SiliaBond®

Reagents

SILICYCLE Inc.®

UltraPure SILICA GELS

Importance of Quality Control

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

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

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

Bare Silica Gel

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

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

Functionalized Silica Gel

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

Quality Control

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

Analysis Descriptions

Elemental Analysis of Organic Compounds

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

Total Trace Metal Analysis

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

Surface Area and Porosity Analysis

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

Particle Size Distribution Analysis

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

Water Content Analysis (*silica gel activity*)

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

pH Analysis

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

Silia*Bond* Reagents

Amide Coupling Reagents

The amide bond is the defining molecular structure of proteins and peptides. In addition, a report estimates that as many as 25% of all synthetic pharmaceutical drugs contain an amide group.[1] Therefore, there is an ongoing scientific endeavor to develop efficient amidation methodologies.[2] Usually, the amide bond formation relies on the use of an excess of toxic coupling reagents such as carbodiimides or supernucleophiles. These chemicals produce a large amount of by-products, which tends to complicate the isolation and purification of the desired amide product.

The use of a reagent linked to an insoluble material has become a widely used tool since the introduction of the solid-phase synthesis concept.[3] Solid-phase reagents are valuable for amide coupling with a carboxylic acid because of the decrease of unwanted side products. Other advantages to using solid-supported reagents include improved stability, toxic chemical immobilization, the ability to run multiple transformations in a single pot, and the flexibility to use both batch reactions and flow chemistry.

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[1] *J. Comb. Chem.* **1999**, *1*, 55.

[2] *Tetrahedron* **2005**, *61*, 10827.

[3] *J. Am Chem Soc.* **1963**, *85*, 2149.

Silia*Bond* Carbodiimide (*R70530B*)

Loading: 1.0 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* Carbodiimide (*Si-DCC*)

1,3-Dicyclohexylcarbodiimide (*DCC*) has arguably become the most commonly used reagent in peptide synthesis and other amide bond-forming reactions of primary and secondary amines with carboxylic acids.[1] 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. However, by using covalently bonded DCC on silica, it is possible to avoid problematic purifications. Only a simple filtration step is needed to remove the unwanted DCU.

[1] *Chem. Rev.* **1981**, *81*, 589.

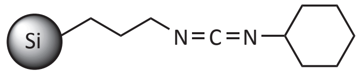
Solvent compatibility

- Aprotic Solvent

Prolonged storage

- Keep cool (*< 8 °C*) and dry, store under argon

Carbodiimide (*Si-DCC*)



Silia*Bond* Ethyl-Dimethylamino Carbodiimide (*EDC*) (*R70630B*)

Loading: 0.8 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* Ethyl-Dimethylaminopropyl Carbodiimide (*Si-EDC*)

A recent literature review shows that 1-ethyl-3 (*3-dimethylaminopropyl*) carbodiimide (*EDC*) has become recognized as one of the best reagents for amide coupling reactions. Unfortunately, using the EDC basic tertiary amine results in the formation of urea, which has to be separated from the product by acidic aqueous extractions.[1] By attaching EDC to silica, it is possible to avoid this potentially problematic work-up without sacrificing the useful carbodiimide reactivity. In fact, Silia*Bond* EDC behaves in a similar fashion as EDC in solution, but the by-product remains on the solid support.

[1] *The Peptides: Analysis, Synthesis, Biology; Academic: New York*, **1979**, *1*, 241.

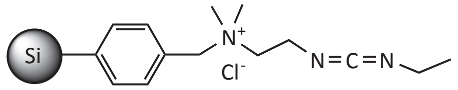
Solvent compatibility

- Aprotic Solvent

Prolonged storage

- Keep cool (*< 8 °C*) and dry, store under argon

Ethyl-Dimethylaminopropyl Carbodiimide (*Si-EDC*)



Silia*Bond* Dichlorotriazine (*R52230B*)

Loading: 0.7 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* Dichlorotriazine (*Si-DCT*)

2,4,6-Trichloro[1,3,5]triazine (*cyanuric chloride*) has been used as a versatile reagent in alkyl chloride and acid chloride synthesis. This triazine has been especially useful as a coupling reagent for amide selective formation.[1] However, cyanuric chloride is toxic, corrosive, and a severe eye, skin and respiratory tract irritant. By anchoring cyanuric chloride on a silica matrix, it is now possible to use this valuable reagent without worrying about its toxicity profile. Silia*Bond* DCT reacts in a similar manner as cyanuric chloride. In addition, excess reagent and by-product elimination is reduced to a simple filtration, which is particularly useful for products where toxicity is a concern such as in the synthesis of active pharmaceutical ingredients (*API*).

[1] *J. Org. Chem.* **1997**, *62*, 982.

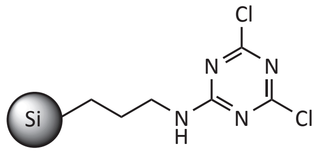
Solvent compatibility

- Aprotic Solvent

Prolonged storage

- Keep cool (*< 8 °C*) and dry, store under argon

Dichlorotriazine (*Si-DCT*)



Silia*Bond* HOBt (*R70730B*)

Loading: 0.7 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

NEW PRODUCT

Silia*Bond* HOBt (*Si-HOBt*)

Hydroxybenzotriazole (*HOBt*) has been used for increasing yield and decreasing racemization during chiral amide synthesis. However, dry HOBt can undergo exothermic decomposition. Bonding HOBt to silica eliminates this risk of explosion. Silia*Bond* HOBt can be easily activated and should ideally be used with a base such as N,N-diisopropylethylamine in the same condition as in homogeneous solution. Moreover, this supported reagent can be reused a few times without adversely affecting its performance.

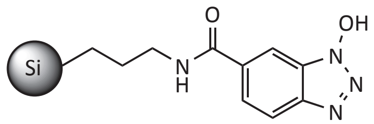
Solvent compatibility

- Aprotic Solvent

Prolonged storage

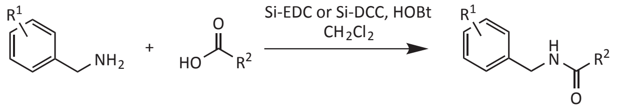
- Keep cool (< 8 °C) and dry, store under argon

HOBt (*Si-HOBt*)



Synthesis of Capsaicin Analogues

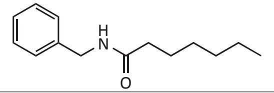
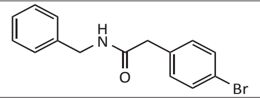
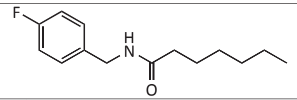
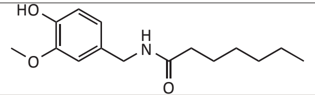
Capsaicin's potential clinical use as an analgesic and peripheral anti-inflammatory effects, as well as the discovery of an ultra-potent analogue (*resiniferatoxin*) has attracted significant interest in finding capsaicin synthesis routes.



General Procedure

The acid (*0.5 mmol*) was placed in an oven-dried reaction vial with anhydrous CH_2Cl_2 (*10 mL*) under N_2. The HOBt (*1.0 mmol*) and the Silia*Bond* Carbodiimide or Silia*Bond* EDC were added to the solution, which was then stirred briefly (*5 min*). The amine (*0.5 mmol*) was then added to the reaction tube, and the mixture was then stirred for 16 h at room temperature. Finally, the reaction was followed by GC-MS.

Capsaicin Analogues Reaction Results

Entry	Product	Yield[a] (Purity[b])	
		Si-DCC	*Si*-EDC
1		99% (> 98%)	81% (> 98%)
2		98% (> 98%)	88% (95%)
3		99% (> 98%)	99% (> 98%)
4		98%[c]	98%[c]

[a]Yield calculated in crude product, [b]Purity determined by GC-MS, [c]Yield determined by GC-MS

Amine Protection Using Benzylcarbamate Group

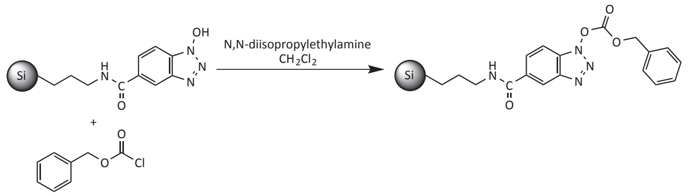
Benzylcarbamate groups are one of the most used amine protecting functions because of the easy deprotection by hydrogenolysis. Silia*Bond* HOBt, as a key reactive, facilitates the protection manipulation and can be reused a few times without loss of reactivity.

General Procedure

Silia*Bond* HOBt (*1 g or 1 eq.*) was introduced in a flask (*oven-dried*) containing anhydrous CH_2Cl_2. Benzylchloroformate (*4 eq.*) was added to the suspension, followed by N,N-diisopropylethylamine 4 eq. The reaction mixture was stirred for 60 minutes at room temperature. Then, the suspension mixture was filtered, and washed with CH_2Cl_2 (*2 x 10 mL*), and the Silia*Bond* HOBt was oven-dried.

The dried, activated Silia*Bond* HOBt was placed in a flask containing anhydrous CH_2Cl_2 under N_2. To this suspension, 0.8 eq. of amine was added, and the reaction mixture was stirred for 4 to 16 h at room temperature. The reaction suspension was filtered and washed with CH_2Cl_2 (*2 x 10 mL*).

Activation Reaction



Activation and recycling Results

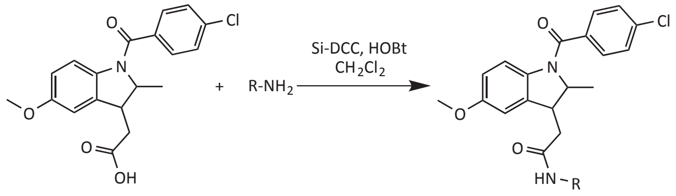
Entry	Yield[a]
Activation	96%
1st Recycling	86%
2st Recycling	95%
3st Recycling	96%

[a]Conversion determined by GC-MS

Synthesis of Amide Derivatives of Indomethacin

A report[1] has shown that indomethacin primary and secondary amide analogues are potent compounds for human COX-2 specific inhibition. Silia*Bond* Carbodiimide can be used as a key reagent in its synthesis.

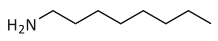
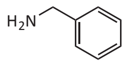
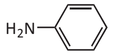
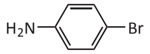
[1] *J. Med. Chem.* **2000**, 2860.



General Procedure

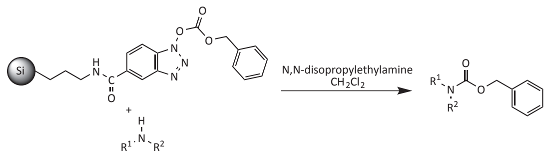
The indomethacin (*0.56 mmol*) was placed in an oven-dried reaction vial in anhydrous dichloromethane (*5 mL*) under N_2. HOBt (*0.95 mmol*) and the Silia*Bond* Carbodiimide (*1.12 mmol*) were added, and the mixture was stirred briefly (*5 minutes*). Then, the amine (*0.56 mmol*) was added to the vial, and the reaction was stirred at room temperature for 16 h. Then, the crude product was directly purified on a short plug of silica gel (*hexane/EtOAc 1/1*) to yield pure amide.

Amide Derivatives of Indomethacin Results

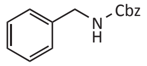
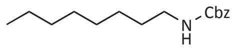
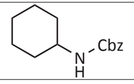
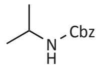
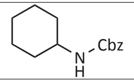
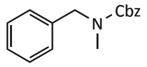
Entry	Amine	Yield[a]
1		90%
2		82%
3		94%
4		78%

[a]Conversion determined by GC-MS

Amine Protection Reaction



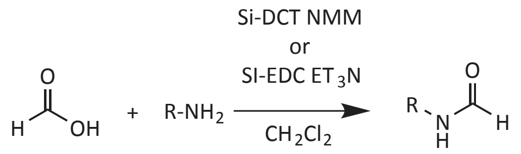
Amine Protection Results

Entry	Product	Conversion[a]
1		98% (4 h)
2		94% (4 h) 96% (16 h) 86% (16 h)[b]
3		81% (16 h)
4		93% (4 h) 98% (16 h)
5		98% (4 h)
6		93% (16 h)

[a]Conversion determined by GC-MS, [b]Polymer HOBt

Synthesis of Formylated Amino Acids

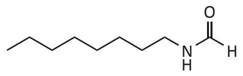
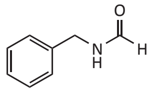
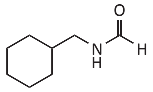
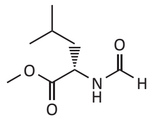
N-formylamino acid esters are useful derivatives for preparing selected N-formylamino acids, incorporating polyfunctional amino acids into peptides, and for other useful starting material preparation. Formylated amino acids have been prepared in high yields by using Silia*Bond* Dichlorotriazine (*DCT*) and Silia*Bond* Ethyl-Dimethylaminopropyl Carbodiimide (*EDC*).



General Procedure

Formic acid (*0.90 mmol*) was placed in an oven-dried reaction vial in anhydrous CH_2Cl_2 (*10 mL*) under N_2. To this solution was added triethylamine (*0.90 mmol*) and either the Silia*Bond* EDC (*2.25 mmol*) or N-methylmorpholine (*0.90 mmol*) and Silia*Bond* DCT (*2.25 mmol*). Then, the mixture was stirred briefly (*5 minutes*). The amine (*0.45 mmol*) was then added to the vial and the reaction was stirred at room temperature for 16 h. Conversion to the desired formamide was followed by GC-MS. Upon completion, the Silia*Bond* EDC or Silia*Bond* DCT was filtered and washed with 2 x 10 mL of CH_2Cl_2. Evaporation of the solvent yielded the desired product.

Synthesis of Formylated Amino Acids Results

Entry	Product	Conversion[a]	
		Si-DCT	*Si*-EDC
1		99%	93%
2		99%	100%
3		99%	99%
4		98%	95%

[a]Conversion determined by GC-MS

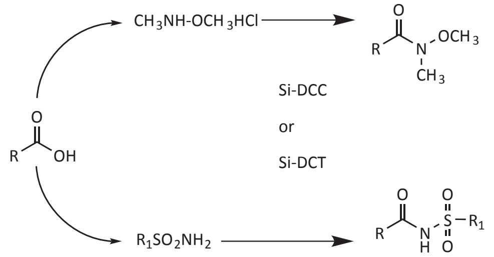
Weinreb and Acylsulfonamide Synthesis

Weinreb synthesis is a reaction often used in medicinal chemistry to produce amides. These functional groups are present in natural products and can be reliably reacted to form new carbon-carbon bonds or converted to other functions. In normal conditions, Weinreb synthesis can tolerate a large variety of functional groups such as N-protected amines, sulfonates, alpha-beta saturation and silyl ethers.

Weinreb Synthesis Results

Acid	Amine	Yield (Purity)[a]	
		Si-DCC	*Si*-DCT
Benzoic Acid	N,O-Dimethylhydroxyamine Hydrochloride	99% (96%)	96% (94%)
t-Cinnamic Acid		87% (95%)	82% (70%)
2-Nitrobenzoic Acid		> 99% (93%)	92% (79%)

[a] Yield and purity determined by GC-MS



Acylsulfonamide Synthesis Results

Acid	Sulfonamide	Yield (Purity)[a]	
		Si-DCC	*Si*-DCT
Benzoic Acid	Benzenesulfonamide	96% (71%)	98% (90%)
	Methanesulfonamide	79% (53%)	71% (82%)

[a] Yield and Purity determined by GC-MS

Silia*Bond* Cyanoborohydride for Reductive Aminations

Reductive amination involves the conversion of a carbonyl group, most of the time a ketone or an aldehyde, to an amine by an intermediate imine or iminium. The intermediate imine is reduced by sodium cyanoborohydride. This is known as direct reductive amination, and is carried out with reducing agents that are more reactive toward protonated imines than ketones and are stable under moderately acidic conditions.

General Procedure

To 1 mmol of Silia*Bond* Cyanoborohydride 5 mL of solvent, 0.5 mmol of aldehydes or ketones and 0.6 mmol of amines were added. The reaction mixture was stirred at room temperature for 16 h. Each solution was then analysed by GC-MS.

Silia*Bond* Cyanoborohydride (*R66730B*)

Loading: 1.0 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* Cyanoborohydride (*Si-CBH*)

Silia*Bond* Cyanoborohydride is the silica-bound equivalent of sodium cyanoborohydride. Bound cyanoborohydride is very useful in reductive amination and in the reduction of imines and aldehydes. Cyanide contamination of the product is a concern, however, when using the solution phase equivalent. This problem is minimized with the use of silica-bound materials since the toxic cyanide residue remains on the silica. To see if any cyanide ion was leaching from the silica, 1 g of Silia*Bond* Cyanoborohydride was washed in 10 mL of methanol for 24 h. Cyanide strips indicated less than 3 ppm in each test performed. In addition to providing superior conversions, acetic acid was not needed (*eliminating issues with acid labile groups*), the workup required only a filtration, and HCN and NaCN were not liberated during workup.

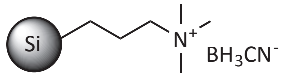
Solvent compatibility

- All solvents, aqueous and organic

Prolonged storage

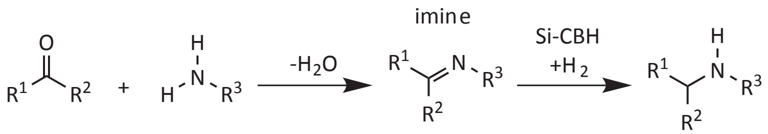
- Keep cool (< *8 °C*) and dry, store under argon

Cyanoborohydride (*Si-CBH*)

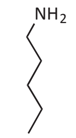
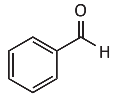
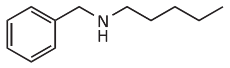
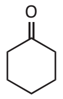
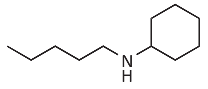
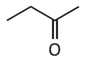
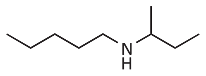
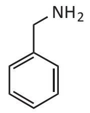
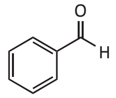
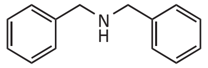
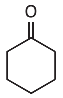
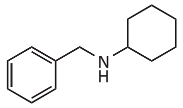
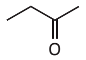
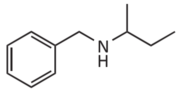
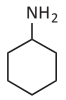
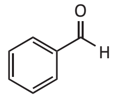
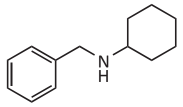
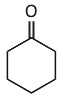
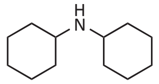
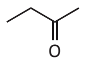
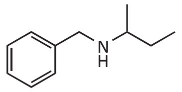


Silia*Bond* Cyanoborohydride for Reductive Aminations

Reduction of Primary Amines

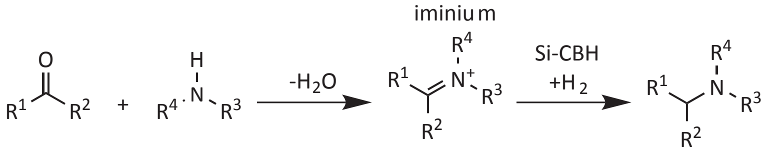


Reduction of Primary Amine Results

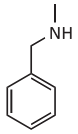
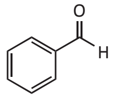
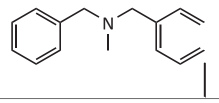
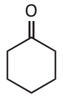
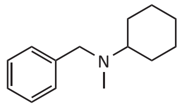
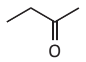
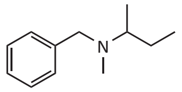
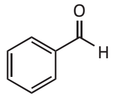
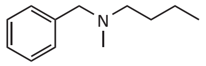
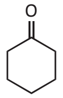
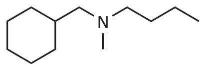
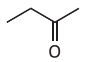
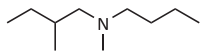
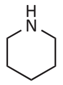
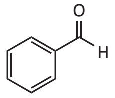
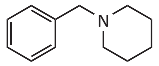
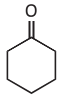
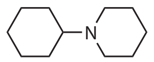
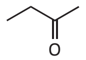
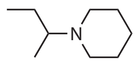
1°Amine	Carbonyl	Conditions (RT 16 h)	Acetonitrile		Ethanol		Methylene Chloride	
		Product	Conversion Product (%)[a]	Imine (%)[b]	Conversion Product (%)[a]	Imine (%)[b]	Conversion Product (%)[a]	Imine (%)[b]
			27	25	64	11	69	12
			97	0	95	5	92	8
			92	0	84	7	78	9
			61	20	71	23	73	24
			92	2	83	17	81	13
			88	3	90	7	91	6
			66	21	97	0	100	0
			91	5	93	5	93	6
			90	0	92	6	86	7

[a]Conversion determined by GC-MS, [b]Unreacted imine was determined by GC-MS

Reduction of Secondary Amines



Reduction of Secondary Amine Results

2°Amine	Carbonyl	Conditions (RT 16 h)	Acetonitrile		Ethanol		Methylene Chloride	
		Product	Conversion Product (%)[a]	SM[c] (%)[b]	Conversion Product (%)[a]	SM[c] (%)[b]	Conversion Product (%)[a]	SM[c] (%)[b]
			90	2	71	0	91	0
			92	5	79	17	93	3
			79	8	79	21	93	2
			94	6	67	0	79	0
			77	23	77	20	87	3
			70	25	61	26	44	2
			97	3	80	0	83	1
			85	15	69	19	88	6
			81	9	70	21	55	2

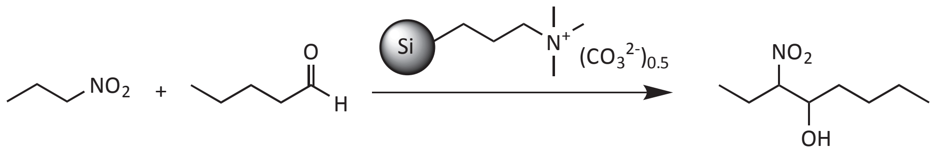
[a]Conversion determined by GC-MS, [b]Unreacted imine was determined by GC-MS, [c]Starting Material

Silia*Bond* Carbonate for Henry Reactions

The Henry reaction is commonly used to form carbon-carbon bonds by addition of nitroalkanes over aldehydes. This reaction is a useful technique in organic chemistry due to the synthetic utility of its corresponding products, as they can be easily converted to other useful synthetic intermediates such as nitroalkenes by dehydrogenation, alpha-nitro ketones by oxidation and ß-amino alcohols by reduction. Usually, the Henry reaction is carried out in presence of bases in homogeneous solution, giving low yield due to side reactions such as retroaldol and Cannizarro reactions.

General Procedure

1-nitropropane (*1 eq.*) was added to a solution containing THF (*5 mL*) and valeraldehyde (*1 eq.*). Silia*Bond* Carbonate (*0.1 eq.*) was added, and the mixture was stirred at room temperature for 6 h. The reaction mixture was then filtered and washed with THF and the crude product was evaporated. Finally, pure product was obtained after flash chromatography purification using a mix of hexane/ethylacetate (*80/20*).



Henry Reaction Results

Entry	Solvent	Reaction Conditions	Conversion[a]
1	THF	0.1 eq. Si-CO_3 room temperature, 6 h	92% (83%)[b]
2	CH_2Cl_2		76%
3	Ethanol		90%
4	Propanol		95%
5	None		92%
6	THF	0.1 eq. Si-CO_3 µwave 100 W, 100˚C 10 min	89%

[a]Conversion determined by GC-MS, [b]Purity determined from the isolated product

Silia*Bond* Carbonate (*R66030B*)

Loading: 0.7 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* Carbonate (*Si-CO_3*)

Used as a heterogenous catalyst in the Henry reaction, Silia*Bond* Carbonate is replacing the use of expensive and toxic heterogeneous catalysts. Silia*Bond* Carbonate in catalytic amounts drive the reaction forward to high yield with or without solvent.

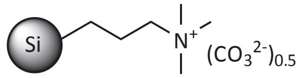
Solvent compatibility

- Aprotic solvents

Prolonged storage

- Keep dry

Carbonate (*Si-CO_3*)



Silia*Bond* DMAP for Baylis-Hillman and Acylation Reactions

Baylis-Hillman Reaction

Coupling of activated alkenes, generally alpha, 1-beta-unsaturated, with aldehydes is named the Baylis-Hillman reaction. This reaction is well known for the formation of carbon-carbon bonds under soft conditions and its compatibility with several functional groups. Furthermore, an organic base can be used to catalyze this reaction with similar success to using transition metals.

Acylation Reaction

It is well-known that DMAP used as a catalyst increases speed and yield of alcohol and phenol acylations over acetic and bezoic anhydrides.

Silia*Bond* DMAP (*R75530B*)

Loading: 0.8 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* DMAP (*Si-DMAP*)

Silia*Bond* DMAP is the heterogenous catalyst equivalent of 4-dimethylaminopyridine, which is used as a nucleophilic catalyst in a wide variety of reactions such as acylations and Baylis-Hillman reactions. These reactions are well known in organic synthesis and are very useful in various applications. Silia*Bond* DMAP has an advantage over its free counterpart as it can be removed by a simple filtration.

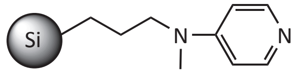
Solvent compatibility

- All organic solvents

Prolonged storage

- Keep cool (*< 8 °C*) and dry, store under argon

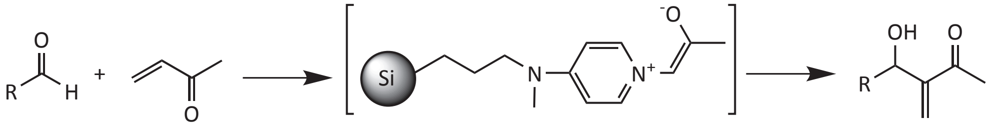
DMAP (*Si-DMAP*)



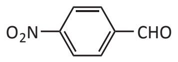
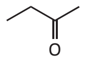
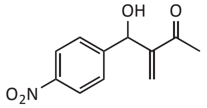
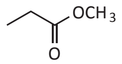
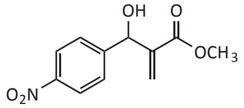
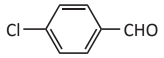
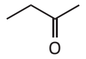
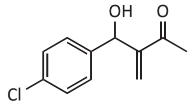
Silia*Bond* DMAP for Baylis-Hillman Reaction

General procedure

Aldehyde (*1 mmol*) was placed in a flask, and THF, Silia*Bond* DMAP (*0.10 mmol*), water and enone (*2 mmol*) were added. The mixture was stirred at room temperature for 6 to 96 h.



Baylis-Hillman Reaction Results

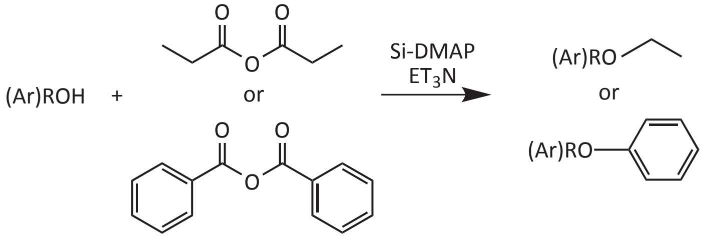
Aldehyde	Enone	Conditions	Product	Yield[a]	
				Si-DMAP	Polymer
		THF/H_2O (3/1) room temperature, 6 h 10% *Si*-DMAP		81%	37%
		DMF/H_2O (3/1) room temperature, 90 min 10% *Si*-DMAP		75%	14%
		CH_2Cl_2 room temperature, 24 h 10% *Si*-DMAP		74%	37%
		No solvent room temperature, 96 h 24% *Si*-DMAP		71%	58%
		THF/H_2O (3/1) room temperature, 96 h 19% *Si*-DMAP		63%	15%

[a] Yield determined from the isolated product

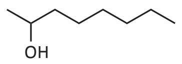
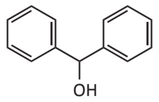
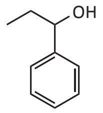
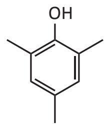
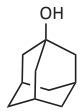
Silia*Bond* DMAP for Acylation Reactions (*Acylation of 1-phenyl-1-propanol*)

General procedure

A mixture of 2 mmol of alcohol, acetic anhydride (*1.3 eq.*), triethylamine (*1.5 eq.*), and 5% Silia*Bond* DMAP in 5 mL CH_2Cl_2 was stirred at room temperature for 90 min. The reaction was quenched by the addition of 0.5 mL of methanol, diluted with Et_2O, and washed twice with saturated aqueous $NaHCO_3$ and once with brine. After drying over Na_2SO_4, the solution was filtered and evaporated to give a colorless oil in quantitative yield.



Acylation Results

Alcohol	Catalyst	Anhydride	Reaction Conditions	Conversion[a]
	None	1.4 eq. Ac_2O	18 h, CH_2Cl_2, room temperature	25%
	5% *Si*-DMAP	1.2 eq. Ac_2O	2 h, CH_2Cl_2, room temperature	> 98%
	None	1.3 eq. Bz_2O	24 h, CH_2Cl_2, room temperature	11%
	5% *Si*-DMAP	1.3 eq. Bz_2O	24 h, CH_2Cl_2, room tremperature	91%
	None	1.3 eq. Ac_2O	18 h, CH_2Cl_2, room temperature	50%
	5% *Si*-DMAP	1.3 eq. Ac_2O	40 min, CH_2Cl_2, room temperature	> 98%
	None	1.3 eq. Bz_2O	18 h, CH_2Cl_2, room temperature	29%
	5% *Si*-DMAP	1.3 eq. Bz_2O	2 h, CH_2Cl_2, room temperature	91%
	None	1.3 eq. Ac_2O	19 h, CH_2Cl_2, room temperature	18%
	5% *Si*-DMAP	1.3 eq. Ac_2O	40 min, CH_2Cl_2, room temperature	> 98%
	None	1.3 eq. Bz_2O	24 h, CH_2Cl_2, room temperature	6%
	5% *Si*-DMAP	1.3 eq. Bz_2O	24 h, CH_2Cl_2, room temperature	88%
	None	1.3 eq. Ac_2O	3 h, CH_2Cl_2, room temperature	89%
	5% *Si*-DMAP	1.3 eq. Ac_2O	25 min, CH_2Cl_2, room temperature	> 99%
	None	1.3 eq. Bz_2O	4 h, CH_2Cl_2, room temperature	63%
	5% *Si*-DMAP	1.3 eq. Bz_2O	4 h, CH_2Cl_2, room temperature	94%
	None	1.3 eq. Ac_2O	24 h, PhH, 80˚C	49%[b]
	5% *Si*-DMAP	1.3 eq. Ac_2O	24 h, PhH, 80˚C	80%[b]

[a] Conversion determined from the isolated product, [b] Determined by GC-FID

Silia*Bond* Tosic Acid in Fischer-Speier Esterifications

The Fischer-Speier reaction is a classic organic process where a carboxylic acid is reacted with an alcohol in the presence of an acidic catalyst to form an ester. All carboxylic acids and only primary and secondary aliphatic alcohols can be use in this reaction. The most commonly used catalysts for this reaction are highly toxic such as H_2SO_4, tosic acid and scandium triflate. Also, a large excess of one of the reagents is used to push the equilibrium towards the product.

Silia*Bond* Tosic Acid (*R60530B*)

Loading: 0.8 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* Tosic Acid (*Si-SCX*)

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. It will not dissolve in methanol or any other solvents.
Silia*Bond* Tosic Acid used as an acid catalyst for Fischer-Speier estherification provides excellent conversion.

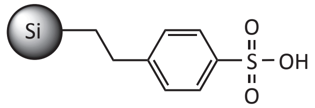
Solvent compatibility

- All solvents, aqueous and organic

Prolonged storage

- Keep dry

Tosic Acid (*Si-SCX*)



Silia*Bond* Tosic Acid for Fischer-Speier Esterifications

General procedure

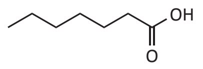
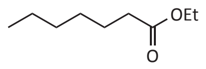
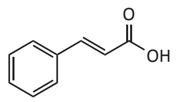
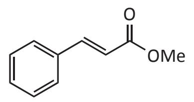
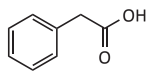
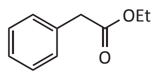
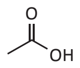
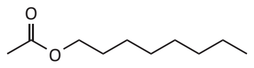
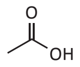
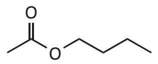
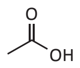
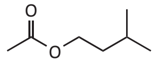
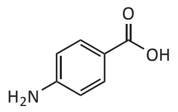
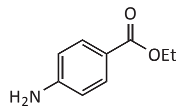
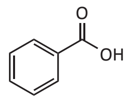
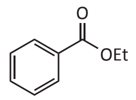
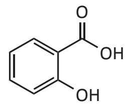
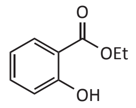
Method A

1.5 mmol of carboxylic acid was added to a mixture of alcohol (*10 mL*) and Silia*Bond* Tosic Acid (*0.1 eq.*). The reaction mixture was maintained at reflux under magnetic agitation for 16 h.

Method B

In a 250 mL round-bottom flask with a magnetic stirrer and a Dean-Stark apparatus, 16.3 mmol of a carboxylic acid was added to alcohol (*4 eq.*) and Silia*Bond* Tosic Acid (*0.1 eq.*). The mixture was then heated to reflux for 20 to 24 h under magnetic agitation.

Fischer-Speier Esterification Results

Alcohol	Carboxylic Acid	Method	Ester	Conversion[a]
Ethanol		A		100%
Methanol		A		98%
Ethanol		A		100%
1-Octanol		A		100%
1-Butanol		A		100% (99%)[b]
3-Methylbutanol		A		100%
Ethanol		A (72 h)		40%[c]
Ethanol		B		94%[c]
Methanol		B		89%[c]

[a] Conversion determined by GC-MS, [b] *Si*-SCX reused 3 times, [c] Conversion determined from the isolated product

Silia*Bond* TBD for Williamson Etherifications

The Williamson etherification is a standard reaction to synthesize asymmetric ethers from alcoholates, prepared from primary and secondary alcohols or phenols with base, in the presence of primary alkyl halides. Because of the high reactivity of alcoholates, they need to be produced during the reaction by strong bases.

Silia*Bond* TBD (*R68530B*)

Loading: 0.9 mmol/g	Endcapping: Yes	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* TBD (*Si-TBD*)

Silia*Bond* TBD is a silica-bound bicyclic guanidine moiety that is sufficiently basic to deprotonate moderately acidic hydrogens. It is most commonly used in Williamson ether synthesis.

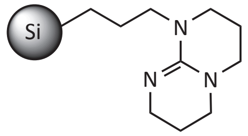
Solvent compatibility

- All solvents, aqueous and organic

Prolonged storage

- Keep cool (< 8°C) and dry, store under argon

TBD (*Si-TBD*)

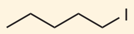
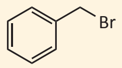
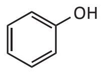
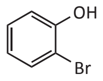
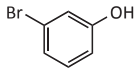
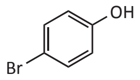
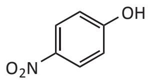
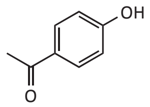
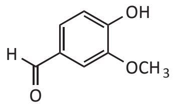
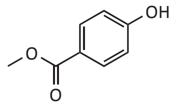
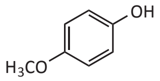


Silia*Bond* TBD for Williamson Etherifications

General procedure

0.15 mmol of alcohol was added to 4 mL of acetonitrile and Silia*Bond* TBD (*0.3 eq.*). The solution was stirred for 1 h at room temperature. Next, 0.12 mmol of the alkyl halide was transferred to the reaction mixture, which was again stirred for 16 h at 60°C. Finally, the mixture was filtered and washed with 2 mL of acetonitrile. Conversion was measured by GC-MS.

Williamson Etherification Results

Alcohol	Alkyl Halide	
		
	83%	89%
	89%	88%
	81%	88%
	80%	80%
	59%	86%
	79%	88%
	87%	94%
	78%	86%
	76%	75%

Silia*Bond* Aluminum Chloride Used as a Catalyst for Friedel-Crafts Alkylations and Acylations

For decades, sulfonated linear alkylbenzenes (*LABs*) have been among the most prolific detergents. LAB synthesis is carried out by Friedel-Crafts alkylation of benzene by linear olefins using hydrogen fluoride or aluminum chloride as catalyst. The use of these catalysts presents severe problems, however. For example, aluminum chloride is difficult to separate after reaction and produces a large amount of waste effluent.

Silia*Bond* Aluminium Chloride (*R74530B*)

Loading: 1.6 mmol/g	Endcapping: No	Category: Reagent	Format: 5g, 10g, 25g, 50g, 100g, 250g, 500g, 1kg, 10kg, 25kg, ..., Multi-Ton

Description

Silia*Bond* Aluminum Chloride (*Si-AlCl$_x$*)

Silia*Bond* Aluminum Chloride is the silica-supported version of the most widely used Lewis acid, aluminum chloride.[1] It is an effective catalyst for Friedel-Crafts alkylations[2-4] and acylations. It also catalyzes the formation of ethers. The silica supported product has several advantages over the free catalyst.[5,6]

- *It is a milder Lewis acid. $AlCl_3$ is so reactive that it often lacks selectivity and causes the formation of unwanted by-products.*
- *The steric bulk of the silica reduces over alkylation and increases shelf life.*

Execution of the reaction is easier. The reagent is removed by a simple filtration, avoiding the destructive water quench which produces large amounts of hazardous waste.

Silia*Bond* Aluminum Chloride's activity can be determined by its color. The material should only be used when it's yellow or violet. The product turns white in presence of moisture.

Solvent compatibility

- All anhydrous organic solvents

Prolonged storage

- Keep cool (< 8°C) and dry, store under argon

Aluminum Chloride (*Si-AlCl$_x$*)

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[1] *Acc. Chem. Res.*, **2002**, *35*, 791

[2] *Org. Process Res. Dev.*, **1998**, *2*, 221

[3] *J. Catal.*, **2000**, *195*, 237

[4] *J. Catal.*, **2000**, *195*, 412

[5] *Chem. Rev.*, **2003**, *103*, 4307

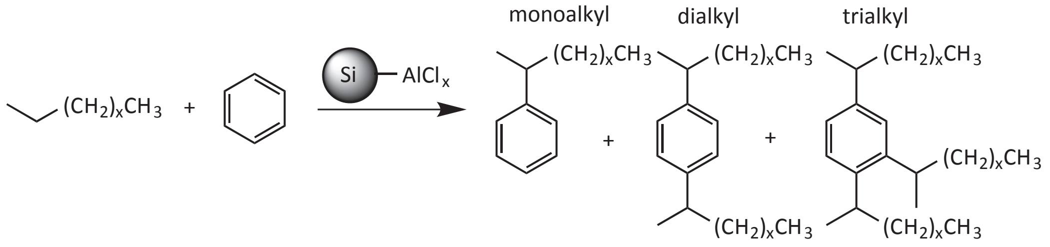
[6] *Tetrahedron*, **2003**, *59*, 1781

Silia*Bond* Aluminum Chloride as a Catalyst for Friedel-Crafts Alkylations

General procedure

Silia*Bond* Aluminum Chloride (*0.03 eq.*) is stirred into anhydrous benzene (*Typical reaction solvent volume: 5 mL/g of SiliaBond Aluminium Chloride*). Add the alkene (*1.0 eq.*) slowly (*a small exothermic reaction should be observed*).

After the addition is completed, remove the catalyst by filtration.



Friedel-Crafts Alkylation Results

Alkene	Catalyst	Alkene Conversion[a]	Selectivity Towards Alkylbenzene		
			% Mono	% Di	% Tri
1-Hexene	$AlCl_3$	100%	58.6	31.1	10.3
1-Hexene	*Si*-$AlCl_x$	100%	71.0	28.0	1.0
1-Decene	$AlCl_3$	100%	68.5	22.5	9.0
1-Decene	*Si*-$AlCl_x$	100%	80.0	20.0	0

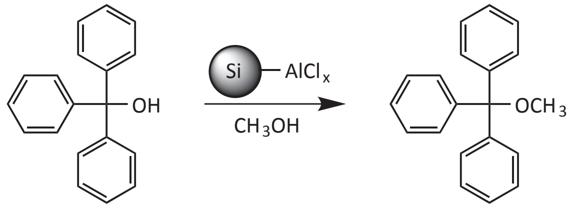
[a] Conversion determined by GC-MS

Silia*Bond* Aluminum Chloride as Catalyst for Friedel-Crafts Acylation

Friedel-Crafts Acylation Results

Alcohol	Catalyst	Conversion[a]
Triphenylmethanol	*Si*-$AlCl_x$	95%
	Polymer-$AlCl_3$	81%
Tert-Butyl Alcohol	*Si*-$AlCl_x$	60%
	Polymer-$AlCl_3$	0%
Benzyl Alcohol	*Si*-$AlCl_x$	40%
	Polymer-$AlCl_3$	0%

[a] Conversion determined by ^{1}H NMR



Silia*Bond* Reagents and Scavengers for Typical Coupling Reactions

Coupling Reactions

Reaction	Reagent / Scavenger
Amide Coupling	
with acid chlorides and amines	Silia*Bond* Carbodiimide
with acids and amines	Silia*Bond* Dichlorotriazine Silia*Bond* Amine (scavenger) - removes excess acid chloride Silia*Bond* Isocyanate/Silia*Bond* Tosic Acid - remove excess of amine
using HOBt or pentafluorophenol	Silia*Bond* Carbonate - removes excess of HOBt
Buchwald Amination	Silia*MetS* Metal Scavengers - remove palladium Silia*Bond* Tosic Acid
Heck Coupling	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*) Silia*MetS* Metal Scavengers - remove palladium
Sonogashira Coupling	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*) Silia*MetS* Metal Scavengers - remove palladium, copper
Stille Coupling	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*) Silia*MetS* Metal Scavengers - remove palladium, tin
Suzuki Coupling	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*) Silia*Bond* Carbonate - removes excess of boronic acid Silia*MetS* Metal Scavengers - remove palladium
Kumada Coupling	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*) Silia*MetS* Metal Scavengers - remove metal residue
Negishi Coupling	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*) Silia*MetS* Metal Scavengers - remove metal residue

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Silia*Bond* Reagents and Scavengers for Common Organic Reactions

Common Organic Reactions

Reaction	Reagent/Scavenger
Acylation/Esterification	Silia*Bond* DMAP Silia*Bond* TBD
Deprotection of Aromatic Ether	Silia*Bond* Tosic Acid
Ether formation	Silia*Bond* Aluminium Chloride (*catalyst*) Silia*Bond* Tosic Acid Silia*MetS* Metal Scavengers - remove metal catalyst
Fmoc, Bsmoc Deprotection of Amino Acid	Silia*Bond* Piperazine (*reagent / scavenger*) - Fmoc deprotection
Friedel-Crafts Alkylation	Silia*Bond* Aluminium Chloride
Fries Rearrangement	Silia*Bond* Tosic Acid
Knoevenagel Condensation	Silia*Bond* Amine Silia*Bond* Dimethylamine Silia*Bond* TBD Silia*Bond* Piperidine Silia*Bond* Piperazine
Michael Addition	Silia*Bond* Dimethylamine Silia*Bond* TBD Silia*MetS* Metal Scavengers - remove metal catalyst
Oxidation	
alcohols to acids	Silia*Bond* Potassium Permanganate
alcohols to ketones or aldehydes	Silia*Cat* TEMPO Silia*Bond* Pyridinium Chlorochromate (PCC) Silia*Bond* Pyridinium Dichromate (PDC)
alkanes	Silia*Bond* Dimethylamine
Reduction	
with borohydride reducing agents	Silia*Bond* Tosic Acid - removes excess and spent borohydride
Reductive Amination	Silia*Bond* Cyanoborohydride Silia*Bond* Tosic Acid - removes excess of amine
Sulfonamide Synthesis	Silia*Bond* Dichlorotriazine Silia*Bond* EDC Silia*Bond* Amine - removes excess of sulfonyl chloride
Tosylate Formation	Silia*Bond* Tosyl Chloride
Urea Synthesis	Silia*Bond* Amine - removes excess of isocyanate
Williamson Ether Synthesis	Silia*Bond* TBD
Grubbs Metathesis	Silia*MetS* Metal Scavengers - remove ruthenium
Sharpless Dihydroxylation	Silia*MetS* Metal Scavengers - remove osmium
Catalytic Hydrogenation	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*)/ Silia*MetS* Metal Scavengers - remove metal catalysts
Cyanation	Silia*Cat* DPP-Pd, Silia*Cat* S-Pd and Silia*Cat* Pd^0 (*catalyst*)/ Silia*MetS* Metal Scavengers - remove metal catalysts
Hydrogenation	Silia*Cat* Pt^0 (*catalyst*)
Debenzylation of Benzyl protected Groups	Silia*Cat* Pd^0 (*catalyst*)
Hydrosilylation	Silia*Cat* Pt^0 (*catalyst*)