





# SOLUTIONS FOR PEPTIDE SYNTHESIS

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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.

# **Solutions for Peptide Synthesis**

SiliCycle Solutions for Peptide Synthesis

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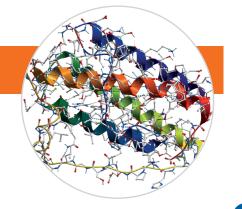
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# SiliCycle Solutions for Peptide Synthesis

- Solutions for peptide synthesis
- Solutions for work-up after peptide synthesis



SiliCycle offers solutions to problems encountered in the peptide research field, either for the peptide synthesis itself or for subsequent work-up.

## Peptide synthesis:

- Supported SiliaBond reagents can be used during peptide synthesis and other amide bond-forming reactions, and excess reagents elimination will be reduced to a simple filtration.
- Some SiliaBond reagents can also be used for Fmoc deprotection of peptides in liquid phase.

## Work-up after peptide synthesis:

- Silia Bond reagents can be used for amines scavenging (catch and release of weak cations), amine free basing, HOBt scavenging,
  TFA removal, or residual azide removal after a click reaction.
- Silia Prep SPE cartridges packed with C18 Widepore (WPD, 125 Å) can be used for trap-elute of relatively polar peptides after cleavage or cysteine oxidation.
- · SiliaMetS are useful to remove residual metal after a catalytic reaction.
- Silia Sep flash cartridges can be used for peptide purification.
- Silia Chrom HPLC columns are available in analytical and preparative dimensions (4.6 mm ID up to 50 mm ID), and in a variety of
  phases, to allow large scale peptide purification. In addition, spherical silica gels Silia Sphere are also offered in bulk to allow DAC
  packing, giving even more options.

# **Quality and Regulatory Documentation**

SiliCycle's products are more and more used in GMP pharmaceutical, biotechnology and fine chemical industries as well as contract research and manufacturing organizations. Many have run their own analysis proving that our products can safely be used without compromising the purity of their compounds.

SiliCycle is committed to high quality standards and all products are manufactured in an ISO 9001:2015 compliant facility and subjected to stringent quality control.

For any inquiries, please contact: <a href="mailto:support@silicycle.com">support@silicycle.com</a>

All products are shipped with the following information:

- Certificate of Analysis (COA)
- Safety Data Sheet (SDS)
- Technical Information

Other statements available upon request:

- BSE / TSE Declaration (non animal-derived)
- GMO-Free Certificate
- · Melamine-Free Certificate, etc.

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

# Manufacturing Capability

Functionalized silica gels are manufactured at our headquarters in Quebec City, where we can meet all customers production needs.

Our state of the art facilities include (but are not limited to):

- 1,000 L to 10,000 L reactors (total capacity of 38,000 L)
- Stainless steel and hastelloy nutsche filters (3 m2)
- Bulk solvent tank farm (60,000 L capacity)



Enjoy a virtual tour of SiliCycle's facility



# **Reagents and Organic Scavengers Portfolio**

| Reagents and Organic Scavengers Technical Information                                    |  |   |  |  |  |  |  |  |  |  |
|--|--|---|--|--|--|--|--|--|--|--|
| Products   | Structure                                      | Brief Description   | Typical Reactions  | Typical Characteristics a, b   |  |  |  |  |  |  |
| SiliaBond Carbodiimide  PN: R70530B  Loading: ≥ 0.91 mmol/g  Endcapping: Yes             | (S) Nε = N                                     | Most commonly used reagents in peptide synthesis and other amide bond-forming   | Amide coupling with acids, acyl chlorides and                            | Color: Orange<br>Density: 0.751 g/mL<br>Solvent Compatibility: 3<br>Prolonged Storage: 3<br>Shelf Life: 2 Years    |  |  |  |  |  |  |
| SiliaBond Ethyl Carbodiimide  PN: R70630B  Loading: ≥ 0.32 mmol/g  Endcapping: Yes       | <b>3</b> — N-c- ✓                              | reactions of primary and secondary amines with carboxylic acids.  | amines   | Color: Orange Density: 0.770 g/mL Solvent Compatibility: 3 Prolonged Storage: 3 Shelf Life: 2 Years                |  |  |  |  |  |  |
| SiliaBond Piperazine  PN: R60030B  Loading: ≥ 0.83 mmol/g  Endcapping: Yes               | © NN NH  | Used deprotecting and scavenging agent for Fmoc and Bsmoc amino protecting groups. Silia <i>Bond</i> Piperazine may also be used to scavenge electrophiles. | Fmoc and Bsoc<br>deprotection, organic<br>scavenger                      | Color: Off-white<br>Density: 0.671 g/mL<br>Solvent Compatibility: 2<br>Prolonged Storage: 2<br>Shelf Life: 2 Years |  |  |  |  |  |  |
| SiliaBond Carbonate  PN: R66030B  Loading: ≥ 0.46 mmol/g  Endcapping: Yes                | (CO <sub>3</sub> <sup>2</sup> ) <sub>0.5</sub> | Used as a heterogeneous catalyst in the Henry reaction in catalytic amounts drive the reaction forward to high yield with or without solvent.               | Free basing of amine   | Color: Off-white<br>Density: 0.608 g/mL<br>Solvent Compatibility: 3<br>Prolonged Storage: 2<br>Shelf Life: 1 Year  |  |  |  |  |  |  |
| SiliaBond Cyano  PN: R38030B Loading: ≥ 1.38 mmol/g Endcapping: Yes                      | S)——≡N   | Less polar than silica, Silia <i>Bond</i> Cyano has a great affinity for polar compounds.   | Residual azide removal,<br>after a click reaction                        | Color: Off-white<br>Density: 0.703 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 2 Years |  |  |  |  |  |  |
| SiliaBond Tosic Acid<br>(SCX)  PN: R60530B Loading: ≥ 0.54 meq/g Endcapping: Yes         |  | SiliaBond Tosic Acid is in a class of strong acids. The aromatic ring makes it slightly more acidic than other supported sulfonic acids.                    | Strong cation exchanger (SCX) for amine "Catch and Release" purification | Color: Off-white<br>Density: 0.698 g/mL<br>Solvent Compatibility: 2<br>Prolonged Storage: 1<br>Shelf Life: 2 Years |  |  |  |  |  |  |
| SiliaBond Propylsulfonic Acid (SCX-2)  PN: R51230B Loading: ≥ 0.63 meq/g Endcapping: Yes | S  | Supported sulfonic acid presenting a slighly more non-polar character than the SCX, thus reducing secondary interactions.                                   | Strong cation exchanger (SCX) for amine "Catch and Release" purification | Color: Off-white<br>Density: 0.728 g/mL<br>Solvent Compatibility: 2<br>Prolonged Storage: 1<br>Shelf Life: 2 Years |  |  |  |  |  |  |

# Spherical Silica Gels in Bulk and HPLC Columns Portfolio

| Spherical Silica Gels in Bulk and HPLC Columns Portfolio (refer to the ordering section for product number) |                  |   |  |  |  |  |  |  |  |
|---|------------------|---|--|--|--|--|--|--|--|
| Sorbent Phase   | Functional Group | Typical Applications  |  |  |  |  |  |  |  |
| C18   | <b>a</b> ~~~~    | Great start for method development. Presents the maximum retention of non-polar compounds. Typically used for peptides, pesticides, PCBs, PAHs, drugs, etc.   |  |  |  |  |  |  |  |
| C8  | (S)~~~~          | Presents less retention compared to C18. Mainly used for highly hydrophobic pesticides, small peptides and heavy drugs.   |  |  |  |  |  |  |  |
| Cyano   | GI——≡N           | Moderate non-polar sorbent with less hydrophobicity than C18 or C8. Purification of cyclosporine and carbohydrates. Les polar sorbent compared to silica, used for the purification of polar organic compounds. |  |  |  |  |  |  |  |
| Silica  | Si               | Most polar sorbent with a slight acidic character. Used for purification of polar and non-ionic compounds.  |  |  |  |  |  |  |  |



# **Metal Scavengers Portfolio**

| Metal Scavengers Technical Information                                    |  |  |   |  |  |  |  |  |  |  |
|---|--|--|---|--|--|--|--|--|--|--|
| Scavengers  | Structure                              | Brief Description  | Metals Removed °  | Typical Characteristics a, b   |  |  |  |  |  |  |
| SiliaMetS Thiol  PN: R51030B  Loading: ≥ 1.20 mmol/g  Endcapping: Yes     | S → SH                                 | Silia <i>MetS</i> Thiol is our most versatile and robust metal scavenger for a variety of metals under a wide range of conditions.   | Ag, Au, Hg, Os, Pd & Ru Cu, Ir, Pb, Rh, Sn & U  | Color: White<br>Density: 0.682 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 4 Years       |  |  |  |  |  |  |
| SiliaMetS DMT  PN: R79030B Loading: ≥ 0.50 mmol/g Endcapping: Yes         | 3H N N N SH                            | 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 ( $i.e.$ $Pd(dppf)Cl_2$ ).   | Au, Bi, Ir, Ni, Os, Pd, Pt,<br>Re, Rh, Ru & U<br>Cd, Co, Cu, Fe, Sc & Zn                | Color: Light brown<br>Density: 0.732 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 2 Years |  |  |  |  |  |  |
| SiliaBond Amine  PN: R52030B  Loading: ≥ 1.20 mmol/g  Endcapping: Yes     | S NH₂                                  | Also known for their electrophile scavenging efficiencies and their base reagent qualities, Silia <i>MetS</i> Amine, Diamine and Triamine have also  | Cd, Cr, Pd, Pt, Rh, Re & Ru<br>Co, Cu, Fe, Hg, Pb, U, W<br>& Zn                         | Color: Off-white<br>Density: 0.700 g/mL<br>Solvent Compatibility: 2<br>Prolonged Storage: 2<br>Shelf Life: 2 Years   |  |  |  |  |  |  |
| PN: R48030B<br>Loading: ≥ 1.11 mmol/g<br>Endcapping: Yes                  | S ↑ ↑ NH2                              | proven to be very useful for the scavenging of the following metals: Pd, Pt, Cr, W and Zn.   | 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: 2 Prolonged Storage: 2 Shelf Life: 2 Years               |  |  |  |  |  |  |
| SiliaMetS Cysteine  PN: R80530B  Loading: ≥ 0.30 mmol/g  Endcapping: Yes  | SH CNa                                 | Silia <i>MetS</i> 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. | Au, Cd, Fe, Ir, Os, Ru, Sc,<br>Sn & U<br>Ca, Cr, Cs, Cu, La, Mg, Pd,<br>Pt, Rh & Zn     | Color: Orange<br>Density: 0.665 g/mL<br>Solvent Compatibility: 2<br>Prolonged Storage: 3<br>Shelf Life: 1 Year       |  |  |  |  |  |  |
| SiliaMetS DOTA  PN: R91030B Loading: ≥ 0.38 mmol/g Endcapping: Yes        | ОН<br>ОН<br>ОН                         | SiliaMetS 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<br>Density: 0.681 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 1 Year |  |  |  |  |  |  |
| SiliaMetS Imidazole  PN: R79230B  Loading: ≥ 0.96 mmol/g  Endcapping: Yes | <b>⊙</b> ~~!♡                          | Silia <i>MetS</i> 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,<br>Ni, Os, U, W & Zn<br>Cr, Pd & Rh                         | Color: Off-white<br>Density: 0.681 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 2 Years   |  |  |  |  |  |  |
| SiliaMetS TAAcOH  PN: R69030B  Loading: ≥ 0.41 mmol/g  Endcapping: No     | Ton (ONL)                              | SiliaMetS 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.  | Au, Ca, Co, Ir, Li, Mg, Ni,<br>Os, Ru, Sc & U<br>Cr, Cs, Fe, Pd, Rh & Sn                | Color: Off-white<br>Density: 0.635 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 2 Years   |  |  |  |  |  |  |
| SiliaMetS TAAcONa  PN: R69230B Loading: ≥ 0.41 mmol/g Endcapping: No      | II g—on (cou)                          | Silia <i>MetS</i> TAAcOH is effective for metals in low or zero oxidation states, compared to Silia <i>MetS</i> TAAcONa which is useful for metals in higher oxidation states (≥ 2).   | Bi, Ca, Cd, Cs, Cu, Fe, Ir,<br>La, Li, Mg, Ni, Os, Rh, Sc,<br>Sn & U<br>Cr, Pd, Ru & Zn | Color: Off-white<br>Density: 0.712 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 2 Years   |  |  |  |  |  |  |
| SiliaMetS Thiourea  PN: R69530B  Loading: ≥ 1.07 mmol/g  Endcapping: Yes  | 3~~\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\ | SiliaMetS 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.  | Au, Pd & Ru  Ag, Cu, Fe, Os, Rh, Sc & Sn  | Color: Off-white<br>Density: 0.767 g/mL<br>Solvent Compatibility: 1<br>Prolonged Storage: 1<br>Shelf Life: 2 Years   |  |  |  |  |  |  |

## <sup>a</sup> Solvent Compatibility:

- 1- All solvents, aqueous and organic
- 2- All organic solvents
- 3- Anhydrous aprotic solvents

## ° Scavenging Efficiency:

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

## <sup>b</sup> Prolonged Storage:

- 1- Keep dry
- 2- Keep cool (≤ 8°C) and dry
- 3- Keep cool ( $\leq 8^{\circ}$ C), dry, and under inert atmosphere



# Peptide Synthesis and Amide Bond-Forming Reactions

1,3-Dicyclohexylcarbodiimide (*DCC*) has arguably become one of the most commonly used reagents in peptide synthesis and other amide bond-forming reactions of primary and secondary amines with carboxylic acids. The major drawback associated with using DCC is the formation of the urea by-product (*DCU*) which remains in solution and requires additional purification steps to remove it. However, by using Silia*Bond* Carbodiimide (*DCC*) it is possible to avoid problematic purifications. Only a simple filtration step is needed to remove the unwanted DCU. For more details on the experimental procedures, see <u>Appn SBR004-0</u>.

| Y   | Yield (%) and Purity (%) of Amides Synthesized Using Silia <i>Bond</i> Carbodiimide ( <i>DCC</i> ) |                                     |                    |                               |                          |     |                    |                    |                       |                               |                             |
|-----|--|-------------------------------------|--------------------|-------------------------------|--------------------------|-----|--------------------|--------------------|-----------------------|-------------------------------|-----------------------------|
| Rn# | Acid   | Amine                               | Meth. #1 Yield (%) | Meth. #2 Yield (%) (% Purity) | SPE Yield (%) (% Purity) | Rn# | Acid               | Amine              | Meth. #1<br>Yield (%) | Meth. #2 Yield (%) (% Purity) | SPE Yield (%) (% Purity)    |
| 1   |  | Aniline                             | 75.5<br>(99.1)     | 70.1<br>(96.4)                | 81.2<br>(97.2)           | 6   | Boc-Phe-OH (L)     |                    | 100.0<br>(97.6)       | 100.0<br>(97.6)               | 99.2<br>(90.1)              |
| 2   | Benzoic acid   | Benzylamine                         | 100.0<br>(95.4)    | 80.1<br>(98.1)                | 100.0<br>(98.7)          | 7   | Fmoc-Phe-C         | HP(A)nylethylamine | N.A.                  | 100.0<br>(> 95.0)             | N.A.                        |
| 3   |  | Phenylethylamine                    | 98.7<br>(97.1)     | 78.7<br>(98.3)                | 100.0<br>(98.8)          | 8   | Z-Val-OH           |                    | 100.0<br>(> 95.0)     | 93.5<br>(> 95.0)              | 100.0<br>(> 95.0)           |
| 4   | Dhanasasastia aaid   | <i>tert</i> -Butylamine             | 100.0<br>(97.4)    | 100.0<br>(94.0)               | 98.2ª<br>(94.5)          | 9   | 3-lodobenzoic acid | Benzylam           | ine 100.0<br>(98.5)   | 100.0<br>(97.1)               | 100.0<br>(94.5)             |
| 5   | Phenoxyacetic acid   | 1,2,3,4-Tetrahydro-<br>isoquinoline | 99.8<br>(95.0)     | 100.0<br>(92.5)               | 97.2<br>(92.4)           | 10  | Heptanoic acid     | Ethanolamine       | 72.3<br>(95.5)        | 84.3<br>(98.0)                | 81.3 <sup>b</sup><br>(93.0) |

Notes: The final amides were analyzed by <sup>1</sup>H and <sup>13</sup>C NMR or GC-MS. Yield corresponds to the mass of isolated product. Purity was determined by GC-FID.

<sup>a)</sup> In DMF; <sup>b)</sup> No HOBt

 SiliaBond Carbodiimide (DCC) has also been succesfully used for the synthesis of Weinreb amides and acylsulfonamides as shown here.

For more details on the experimental procedures, see <u>Appn\_SBR004-0</u>.

| <b>Y</b> | Yield (%) and Purity (%) of Weinreb Amides and Acylsulfonamides Synthesized Using SiliaBond Carbodiimide (DCC) |                       |                                  |     |                  |                    |                                   |  |  |  |
|----------|--|-----------------------|----------------------------------|-----|------------------|--------------------|-----------------------------------|--|--|--|
|          |  | Weinreb Amides        |                                  |     | Acylsulfonamides |                    |                                   |  |  |  |
| Rn#      | Acid   | Amine                 | Yield (%)<br>(% <i>Purity</i> )* | Rn# | Acid             | Amine              | Yield (%)<br>(% <i>Purity</i> )** |  |  |  |
| 1        | Benzoic acid   | N.O-                  | 98.8 (95.5)                      | 1   |                  | Benzenesulfonamide | 95.5 (71.3)                       |  |  |  |
| 2        | t-Cinnamic acid  | dimethylhydroxylamine | 87.3 (94.7)                      | 2   | Benzoic acid     | Methanesulfonamide | 78.8 (53.1)                       |  |  |  |
| 3        | 2-Nitrobenzoic acid  | hydrochloride         | 99.5 (93.2)                      |     |                  | Wethanesunonamide  | 76.6 (55.7)                       |  |  |  |

<sup>\*</sup> Determined by GC-FID. \*\* Purity was determined by GC-FID (the purity obtained is lower than in the previous synthesis because scavenging step using SiliaBond Amine, to eliminate the acid in excess, hasn't been done).

In this particular example, the Silia Bond Carbodiimide was used as the coupling reagent, followed by Silia Bond Carbonate to remove HOBt (the catalyst). As TFA salt of the amide was formed by the removal of the Boc protecting group, Silia Bond Carbonate was used a second time to remove it. Yields in the above figure refer to the mass of isolated product and purity is determined by GC-FID.

For more details, see Appn\_SB012-0.



# **Amine Free Basing**

Supported sulfonic acids are in a class of strong acids (pKa < 1) widely used in different fields of synthetic organic chemistry. Their applications are very well-known in a large number of settings, from drug discovery laboratories up to manufacturing processes. Among these applications are: acid catalysts, stationary phases for ion chromatography, basic impurity scavengers, and they are very useful for more specific organic synthesis applications, like amine free basing and Boc group deprotection. Their most common use is probably as a strong cation exchanger (SCX) for the "Catch and Release" purification of amines in SPE cartridges. For more details, see Appn SP004-0.

## Procedure - Tosic Acid (SCX) and Propylsulfonic Acid (SCX-2) in SPE cartridges

| Catch and Release of Amines with SCX and SCX-2 |  |  |  |  |  |  |
|--|--|--|--|--|--|--|
| Cartridges used                                | Silia Prep Tosic Acid (SCX) 6 mL / 500 mg (SPE-R60530B-06P) Silia Prep Propylsulfonic Acid (SCX-2) 6 mL / 500 mg (SPE-R51230B-06P) |  |  |  |  |  |
| Samples  | Amine (1 equiv) dissolved in methanol (2,500 ppm)  |  |  |  |  |  |
| Conditioning step                              | 6 mL of methanol   |  |  |  |  |  |
| Loading step                                   | Samples slowly aspirated through the cartridges  |  |  |  |  |  |
| Washing step                                   | 6 mL of methanol (1 mL/min)  |  |  |  |  |  |
| Elution step                                   | 6 mL of 2 M ammonia / methanol   |  |  |  |  |  |

## Results

|                  | Catch and Release of Amines with SCX and SCX-2 |             |                |                       |     |                   |       |                     |     |              |                 |
|------------------|--|-------------|----------------|-----------------------|-----|-------------------|-------|---------------------|-----|--------------|-----------------|
| Amine            | рКа  | Catc<br>SCX | h (%)<br>SCX-2 | Release (%) SCX SCX-2 |     | Amine             | рКа   | Catch (%) SCX SCX-2 |     | Relea<br>SCX | se (%)<br>SCX-2 |
| 4-nitroaniline   | 0.98   | 98          | 97             | 100                   | 100 | Benzylmethylamine | 9.58  | 100                 | 100 | 100          | 97              |
| Aniline          | 4.62   | 100         | 100            | 95                    | 96  | Cyclohexylamine   | 10.64 | 100                 | 96  | 95           | 96              |
| 4-methoxyaniline | 5.29   | 100         | 100            | 100                   | 100 | Tributylamine     | 10.75 | 100                 | 100 | 100          | 98              |
| Morpholine       | 8.36   | 100         | 100            | 100                   | 89  | Quinuclidine      | 11.00 | 100                 | 100 | 94           | 98              |

Although the aromatic ring of the Tosic Acid makes it slightly more acidic than Propylsulfonic Acid, these studies demonstrate that they have comparable strength. In fact, the difference between the two products is mainly in the selectivity.

# **HOBt Scavenging**

The use of functionalized silica greatly simplifies not only organic synthesis but also purification. In some cases, the work-up is reduced to a simple filtration and evaporation of the solvent. As demonstrated by the examples below, Silia*Bond* Carbonate could play a key role in further simplifying the work-up in amide coupling reactions. For more details, see <u>Appn SB012-0</u>.

## Procedure - Silia**Bond** Carbonate in bulk

| Υ | HOBt Scavenging - Bulk  |  |  |  |  |  |  |  |  |
|---|---|--|--|--|--|--|--|--|--|
| 1 | Add 2 - 4 equivalents of Silia Bond Carbonate to the HOBt solution (in DMF) |  |  |  |  |  |  |  |  |
| 2 | Stir for 1 hour at room temperature   |  |  |  |  |  |  |  |  |
| 3 | Remove the Silia <i>Bond</i> carbonate by filtration and rinse with DMF     |  |  |  |  |  |  |  |  |
| 4 | Solvent evaporation gives the HOBt free solution                            |  |  |  |  |  |  |  |  |

# Procedure - SiliaBond Carbonate in SPE cartridges

| HOBt Scavenging - SPE Cartridges |                        |  |  |  |  |  |
|----------------------------------|------------------------|--|--|--|--|--|
| Conditioning step                | 1 x CV of DMF          |  |  |  |  |  |
| Loading step                     | Load the HOBt solution |  |  |  |  |  |
| Rinsing step                     | 1 x CV of DMF          |  |  |  |  |  |

Note: CV = Column Volume

### Results

|                       | Scavenging with Silia <i>Bond</i> and Silia <i>Prep</i> Carbonate |                                 |                            |                         |                          |                   |                                 |                            |                         |  |  |
|-----------------------|---|---------------------------------|----------------------------|-------------------------|--------------------------|-------------------|---------------------------------|----------------------------|-------------------------|--|--|
| Number of Equivalents | Product   | Reaction<br>Time ( <i>min</i> ) | Final HOBt<br>Conc.* (ppm) | Scavenging<br>Yield (%) | Number of<br>Equivalents | Product           | Reaction<br>Time ( <i>min</i> ) | Final HOBt<br>Conc.* (ppm) | Scavenging<br>Yield (%) |  |  |
|                       | Silia <i>Bond</i>   | 5                               | 32                         | 99.4                    |                          | Silia <i>Bond</i> | 5                               | 22                         | 99.6                    |  |  |
| 3                     | SiliaBona   | 60                              | 32                         | 99.4                    | 4                        |                   | 60                              | 21                         | 99.6                    |  |  |
|                       | Silia <i>Prep</i>   | -                               | < 5                        | > 99.9                  |                          | Silia <i>Prep</i> | -                               | < 5                        | > 99.9                  |  |  |

<sup>\*</sup> Determined by GC-MS. Initial HOBt concentration: 5,000 ppm in DMF.



# **TFA Removal**

Trifluoroacetic acid (*TFA*) is certainly the most commonly used ion-pairing agent for the separation of peptides in reversed-phase ion-pairing chromatography. This is due to TFA being a volatile solvent and therefore easier to remove, having low absorption within detection wavelengths, and its effectiveness is well established.

The role of TFA is to act as a buffer (*keeping the charge on the analyte and avoiding precipitation*), to impart some hydrophobicity to the amino groups, and to neutralize cationic charges.

Usually after HPLC separation and evaporation of the solvent, the peptide is isolated in its TFA salt form and it is well-known that peptides stored this way exhibit reduced stability. Hence it is necessary to use a method to freebase the peptides prior to their storage. The use of SiliaBond Carbonate was investigated in the following study as an efficient and convenient solution to this problem. For more details, see Appn SB012-0.

# SPE Cartridges Packed With SiliaBond Carbonate

Non-retentive SPE (Catch and Release) allows peptides to be eluted directly during the loading and rinsing steps (i.e., won't be retained on the sorbent) while the TFA remains in the SPE cartridge.

#### **Procedure**

| Catch and Release of the Analyte |                                  |  |  |  |  |  |  |
|----------------------------------|----------------------------------|--|--|--|--|--|--|
| Conditioning step                | 1 x CV of THF                    |  |  |  |  |  |  |
| Loading step                     | Load the amine solution (in THF) |  |  |  |  |  |  |
| Rinsing step                     | 1 x CV of THF                    |  |  |  |  |  |  |

Note: CV = Column Volume

### Results

| Salt Removal Using SiliaPrep Carbonate SPE Cartridges |        |                        |                         |  |  |  |  |  |
|---|--------|------------------------|-------------------------|--|--|--|--|--|
| Amine   | Salts  | Yield <sup>A</sup> (%) | Purity <sup>B</sup> (%) |  |  |  |  |  |
|   | HCI    | 98.7                   | 94.4                    |  |  |  |  |  |
| Ephedrine -   | TFA    | 100                    | 98.9                    |  |  |  |  |  |
|   | - AcOH | 100                    | 99.2                    |  |  |  |  |  |

A Yields refer to the mass of isolated product.

# Residual Metal Removal After a Catalytic Reaction

Nishimura's team at Shinshu University synthesized supramolecular hydrogels (*i.e. cross-linked fiber networks that swell*) encapsulated with enzymes. The biocatalytic supramolecular shear-thinning hydrogels are fabricated by self-assembly of amphiphilic carbohydrate-conjugated diphenylalanine derivatives. The amphiphilic glycopeptides are synthesized by a copper-catalyzed Huisgen reaction. Residual copper was scavenged using Silia*MetS* Triamine (*r.t. in DMF, number of equivalent, reaction time, concentration of Cu before and after scavenging as well as scavenging yield are unknown*). For more details, see <u>CS\_SM014-0</u>.

Sakamoto, Y. et al. Langmuir 2022, 38, 5883-5890.



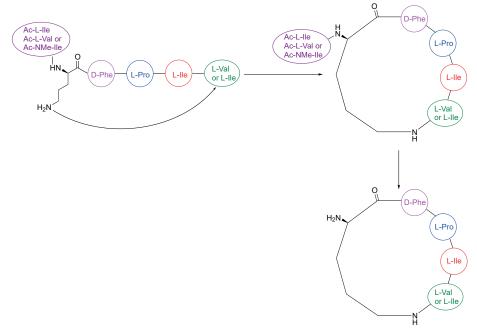
<sup>&</sup>lt;sup>B</sup> Purities determined by GC-FID.

# Peptide Purification by Flash Chromatography

Voyer's team reported the first total synthesis of the cycletail peptides known as pseudacyclins A-E with high overall yields. The strategy was based on the use of orthogonally protected ornithine that yielded protected-cyclic peptides that were later hydrogenolyzed to give the exocyclic amines. The hydrogenolysis step of these types of syntheses is usually purified by HPLC, and the purification is long, tedious, and gives poor yields.

Voyer's team developed a powerful normal-phase method for rapid separation of the monomers from the dimers using Silia Sep PREMIUM Spherical Flash Cartridges obtaining yields from 52 to 56 % with a purity of 98 to 99 %. The chromatographic conditions are reported on the right. For more details, see <u>CS\_SS002-0</u>.

| Chromatographic Conditions |   |  |  |  |  |
|----------------------------|---|--|--|--|--|
| Parameter                  | Value   |  |  |  |  |
| Cartridge                  | SiliaSep PREMIUM Flash Cartridge, Silica-Based, 25 µm, 90 Å                     |  |  |  |  |
| Part Number                | FLH-10095D-A-ISO40  |  |  |  |  |
| Gradient                   | Linear gradient 100 % dichloromethane to 80:20 dichloromethane:methanol (19 CV) |  |  |  |  |
| Flow Rate                  | 25 mL/min   |  |  |  |  |

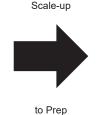


Bérubé, C. et al. Tetrahedron Letters 2018, 59, 4176-4179.

# Peptide Purification by Preparative HPLC and DAC

In large scale purification using high pressure chromatography, it is paramount to first screen & scout analytical columns and then be able to scale-up using prep columns of the same silica (*phase and particle size*). That's why our HPLC columns are available in analytical dimensions (4.6 mm ID) and preparative dimensions (10, 21.2, 30, and 50 mm ID). In addition, bulk silica is also offered to allow DAC packing, giving the purification scientist even more options.









10 mm ID 21.2 mm ID 30 mm ID

+ Bulk for DAC packing (available in -50G, -250G, -500G, and -1KG formats)



50 mm ID

# **Other Applications**

# **Trap-Elute of Polar Peptides**

Silia Prep SPE cartridges packed with C18 Widepore (WPD, 125 Å) can be used for trap-elute of relatively polar peptides after cleavage or cysteine oxidation.

# **Fmoc Deprotection of Peptides**

SiliaBond Piperazine (Si-PPZ) is a useful deprotecting and scavenging agent for Fmoc and Bsmoc amino protecting groups, and can also be used as a solid-phase Knoevenagel catalyst.

## Removal of Residual Azide

SiliaBond Cyano can be useful to remove residual azide (starting material) after a click reaction.

# **Ordering Information**

# **Bulk Irregular Silica Gels**

Our silica gels are available from 5 g up to 25 kg formats. All particle size and pore size are respectively 40 - 63 µm, 60 Å for theseproducts. To build your own product number, just add the quantity to the Phase PN: [Phase PN]-[Quantity Code]

Example: 100 g of Thiol silica gel, 40 - 63 µm, 60 Å: R51030B-100G

| Reagents and Organic Scavengers       |          |  |  |
|---------------------------------------|----------|--|--|
| Product Names                         | Phase PN |  |  |
| Silia <i>Bond</i> Carbodiimide        | R70530B  |  |  |
| SiliaBond Ethyl Carbodiimide          | R70630B  |  |  |
| SiliaBond Piperazine                  | R60030B  |  |  |
| Silia <i>Bond</i> Carbonate           | R66030B  |  |  |
| Silia <i>Bond</i> Cyano               | R38030B  |  |  |
| SiliaBond Tosic Acid (SCX)            | R60530B  |  |  |
| SiliaBond Propylsulfonic Acid (SCX-2) | R51230B  |  |  |

| Metal Scavengers        |          |
|-------------------------|----------|
| Product Names           | Phase PN |
| SiliaMetS Thiol         | R51030B  |
| SiliaMetS DMT           | R79030B  |
| Silia <i>Bond</i> Amine | R52030B  |
| SiliaMetS Triamine      | R48030B  |
| SiliaMetS Cysteine      | R80530B  |
| SiliaMetS DOTA          | R91030B  |
| SiliaMetS Imidazole     | R79230B  |
| SiliaMetS TAAcOH        | R69030B  |
| SiliaMetS TAAcONa       | R69230B  |
| SiliaMetS Thiourea      | R69530B  |

# **Bulk Spherical Silica Gels**

The table below presents the most popular Silia Sphere bonded phases available from SiliCycle.

To build your own product number, just add the Particle and Pore Size Code to the Phase Code: [Phase]-[Particle and Pore] Example: S03205E-A for a C18 silica gel, 5 µm, 100 Å

## **Phase Codes**

| SiliaSphere Phase Codes |      |  |  |
|-------------------------|------|--|--|
| Phase Code              |      |  |  |
| C18                     | S032 |  |  |
| C8 S308                 |      |  |  |
| Cyano                   | S380 |  |  |
| Silica S100             |      |  |  |

## **Particle and Pore Size Codes**

| Ya.           | SiliaSphere Particle and Pore Size Codes |       |       |         |  |
|---------------|--|-------|-------|---------|--|
| Particle Size | Pore Diameter                            |       |       |         |  |
|               | 60 Å                                     | 100 Å | 300 Å | 1,000 Å |  |
| 3 µm          | 03B                                      | 03E-A | 03M   | -       |  |
|               |  |       |       |         |  |
| 5 μm          | 05B                                      | 05E-A | 05M   | -       |  |



# **Packed in Cartridges**

# Silia Prep SPE Cartridges and Silia Sep Flash Cartridges

To build your SPE or flash cartridge Product Number, simply start with the **Prefix SPE** or **FLH**, followed by the **Phase of the silica gel** you wish your cartridge to be packed with, followed by the **Format code**.

• Silia*Prep* Cyano, 6 mL, 500 mg = SPE-R38030B-06P

- Silia Sep Open-Top Carbonate, 70 mL, 10 g = FLH-R66030B-70Y
- SiliaSep Thiol, 4 g = FLH-R51030B-ISO04

| Silia <i>Prep</i> SPE and SiliaSep OT Cartridges |        |      |                |  |  |
|--|--------|------|----------------|--|--|
| Formats available                                | Prefix | Code | Units /<br>Box |  |  |
| 3 mL / 200 mg                                    | SPE    | 03G  | 50             |  |  |
| 3 mL / 500 mg                                    | SPE    | 03P  | 50             |  |  |
| 6 mL / 500 mg                                    | SPE    | 06P  | 50             |  |  |
| 6 mL / 1 g                                       | SPE    | 06S  | 50             |  |  |
| 6 mL / 2 g                                       | SPE    | 06U  | 50             |  |  |
| 12 mL / 2 g                                      | SPE    | 12U  | 20             |  |  |
| 25 mL / 5 g*                                     | FLH    | 20X  | 20             |  |  |
| 70 mL / 10 g*                                    | FLH    | 70Y  | 16             |  |  |
| 70 mL / 15 g*                                    | FLH    | 70i  | 16             |  |  |
| 70 mL / 20 g*                                    | FLH    | 70Z  | 16             |  |  |
| 150 mL / 25 g*                                   | FLH    | 95K  | 10             |  |  |
| 150 mL / 50 g*                                   | FLH    | 95M  | 10             |  |  |
| 150 mL / 70 g*                                   | FLH    | 95N  | 10             |  |  |
| * Commercialized under Silia Sen OT branding     |        |      |                |  |  |



| SiliaSep Flash Cartridges |           |             |   |  |  |
|---------------------------|-----------|-------------|---|--|--|
| Formats available         | Prefix    | Prefix Code |   |  |  |
| 4 g                       | FLH       | ISO04       | 2 |  |  |
| 12 g                      | FLH       | ISO12       | 1 |  |  |
| 25 g                      | g FLH IS  |             | 1 |  |  |
| 40 g                      | FLH ISO40 |             | 1 |  |  |
| 80 g                      | FLH IS    |             | 1 |  |  |
| 120 g                     | FLH       | IS120       | 1 |  |  |
| 220 g                     | FLH       | IS220       | 1 |  |  |
| 330 g                     | FLH       | IS330       | 1 |  |  |
| 800 g                     | FLH       | IS750       | 1 |  |  |
| 1,600 g                   | FLH       | I1500       | 1 |  |  |

# Silia Chrom Plus HPLC Columns Ordering Information

How to build your PN for HPLC Column: HPLC-[Phase Code]-[Format Code]

Example: HPLC-S03203E-A-N150 for a Silia*Chrom* Plus C18, 3 µm, 4.6 x 150 mm HPLC column

## **Phase Codes**

| Silia Chrom Plus Phase Codes |           |               |           |  |
|------------------------------|-----------|---------------|-----------|--|
| Phase                        |           | Particle Size |           |  |
|                              | 3 µm      | 5 μm          | 10 µm     |  |
| C18                          | S03203E-A | S03205E-A     | S03207E-A |  |
| C18-300                      | S03203M   | S03205M       | S03207M   |  |
| C8                           | S30803E-A | S30805E-A     | S30807E-A |  |
| C8-300                       | S30803M   | S30805M       | S30807M   |  |
| Silica                       | S10003E-A | S10005E-A     | S10007E-A |  |
| Silica-300                   | S10003M   | S10005M       | S10007M   |  |
| Cyano                        | S38003E-A | S38005E-A     | S38007E-A |  |

## **Format Codes**

| Format Codes  |         |      |          |          |          |  |
|---------------|---------|------|----------|----------|----------|--|
| Dimension     | Qty/box | Code | 3 µm     | 5 μm     | 10 µm    |  |
| 4.6 x 50 mm   | 1       | N050 | <b>✓</b> | <b>✓</b> |          |  |
| 4.6 x 100 mm  | 1       | N100 | <b>✓</b> | ✓        |          |  |
| 4.6 x 150 mm  | 1       | N150 | 1        | <b>✓</b> | 1        |  |
| 4.6 x 250 mm  | 1       | N250 | <b>✓</b> | <b>✓</b> | <b>✓</b> |  |
| 10 x 150 mm   | 1       | Q150 |          | <b>✓</b> | <b>✓</b> |  |
| 10 x 250 mm   | 1       | Q250 |          | <b>✓</b> | <b>✓</b> |  |
| 21.2 x 150 mm | 1       | T150 |          | <b>✓</b> | <b>✓</b> |  |
| 21.2 x 250 mm | 1       | T250 |          | <b>✓</b> | <b>✓</b> |  |
| 30 x 150 mm   | 1       | V150 |          | <b>✓</b> | <b>✓</b> |  |
| 30 x 250 mm   | 1       | V250 |          | <b>✓</b> | <b>✓</b> |  |
| 50 x 150 mm   | 1       | W150 |          |          | <b>✓</b> |  |
| 50 x 250 mm   | 1       | W250 |          |          | 1        |  |



Commercialized under Silia Sep OT branding.



# We Redefine Purity

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

## **DISCOVER AND DOWNLOAD OUR BROCHURES**

### **METAL AND ORGANIC SCAVENGING**

SiliaMetS® - Metal Scavengers

SiliaBond® - Organic Scavengers

E-PAK® - Fixed Bed Flow-Through Purification Cartridges



### CHROMATOGRAPHY AND PURIFICATION

SiliaFlash® - Irregular Silica Gels | SiliaSphere™ PC - Spherical Silica Gels

**Silia**Bond® - Chromatographic Phases

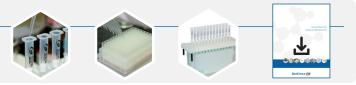
SiliaSep™ - Flash Cartridges | SiliaPlate™ - TLC Plates



### SAMPLE PREPARATION

SiliaPrep™ - Silica-based SPE Cartridges and Well Plates

SiliaPrepX™ - Polymeric SPE Cartridges and Well Plates



## **ANALYTICAL AND PREPARATIVE CHROMATOGRAPHY**

SiliaSphere™ - Spherical Silica Gels SiliaChrom® - HPLC Columns









### **ORGANIC SYNTHESIS**

SiliaBond® - Reagents and Oxidants

Silia Cat® - Heterogeneous Catalysts









#### **PEPTIDE SYNTHESIS**

Peptide Synthesis and Purification Solutions Amine Free Basing and TFA Removal









## **R&D SERVICES**

Metal and Organic Scavenging Screenings | Organic Synthesis Chromatography and Purification | Material Science Method Development, Optimization, and Transfer









# **Technical Support**

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

Our worldwide Technical Support Group of highly qualified M. Sc., Ph. D. Chemists and Engineers will answer your questions and provide solutions to your most advanced chemistry and purification needs. Contact us at <a href="mailto:support@silicycle.com">support@silicycle.com</a> or call us.



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