



Supra Sciences

Solid-Supported Reagents & Scavengers- Applications

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Who Are We?

We are a team of chemists providing high quality solid supported reagents and scavengers for organic synthesis and purification, resins for peptide synthesis and custom resins for your personalized applications

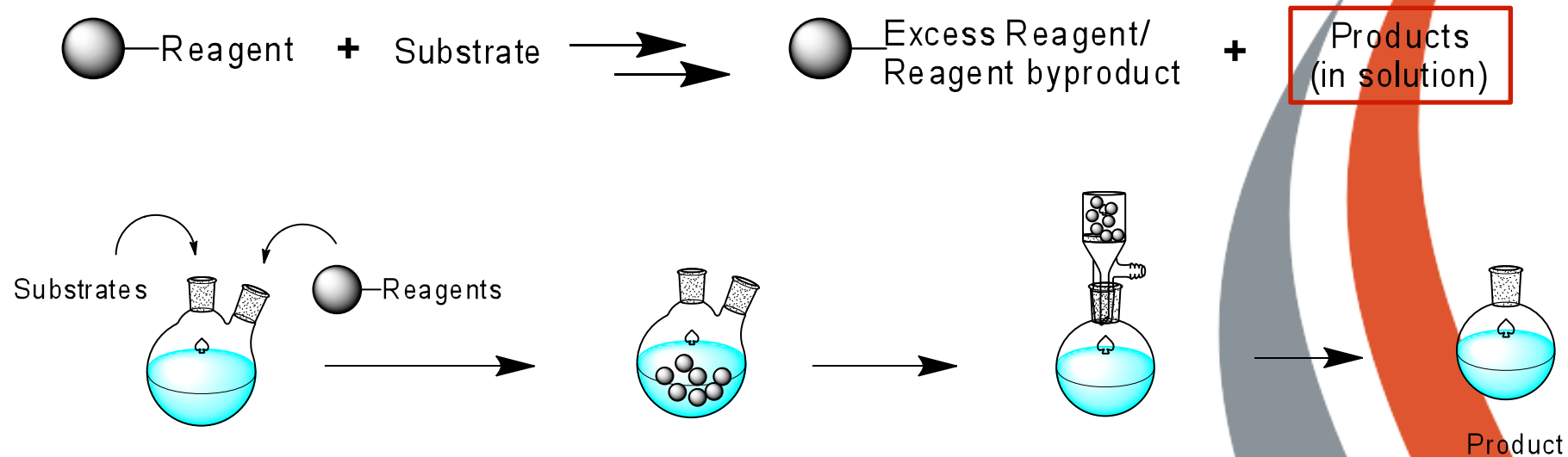
- Incorporated both in the SF Bay Area, California, USA & Hyderabad, India
- Strong scientific background of the tech team
 - More than 20 yrs of Med & Organic Chemistry experience in Biotech and Pharma
 - Industry expert in production and utilization of polymer supported reagents and scavengers.

Why Solid Supported Materials?

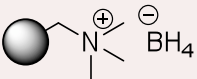
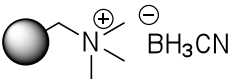
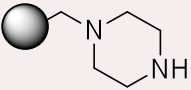
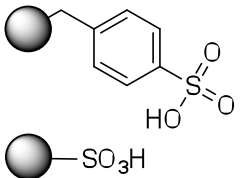
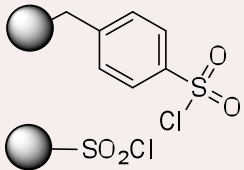
- Perform the same reactions as a solution phase reagent.
- Equivalent stability and storage conditions.
- Potential toxic artifacts remain on solid support minimizing safety issues.
- Eliminates the tedious and risky aqueous work-up procedures.
 - Option 1: Simple catch/release procedures isolate only products.
 - Option 2: SPE provides desired product by simple filtration.
- Increased simplicity and speed result in increased efficiency.
- Significant cost savings:
 - Time
 - Energy
 - Materials
 - Waste

Reagents

Solid Supported **Reagent** Assisted Synthesis

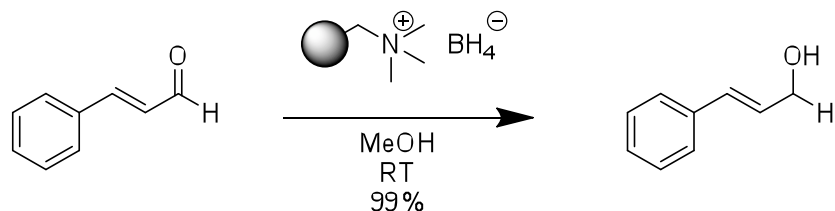


Reagents

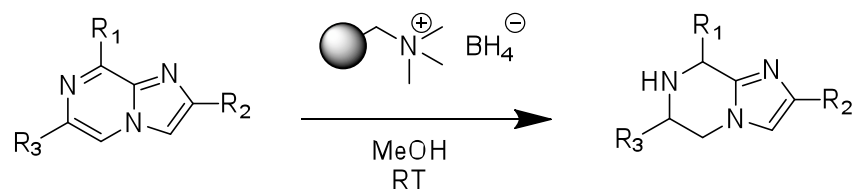
Reagent	Structure	Application
Borohydride		Reduction of carbonyls and Schiff bases.
Cyanoborohydride		Reductive aminations
Piperizine		Knovoenagel, Vilsmeier and Mannich
Sulfonic Acid		PG cleavage, acid catalysis
Sulfonyl Chloride		Alcohol activation, protecting group

Reduction Examples

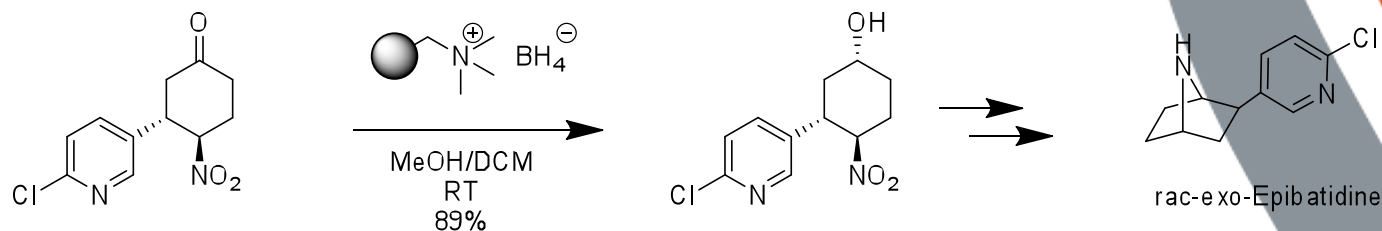
Standard reduction



Somatostatin receptor agonists

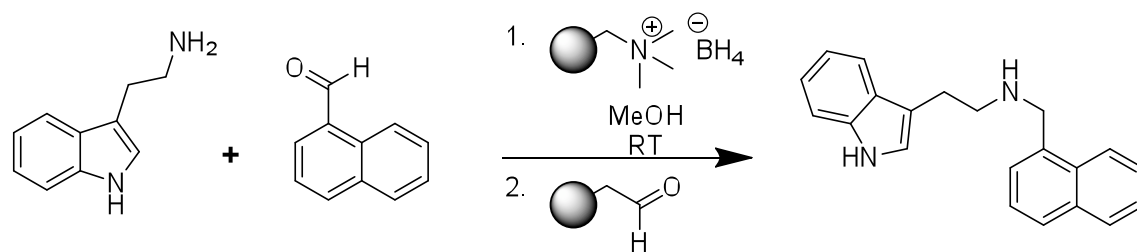


Epibatidine

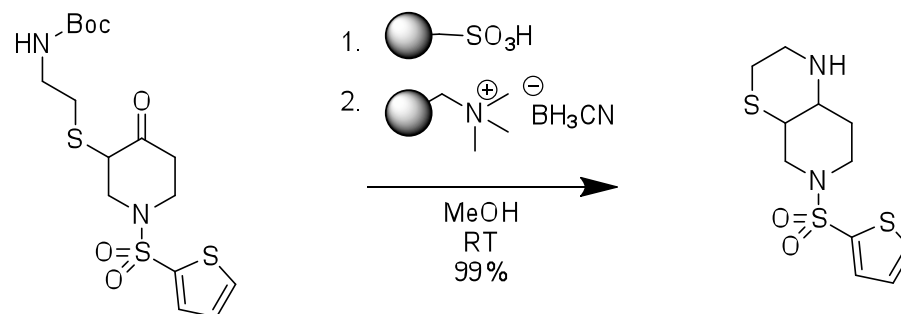


Reductive Aminations

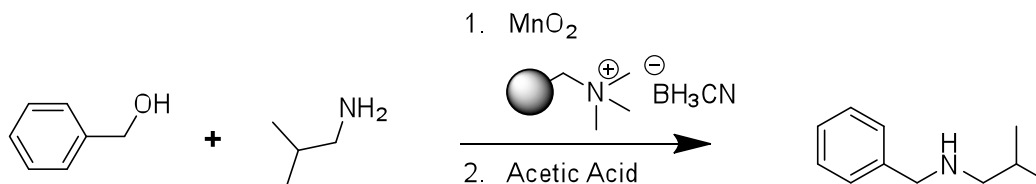
Oxomaritidine



Tandem

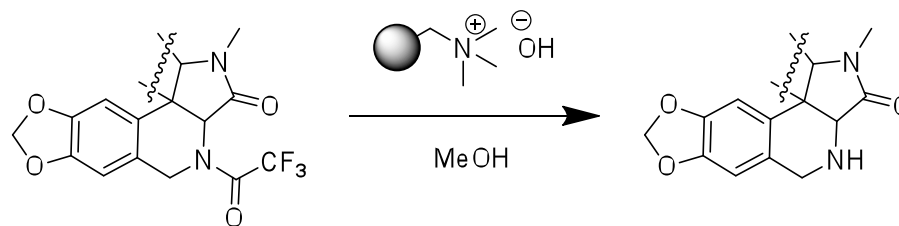


Combination

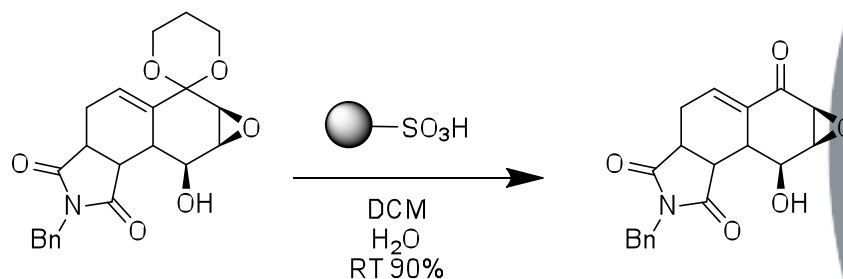


Protection/Deprotection

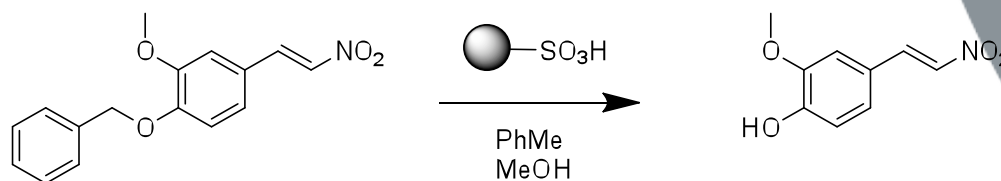
Trifluoroacetamide Removal



Ketal deprotection

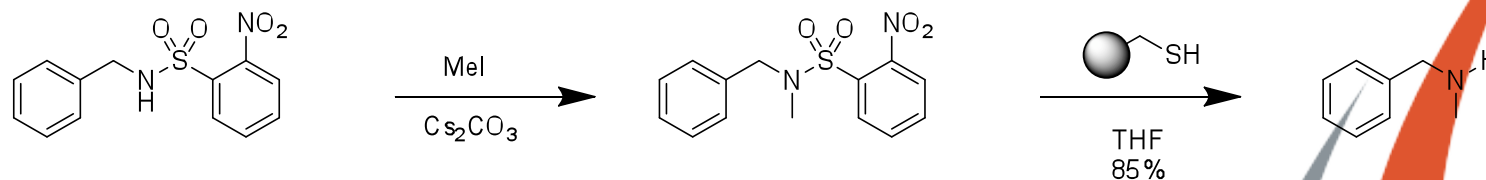


Benzyl ethers

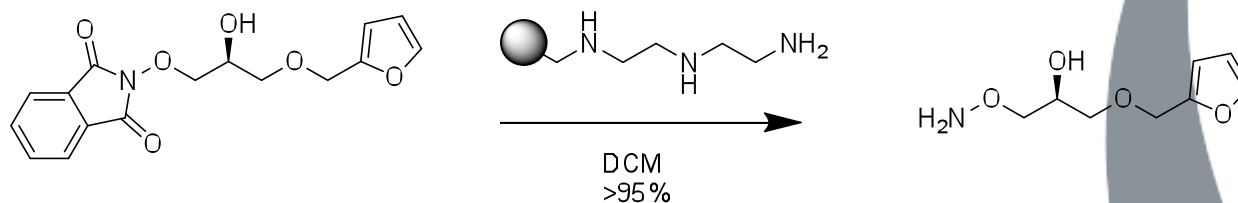


Protection/Deprotection

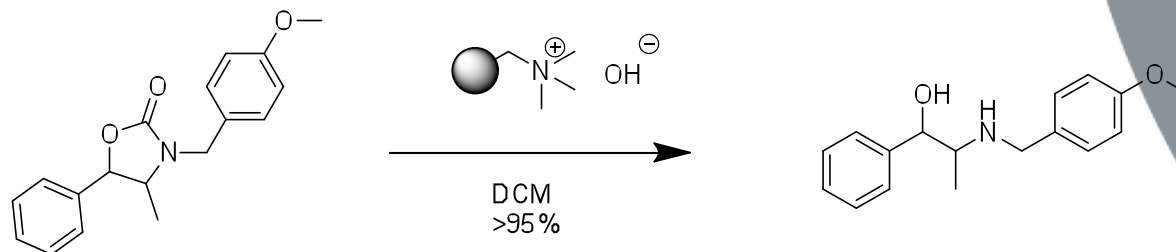
Amine Mono-alkylation



Oximes as antimicrobial mimics

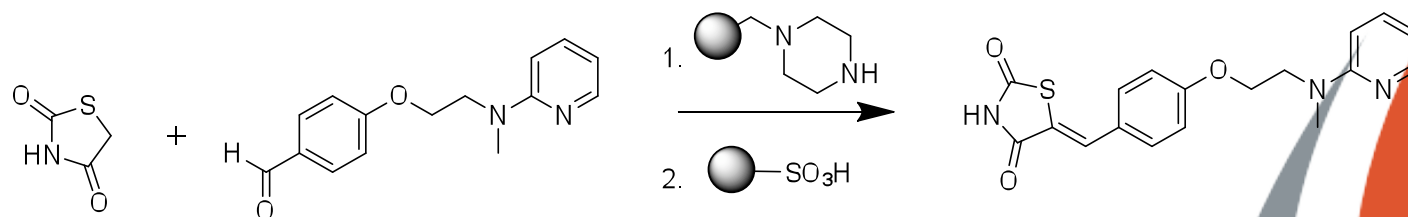


Amino Alcohols

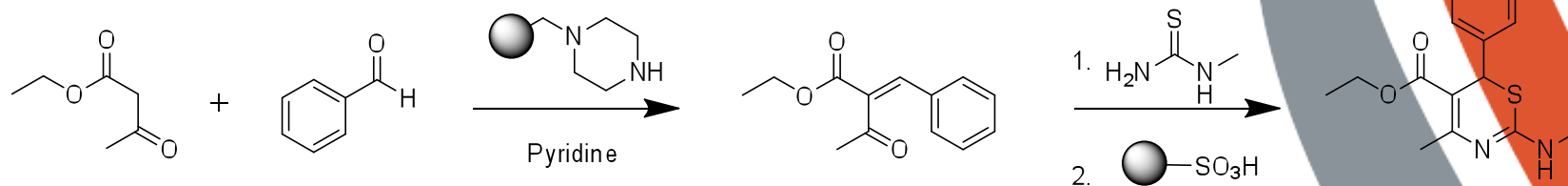


Knoevenagel

Rosiglitazone

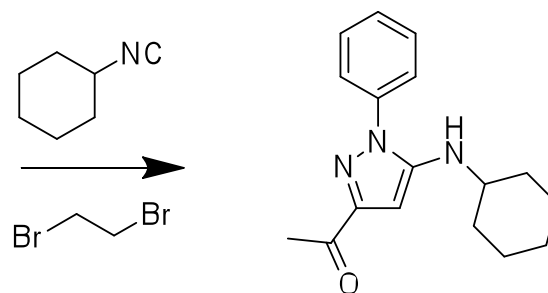
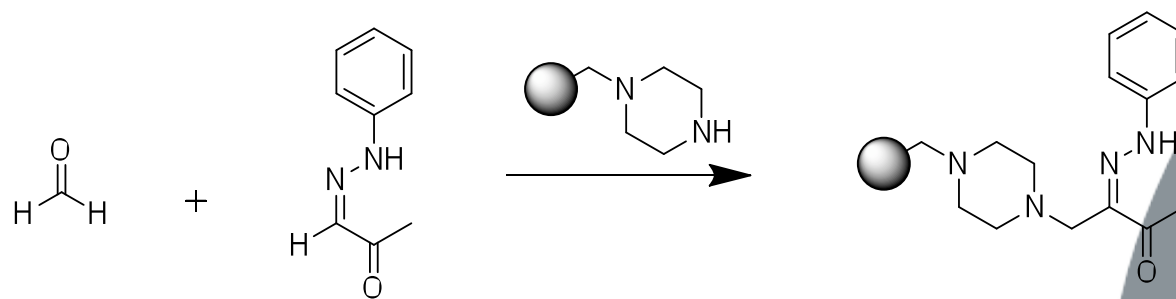


Substituted Thiazines



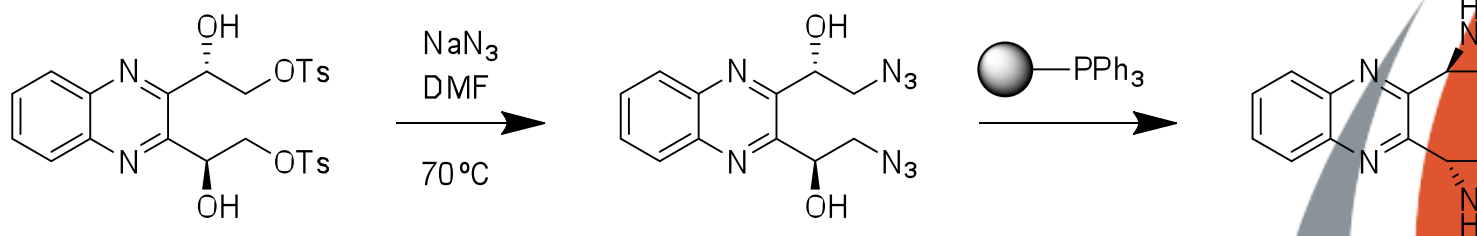
Mannich

Substituted Aminopyrazoles

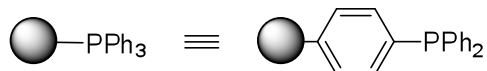
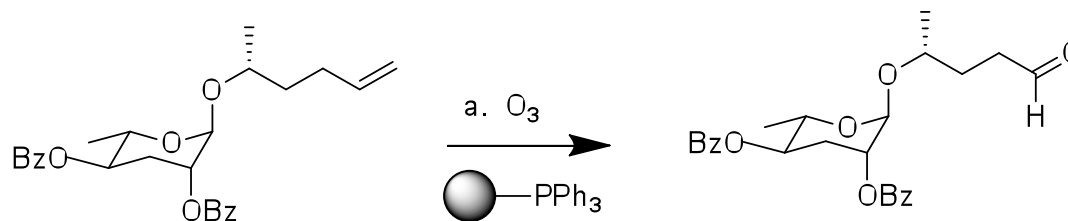


Staudinger and Ozonolysis

Glycosidase inhibitors

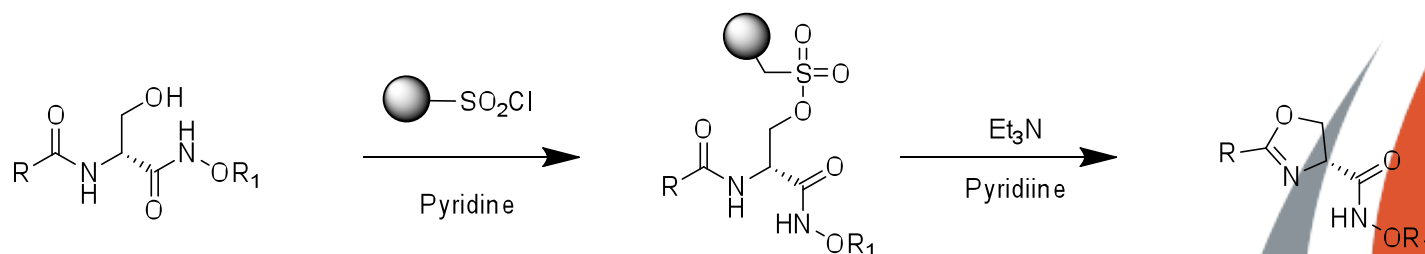


Nematode larvae killer

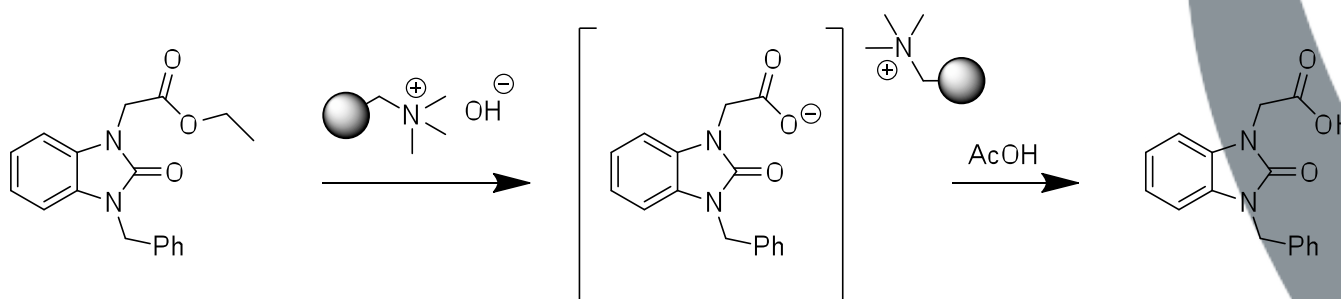


Combination Uses

Antibacterials

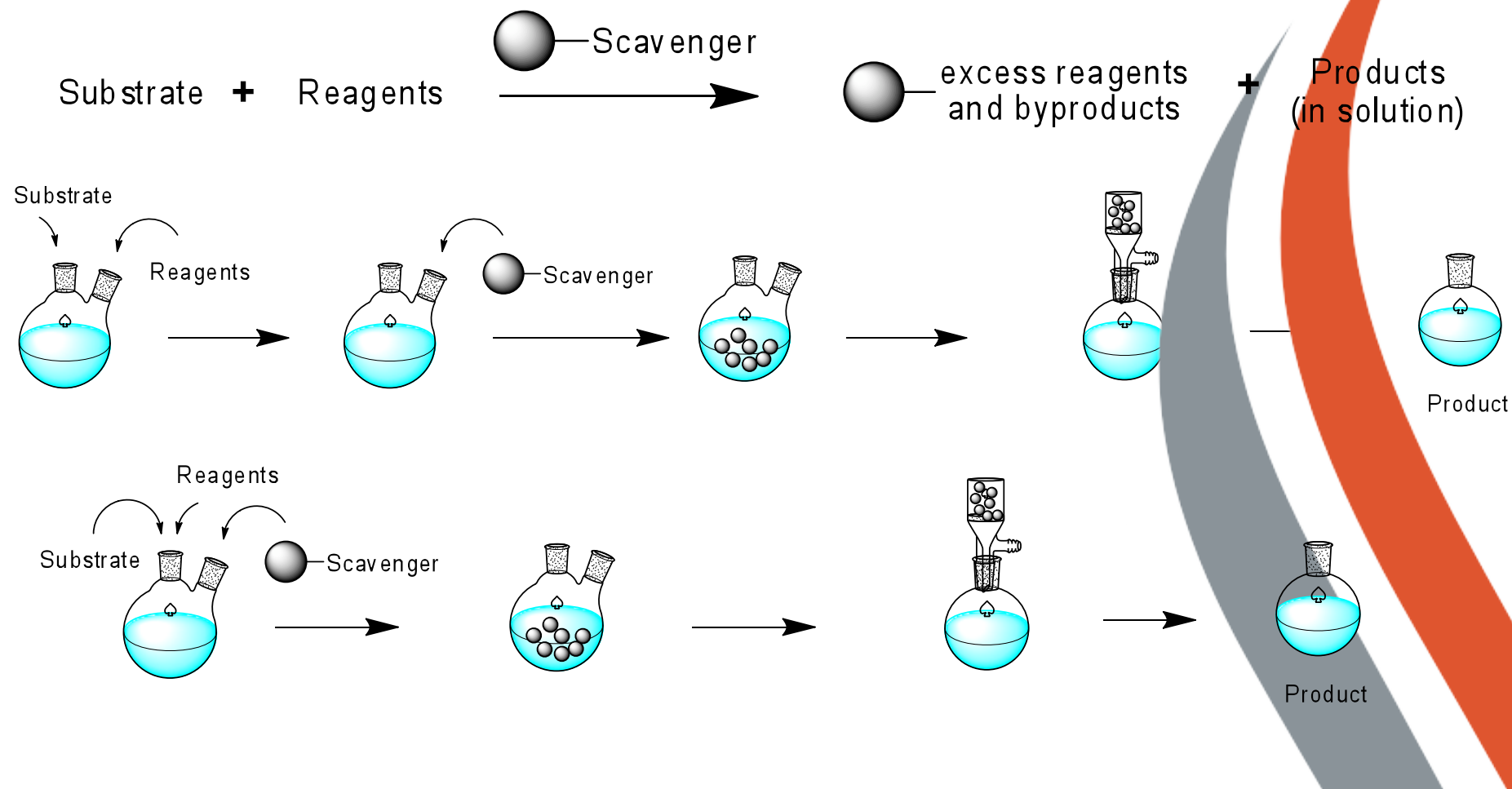


Aldose reductase inhibitor



Scavengers

Solid Supported Scavenger Assisted Synthesis



Scavengers

Base/Nucleophile

Reagent	Structure
Aldehyde	
Carboxylic Acid	
Isocyanate	
Sulfonic Acid	
Sulfonyl Chloride	

Acid/Electrophile

Reagent	Structure
Carbonate	
DIEA	
Hydroxide	
Morpholine	
Sulfonyl Hydrazide	
TEA	
TRIS	

Metals

Reagent	Structure
DEAM	
Thiol	
Thiourea	
TMT	
TRIS	

Scavenging – Metals

	Ag	Au	Co	Cu	Fe	Pb	Hg	Ni	Pd	Pt	Rh	Ru	Ti	Al	Sn	Zn
Triphenylphosphine									★		★	★				
Diethanolamine				★	★								★	★	★	
Thiol/Thiophenol	★	★		★		★	★	★	★		★	★			★	
Thiourea	★	★		*			★		★		★				★	
TMT/DMT	★	★					*	★	★	★	★	★			★	
Trisamine			★	★	★	★		★	★	★	★	★				★

Scavenging - Acids

HPLC fractions

Issue :

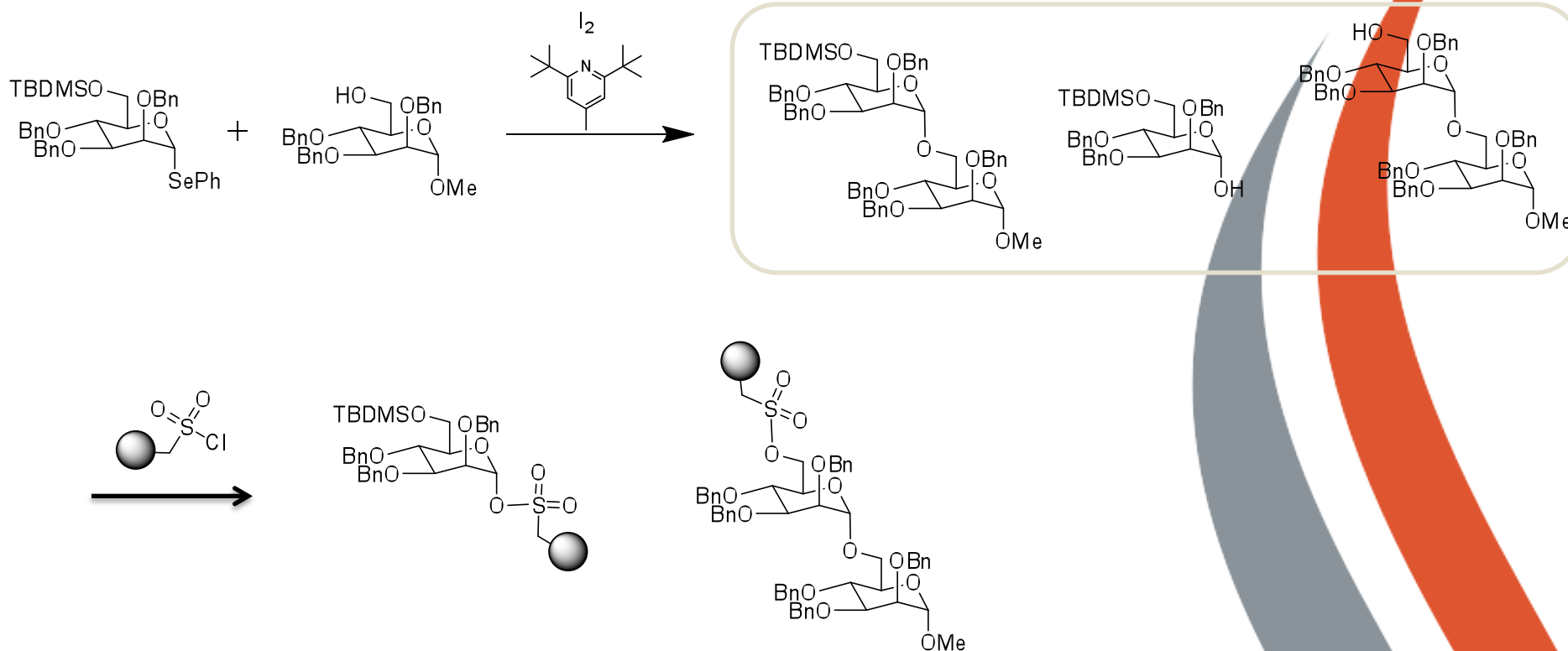
- CH₃CN/Water with TFA or Formic Acid buffers
- Lyophilization of TFA salts produces difficult to manage solid.
- Formic acid converts to formamide over time.
- Material decomposition and long term storage is a concern.

Solution :

- Freebasing fractions with MP-Carbonate.
- No loss of material in water layer during aqueous neutralization.
- Product integrity maintained over time.

Scavenging - Alcohols

Carbohydrates

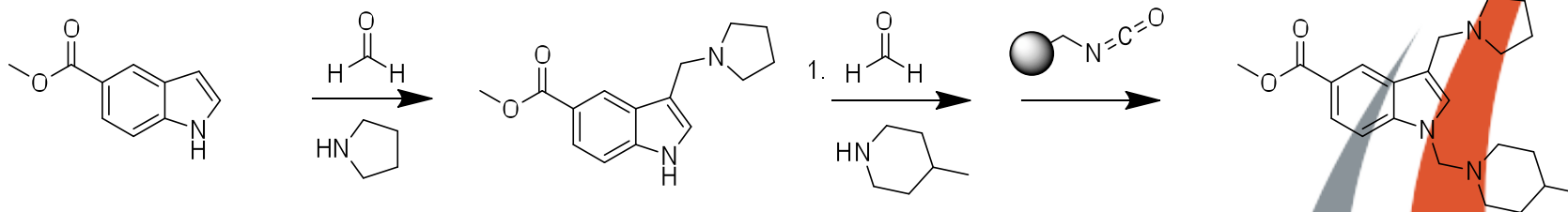


Byproducts are simply removed by filtration leaving only desired ether behind. Sulfonyl Chloride can be used to scavenge alcohols.

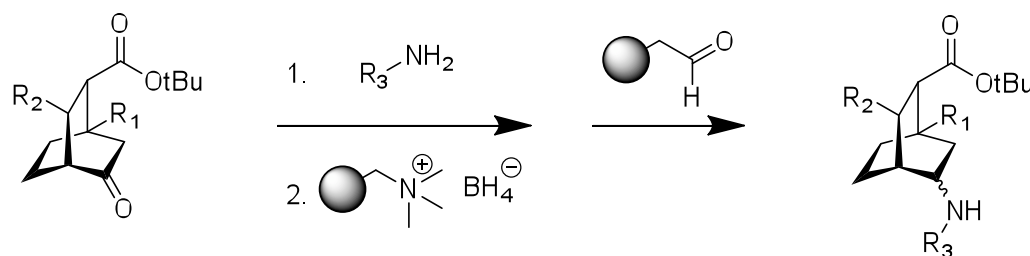
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Scavenging - Amines

Mannich Rxn

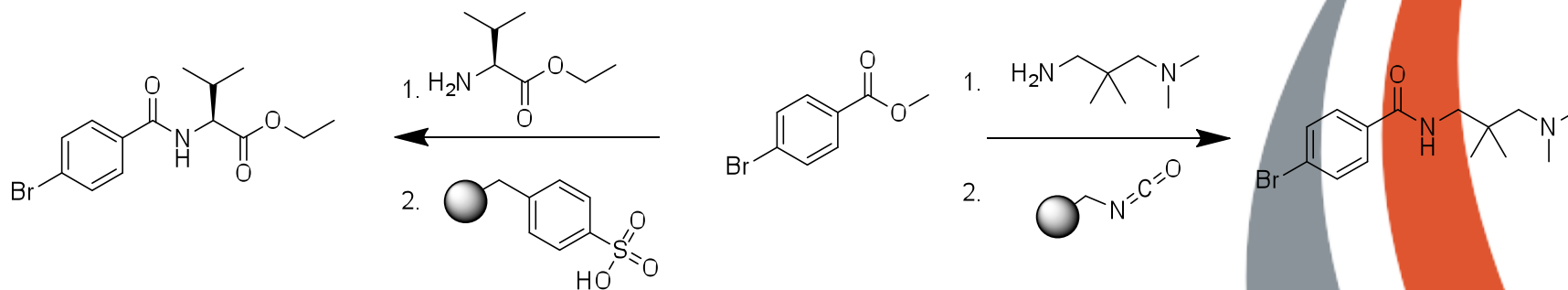


Reductive Aminations



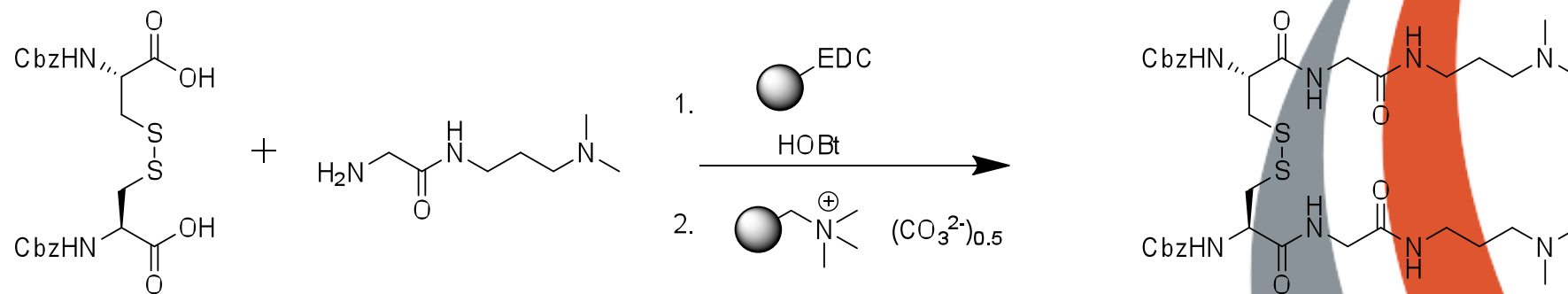
Scavenging - Amines

Amide Formation



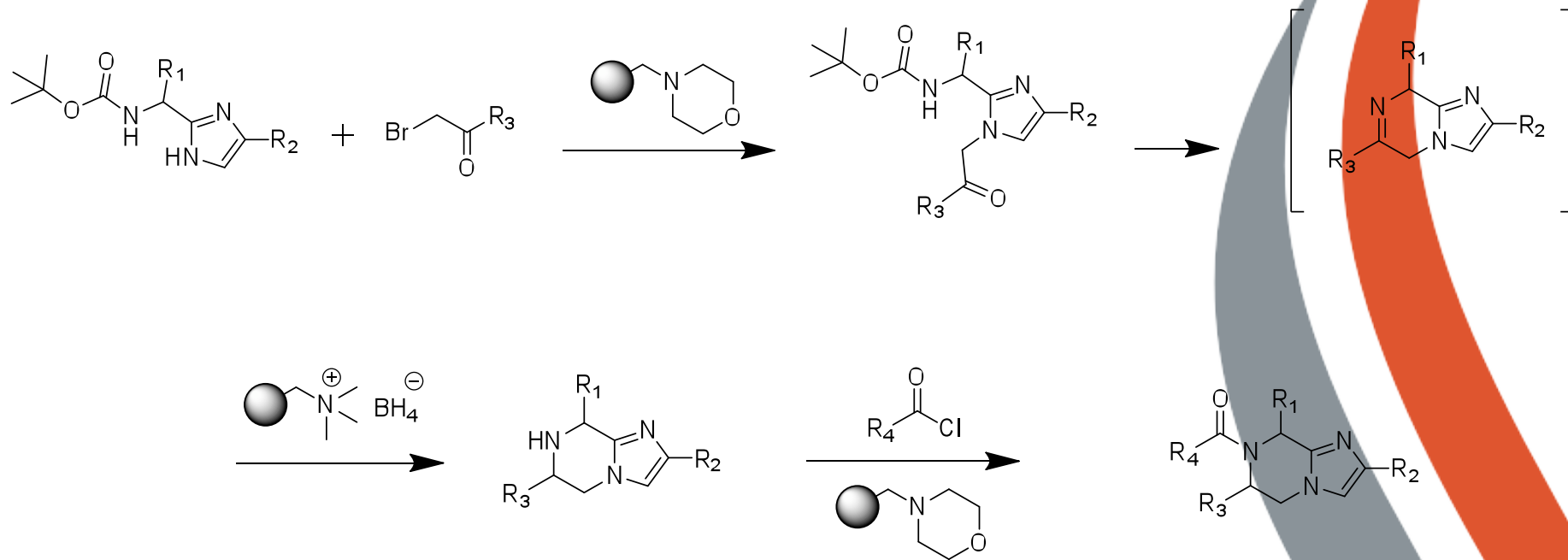
Scavenging – Amide Coupling

HOBt Removal



Scavenging – Acid byproduct

Human Somatostatin Receptor Subtype 5



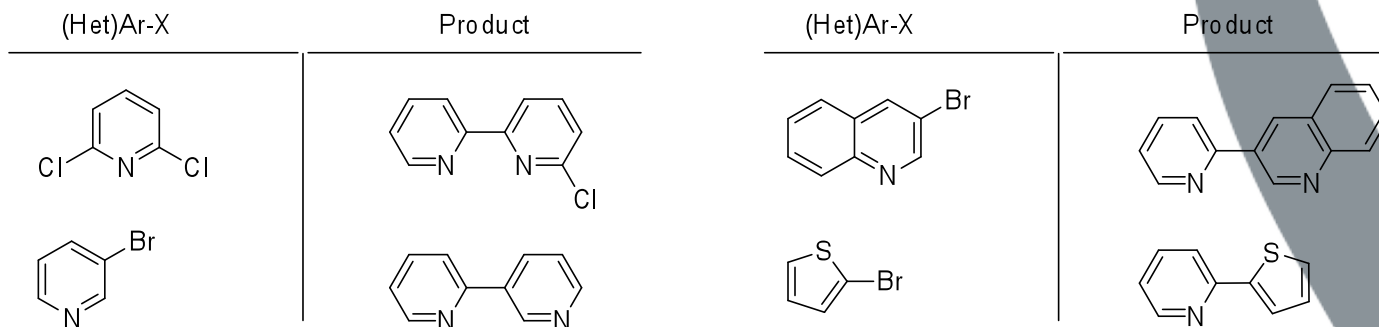
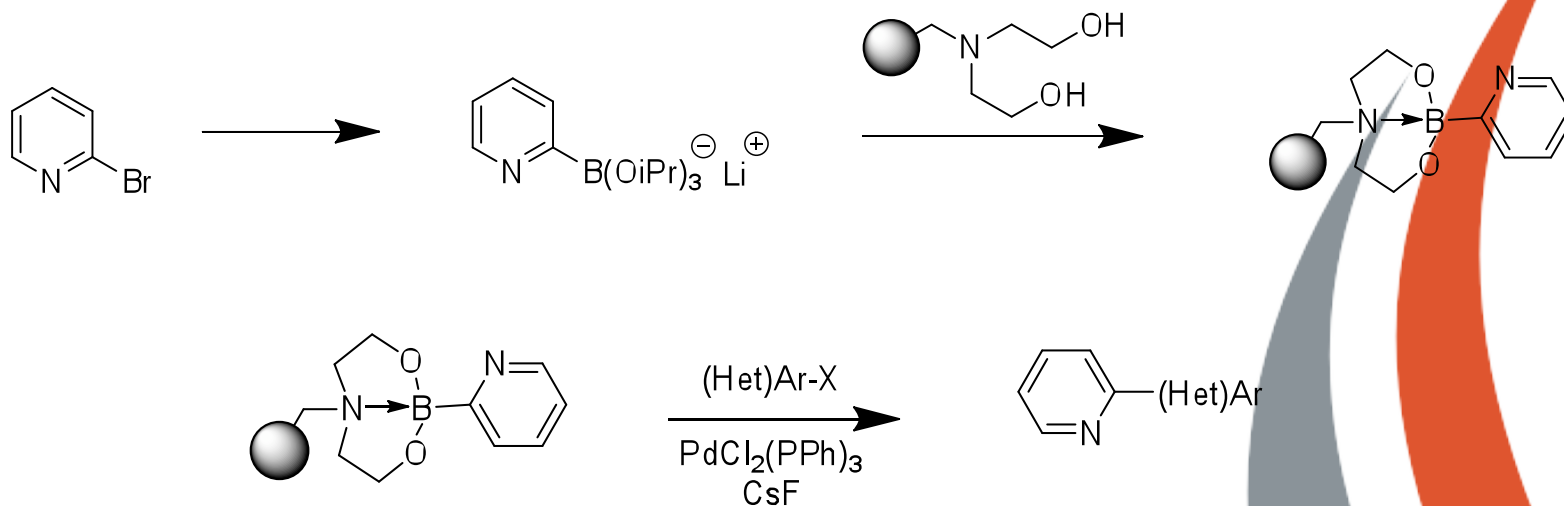
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Contour-Galerera, M.-O. *Bioorg. Med. Chem. Lett.* 2001, 11, 741-745

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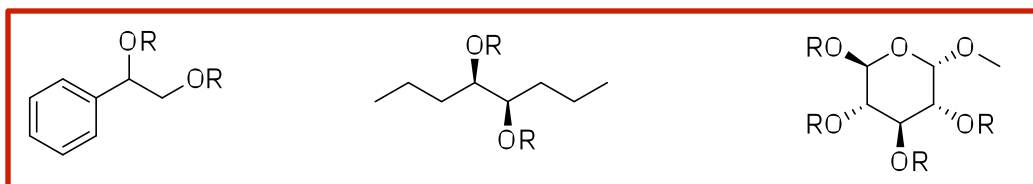
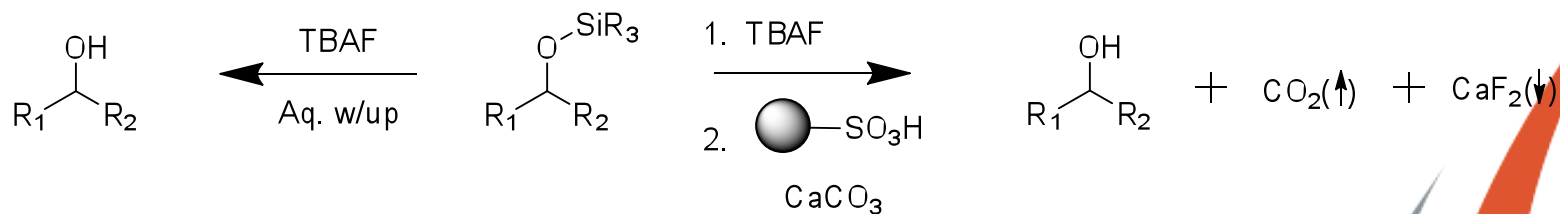
Scavenging – Boronic Acid

Boronic Acids

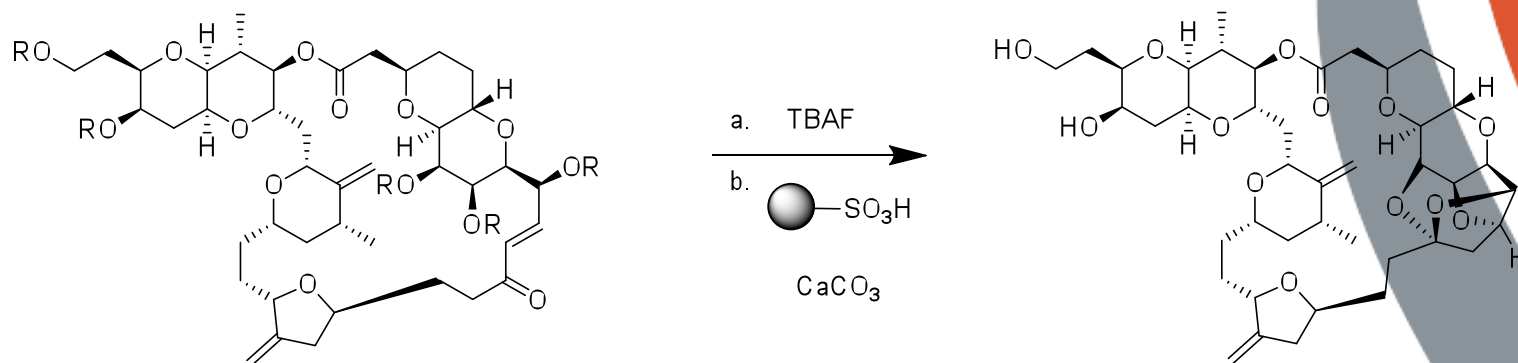


Scavenging – TBAF

TBAF




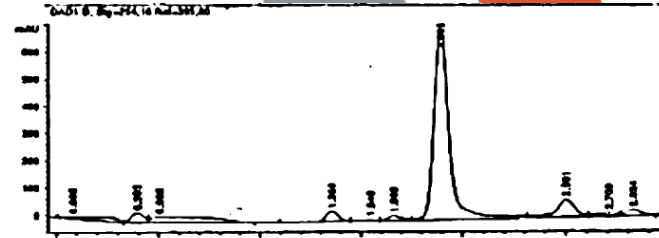
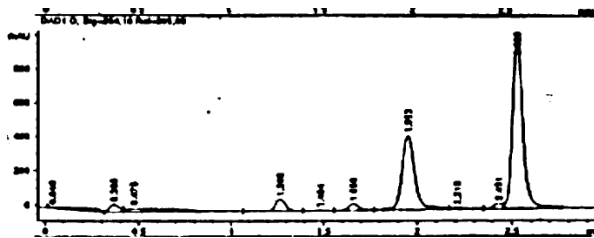
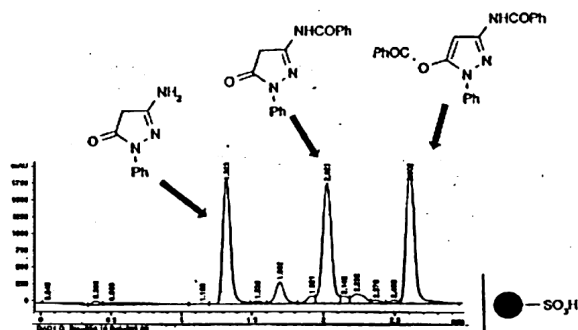
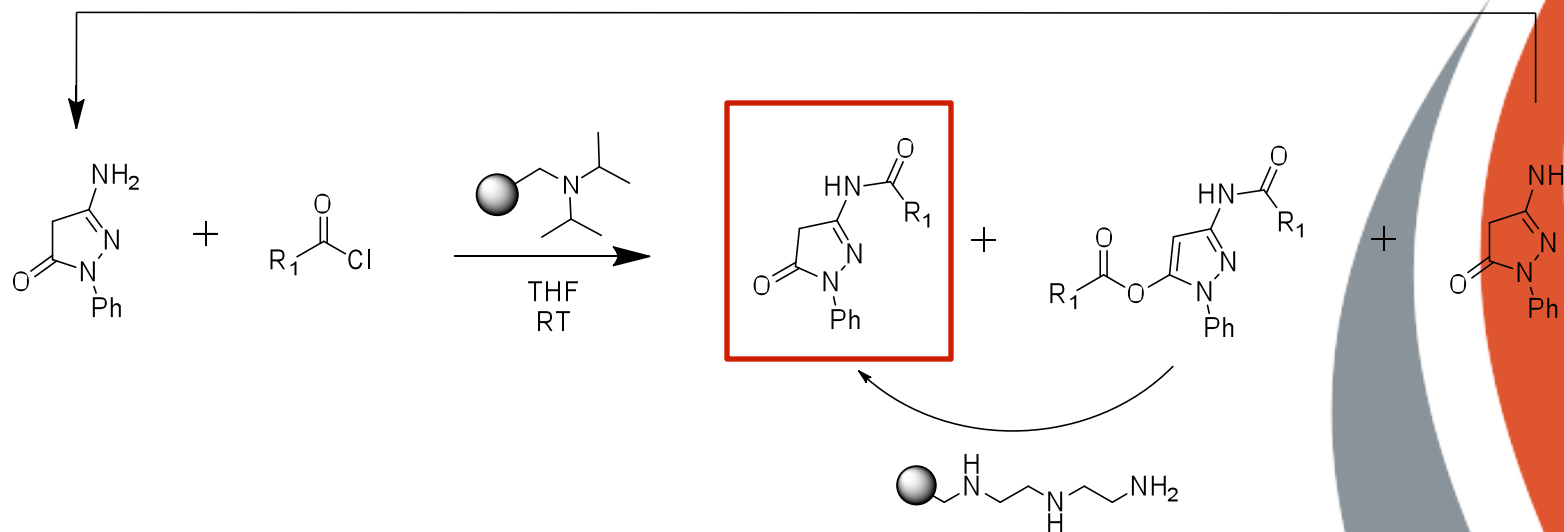
Halichondrin's



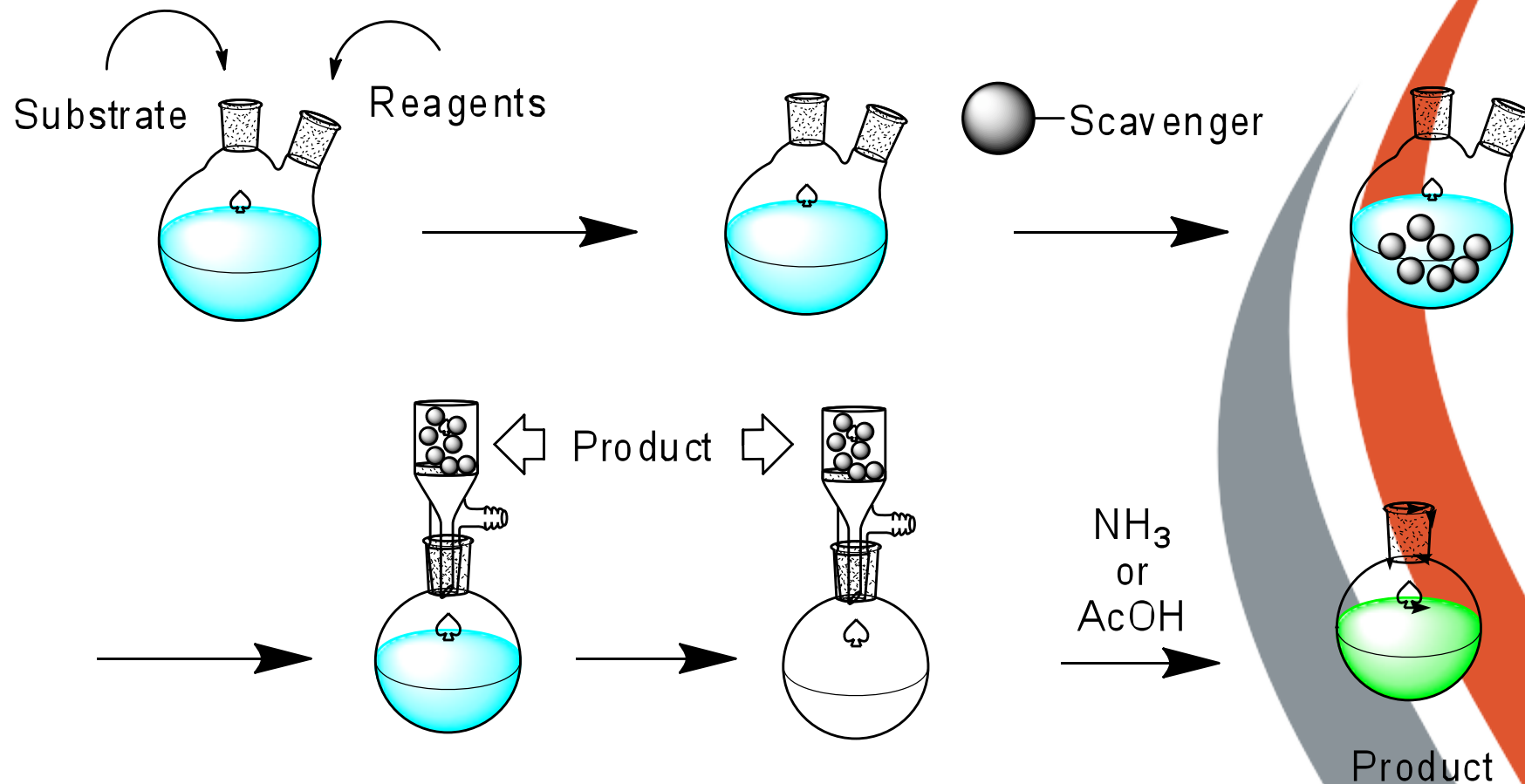
Medchem– Acid Chlorides

Managing byproducts

1. -SO₃H
2. NH₃/EtOH

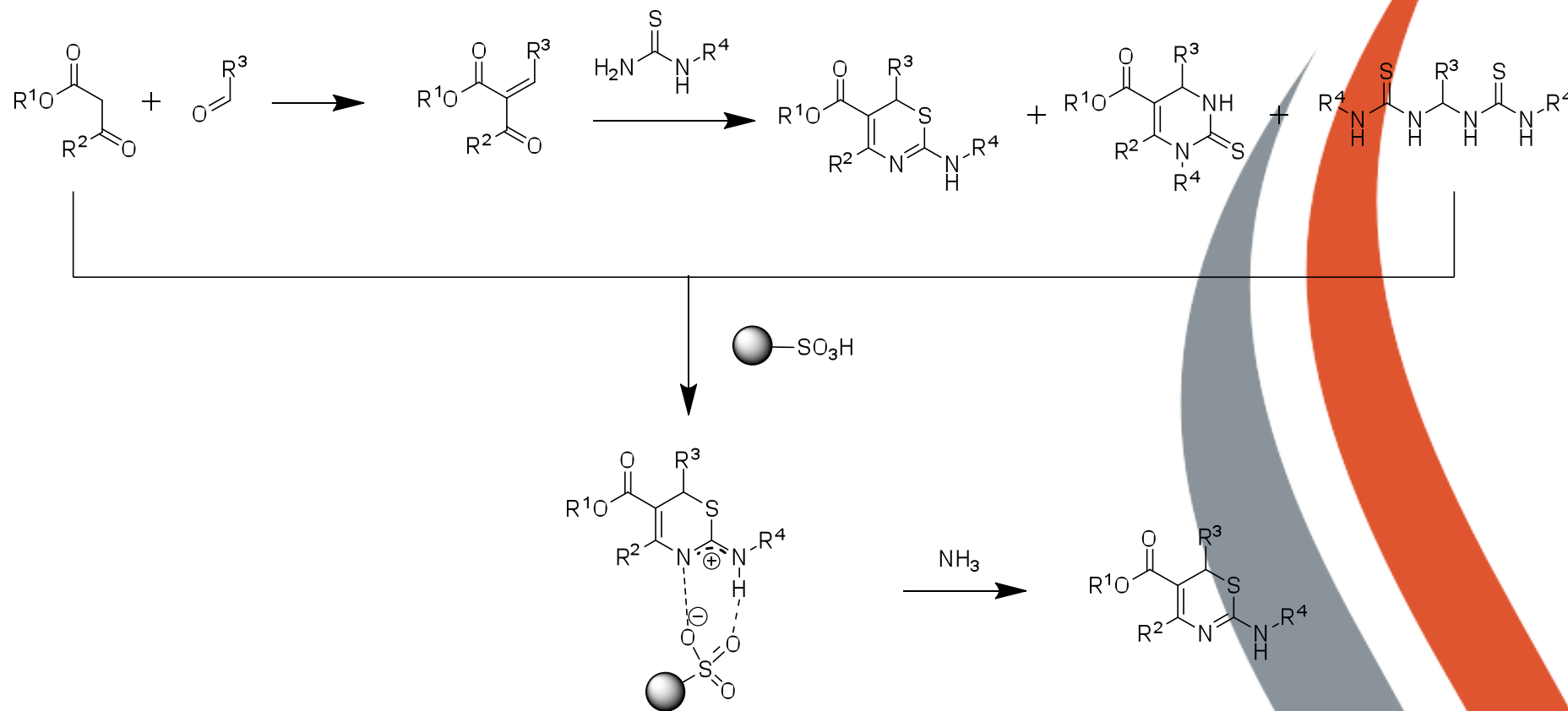


Catch and Release



Catch and Release

Thiazine Library



SPOS: Chemistry on Beads

Solid Phase Organic Synthesis: General Considerations

- Bead Size :
- Resins comprise of a distribution of bead sizes
 - 100 – 200 mesh most common
 - 200 – 400 mesh also used
 - Larger beads display sluggish reaction
 - Fines may plug frits

- Resin matrix :
- Inert carrier of a synthetic substrate
 - Polystyrene matrix most popular solid support
 - Lightly cross-linked with 1-2% DVB

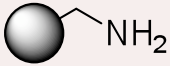
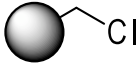
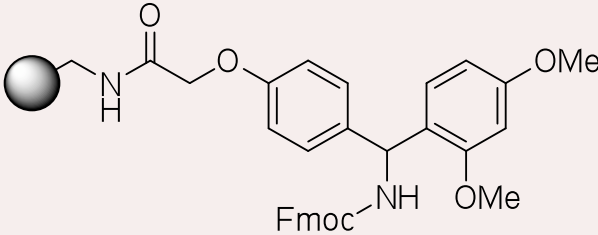
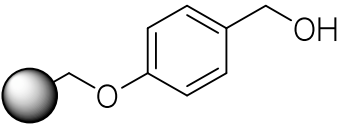
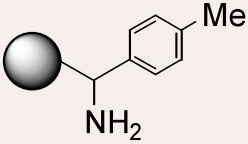


SPOS: Chemistry on Beads

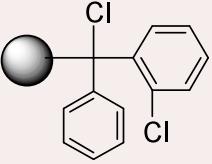
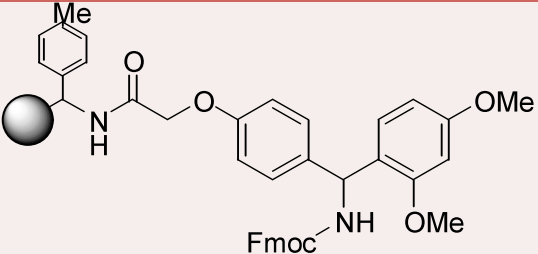
Solid Phase Organic Synthesis: Chemistry Considerations

- Chemistry on beads requires diffusion of reagents into the beads
- Resin swelling is important to achieve diffusion of reagents
- Swollen polymers are like reaction solvents in SPOS
- The micro-environment associated with the neighboring polymer may affect a reaction
- Low loaded functional resins typically provide better results with longer sequences

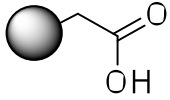
SPOS: Supra Peptide Resins

Resin	Structure	Bead Size
Aminomethyl (AM)		100-200 mesh 200-400 mesh
Merrifield		100-200 mesh 200-400 mesh
Rinkamide AM		100-200 mesh 200-400 mesh
Wang		100-200 mesh 200-400 mesh
MBHA		100-200 mesh

SPOS: Supra Peptide Resins

Resin	Structure	Bead Size
2-CTC		100-200 mesh
2-CTC-Amino Acid (AA)	2-CTC-AA	100-200 mesh
Rinkamide MBHA		100-200 mesh
Rinkamide MBHA-Amino Acid	Rinkamide-MBHA-AA	100-200 mesh
Wang Resin-Amino Acid	Wang-AA	100-200 mesh

Supra Peptide Purification Tools

Resin	Active Functionality	Application
Reverse-Phase Silica	C-18, C-8 and C-4	Hydrophobic silica for Peptide purification
MP-Carboxylic Acid		Weakly acidic resin suitable for affinity chromatography
Basic Resins	Carbonate, Hydroxide, Triethylamine	Neutralization and pH adjustment to your desired levels
Anion-Exchange resins	Acetate, Chloride, Sulfate	Exchange to your desired anions
Cation-Exchange Resins	Sulfonic Acid	SPE, Strong cation exchange

Thank You

Thank You