	95K	10
150 mL / 50 g	95M	10
150 mL / 70 g	95N	10
276 mL / 100 g	276F	12

Silia*Chrom*® Guard Cartridges

Silia*Chrom* Guard Cartridges are available in lengths of 10 - *20 mm* and three internal diameters *(ID: 4.0, 10 and 21.2 mm)*.
The Guard Cartridges internal diameter should be the same as the HPLC column or one size smaller.

Never use a guard cartridges with a larger ID than that of the HPLC column (*risk of efficiency loss*).

Silia*Chrom* Scavenger Guard Cartridges, 5 µm

Formats Available (*internal diameter x length in mm*)	PN	Qty	Guard Holder PN
4.0 x 10	HPLG-K34605E-A-N010	4/box	HPH-N010
4.0 x 20	HPLG-K34605E-A-N020	4/box	HPH-N020
10 x 10	HPLG-K34605E-A-Q010	2/box	HPH-Q010
21.2 x 10	HPLG-K34605E-A-T010	1/box	HPH-T010
30 x 10	HPLG-K34605E-A-V010	1/box	HPH-V010
30 x 20	HPLG-K34605E-A-V020	1/box	HPH-V020
30 x 30	HPLG-K34605E-A-V030	1/box	HPH-V030

Silia*Chrom* Scavenger Guard Cartridges, 10 µm

Formats Available (*internal diameter x length in mm*)	PN	Qty	Guard Holder PN
4.0 x 10	HPLG-K34607E-A-N010	4/box	HPH-N010
4.0 x 20	HPLG-K34607E-A-N020	4/box	HPH-N020
10 x 10	HPLG-K34607E-A-Q010	2/box	HPH-Q010
21.2 x 10	HPLG-K34607E-A-T010	1/box	HPH-T010
30 x 10	HPLG-K34607E-A-V010	1/box	HPH-V010
30 x 20	HPLG-K34607E-A-V020	1/box	HPH-V020
30 x 30	HPLG-K34607E-A-V030	1/box	HPH-V030

Contact us

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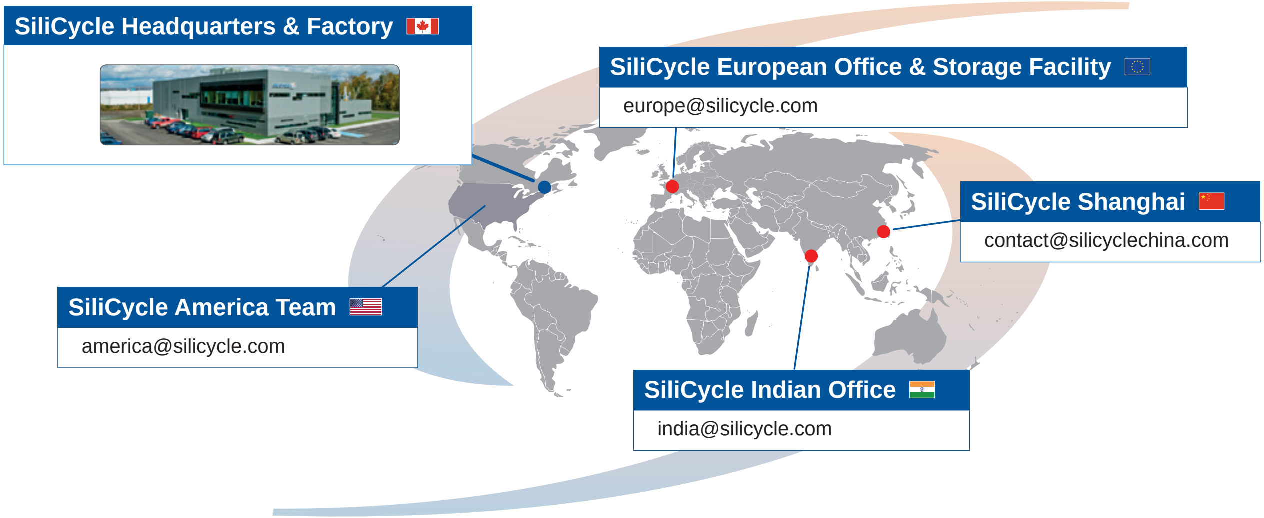

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SiliCycle Indian Office
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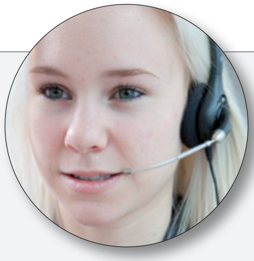


Technical Support

At SiliCycle, we are committed to providing the best technical support possible.

Our worldwide Technical Support Group is comprised of a team of highly qualified M. Sc., Ph. D. Chemists and Engineers, Technical Support Professionals and Service Coordinators who are prepared to troubleshoot, answer questions and provide solutions for your service and applications needs.

In order to better respond to your technical inquiries, feel free to contact us in three different ways:

E-mail: **support@silicycle.com**

Phone:
- International **+1 418.874.0054**
- USA and Canada **+1 877.745.4292** (*Toll Free*)

CERTIFIÉE ISO 9001:2015 CERTIFIED

High Value Silica-based and Specialty Products for Chromatography, Analytical and Organic Chemistry, and Purification

DISCOVER OUR BROCHURES

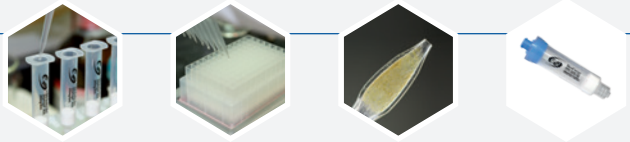
METAL & ORGANIC SCAVENGING

Silia*MetS*® – Metal Scavengers
Silia*Bond*® – Organic Scavengers
***E-PAK*®** – Fixed Bed Flow-Through Purification Cartridges

CHROMATOGRAPHY & PURIFICATION

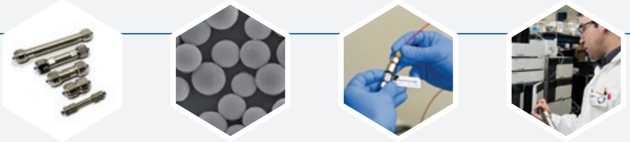
Silia*Flash*® – Irregular Silica Gels
Silia*Sphere*™ PC – Spherical Silica Gels
Silia*Bond*® – Chromatographic Phases
Silia*Sep*™ – Flash Cartridges
Silia*Plate*™ – TLC Plates

SAMPLE PREPARATION



Silia*Prep*™ – Silica-based SPE Cartridges & Well Plates
Silia*PrepX*™ – Polymeric SPE Cartridges & Well Plates
Silia*Prep*™ – Micro-SPE Tips
Silia*Fast*™ – FaPEx® Cartridges for Pesticide Residue Analysis

ANALYTICAL & PREPARATIVE CHROMATOGRAPHY



Silia*Sphere*™ – Spherical Silica Gels
Silia*Chrom*® – HPLC Columns

ORGANIC SYNTHESIS

Silia*Bond*® – Reagents & Oxidants

R&D SERVICES

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Custom Column Packing
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