

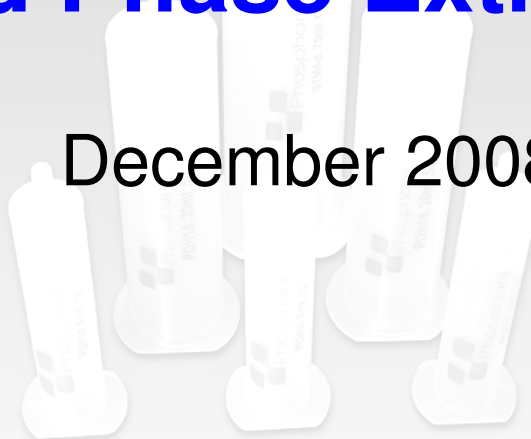
46 Rh Rhodium 102.905	Palladium	47 Ag Silver 107.868
78 Pt Platinum	79 Au Gold	



Novel Functionalised Silicas for Medicinal Chemistry Applications

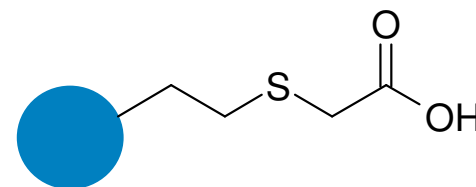
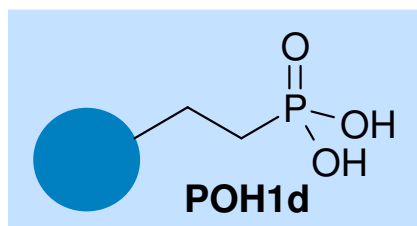
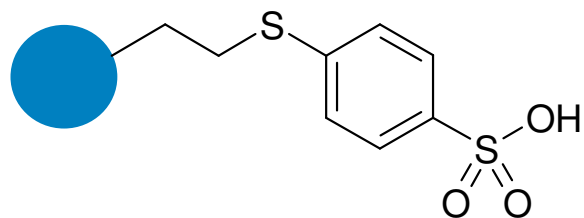
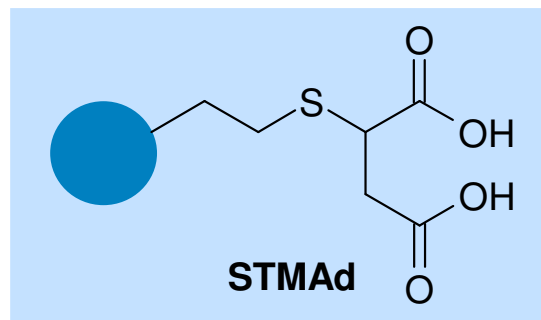
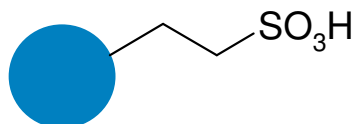
Solid Phase Extraction

December 2008



SPE : SCX 'Catch & Release' Portfolio

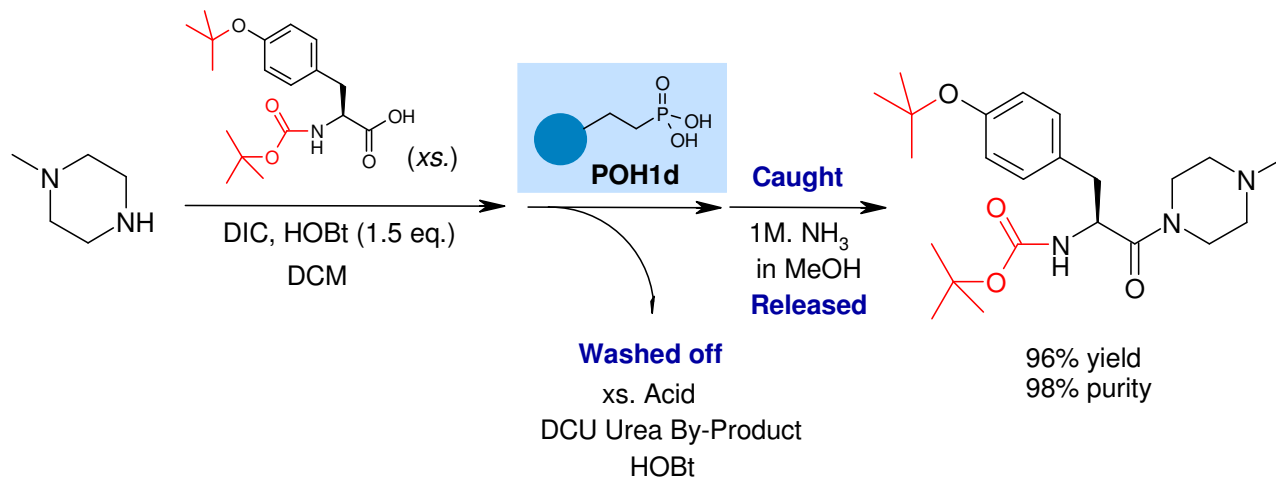
Increased Acidity
Lower pKa



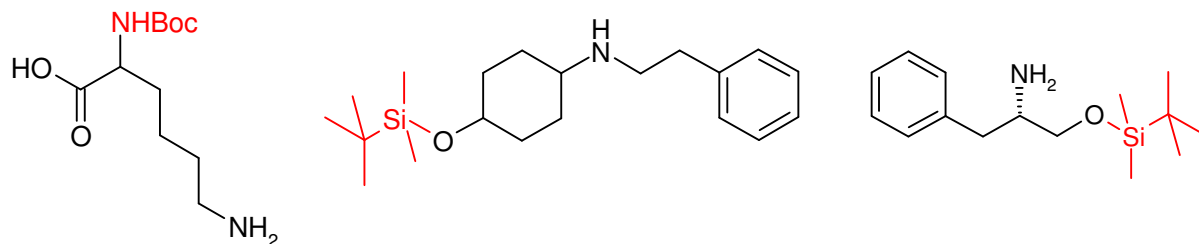
PhosphonicS™ acidity-modified cation exchange materials offer...

- Selective separations of basic materials
- Increased sensitivity to acid-labile groups
- Easier & high-yielding purifications
- Isolation of basic (*catch and release*) and non-basic (*not retained*) compounds
- Accelerated reaction work-ups

SPE - No Loss of Acid-Sensitive PGs

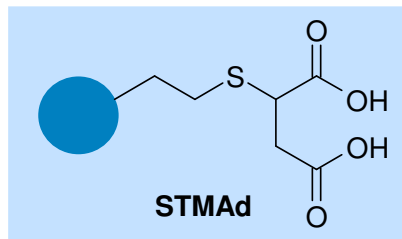
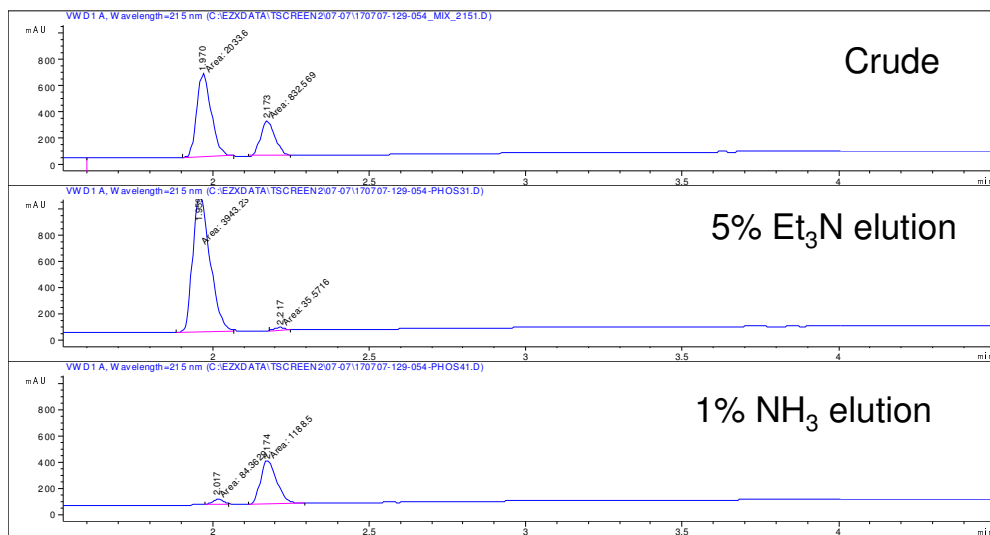
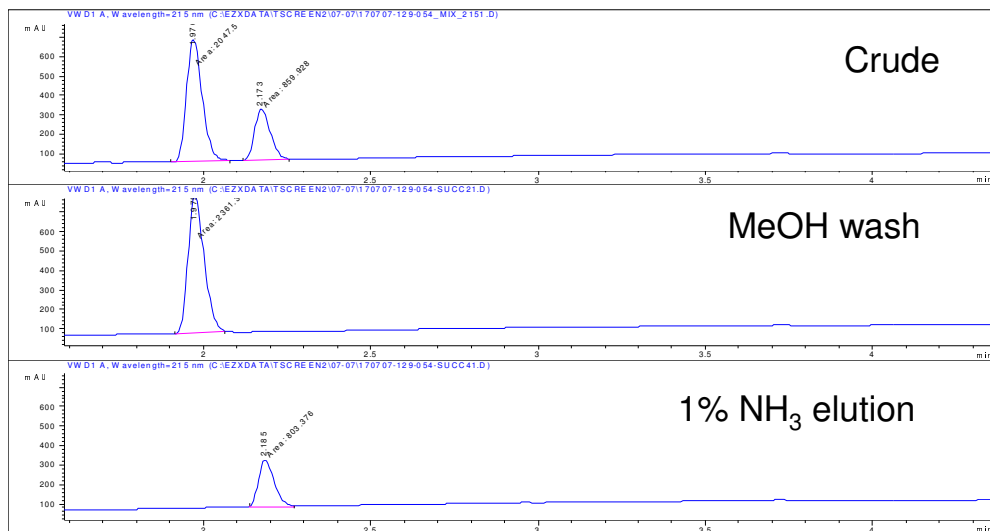
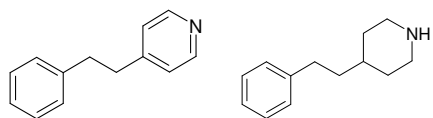


- Use of commercial SCX sulfonic acids causes removal of acid-sensitive groups
- No PG cleavage observed with phosphonic acid **POH1d**
- Further products isolated in high yield & purity with tailored SCX materials



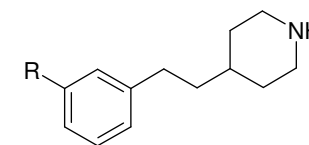
- Now successfully utilised for purification of a variety of highly-functionalised molecules including carbohydrates, iminosugars and heterocycles

Selective Separations of Basic Heterocycles



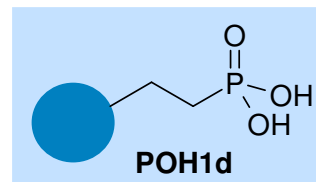
Catch & release

Retains solely



R = H or CO₂H

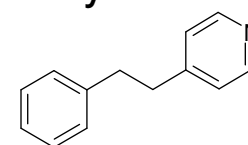
Compound Recovery : >95%



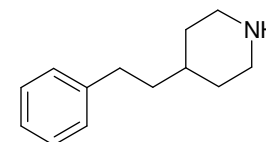
Catch : Selective elution

Both piperidine and pyridine retained, but selectively eluted

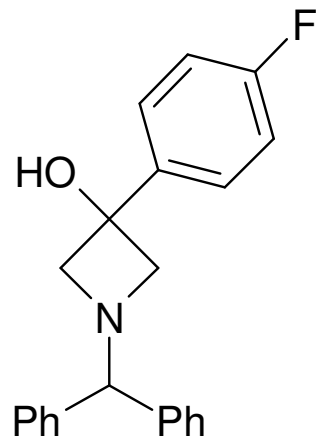
5% Et₃N / MeOH



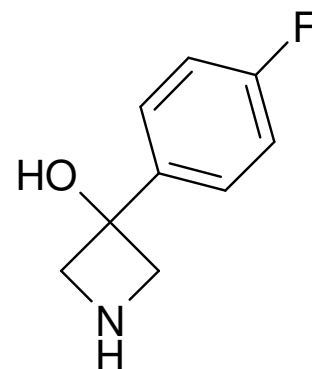
1% NH₃ / MeOH



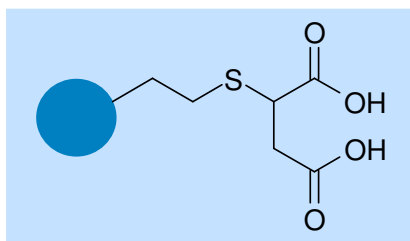
Selective Separation of 2° and 3° Amines



A

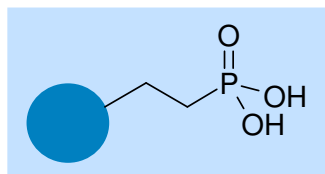


B



Catch & release

A : >95%* (MeOH wash); **B** : >95% (5% Et₃N)



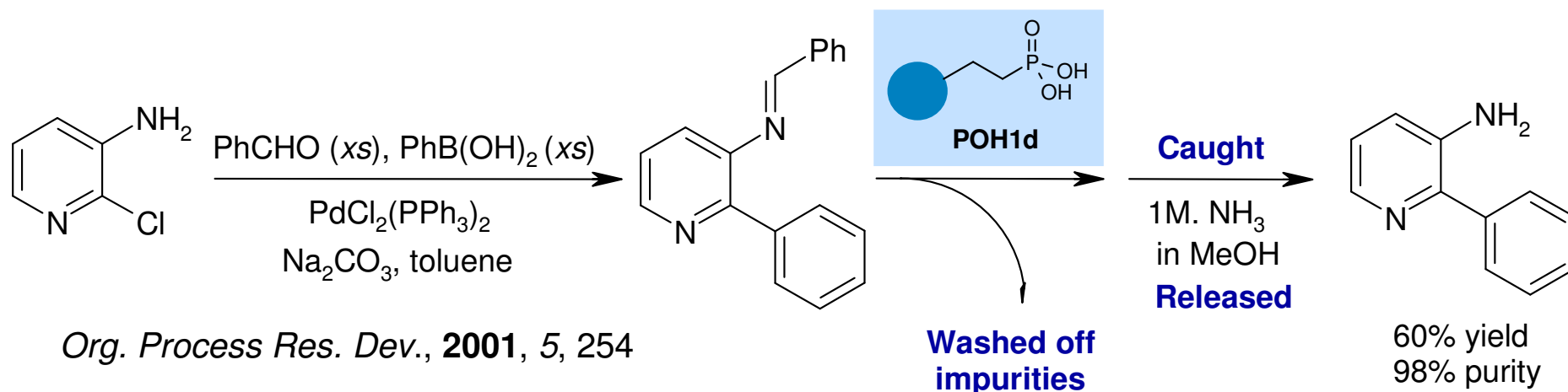
Selective elution

A : >95% (5% Et₃N); **B** : >95% (1% NH₃)

* Isolated yields, purities >95% in each case

● **A & B** not separable by column chromatography or with SCX sulfonic acids

Simplified Work-ups, Quicker to Products



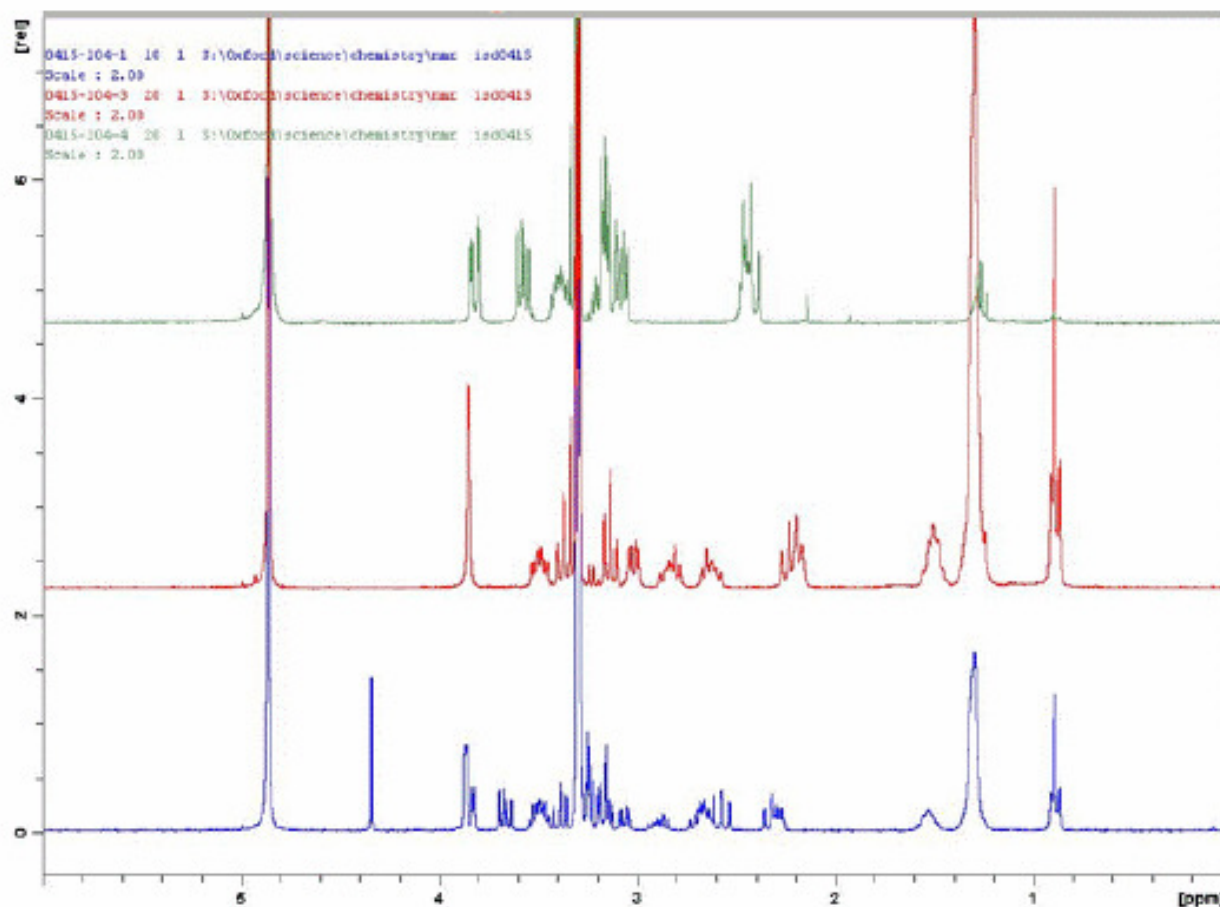
- Precursor to piperidine pharmacophore present in NK1 receptor antagonists
- 3-Amino protection required for reasonable yield in Suzuki reaction
- Literature : PG removal with acid, aq. extractive work-up & recrystallisation required
- SPE clean-up allows larger excess of PhCHO to be used to drive imine formation
- **POH1d** provides easier product isolation & reduced times to product

Purifications at Summit



summit_{plc}

A Typical POH Clean-Up (50mg scale, >50% yield)



Mixture after MeOH /
NH₃ rinse
(Secondary amine sm)

Mixture after MeOH
/ Et₃N rinse
(Tertiary amine tm)

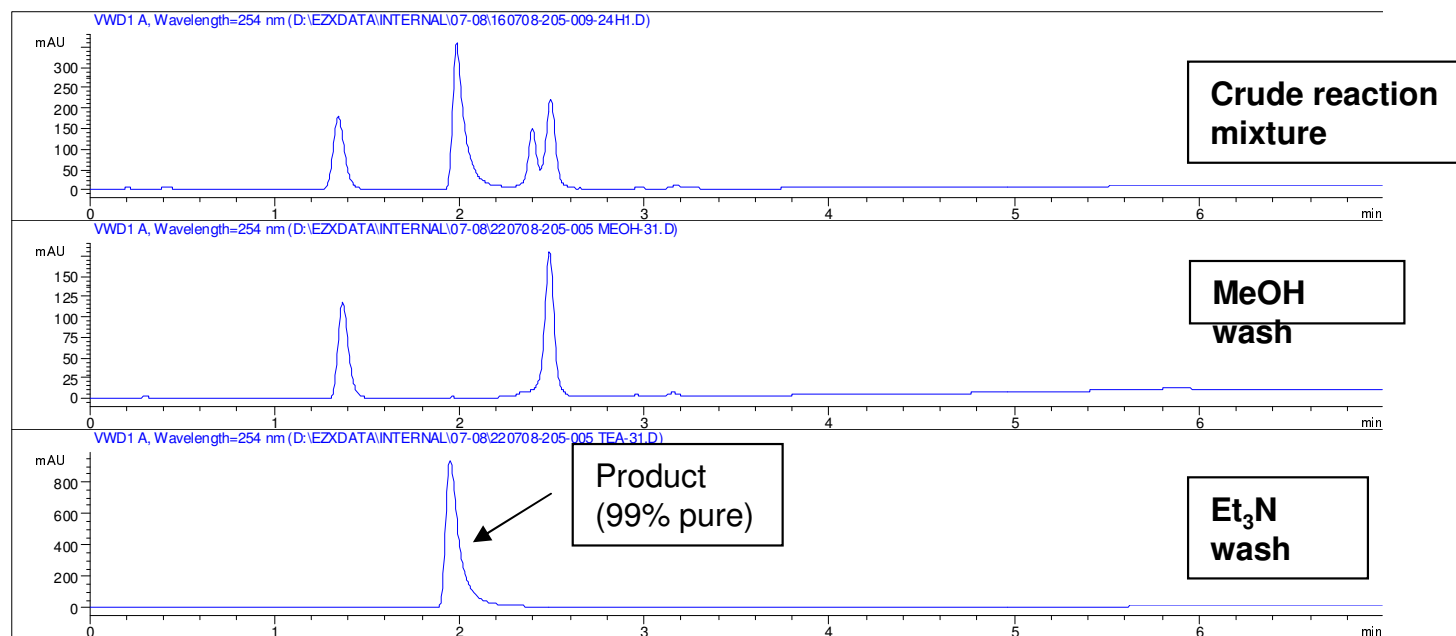
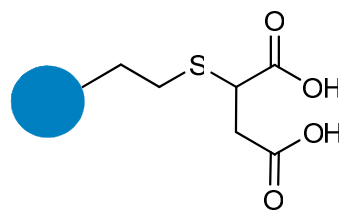
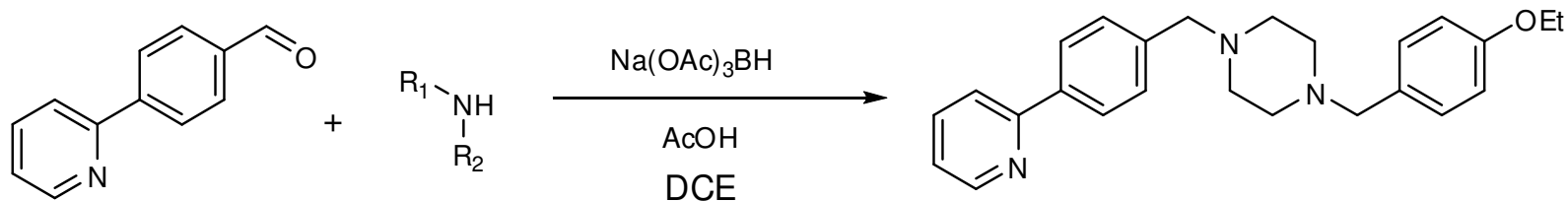
Mixture after SCX

● POH1d excellent for iminosugar purifications

● No separation of products with sulfonic acid SCX materials

Presented at UKASF Meeting, Pfizer Sandwich, November 2008

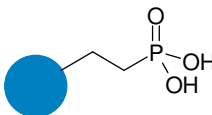
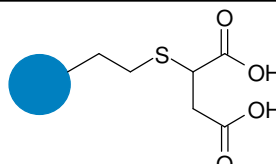
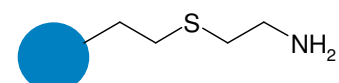
Purifications at Sygnature



- **STMA**d used to purify crude reductive amination product
- Product cleanly separated from other basic components – SMs, by-products

SPE Cartridges Available

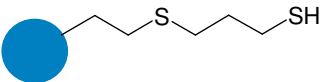
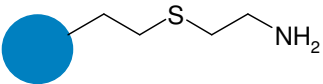
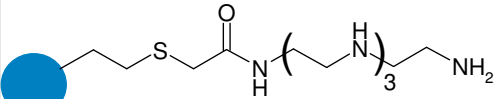
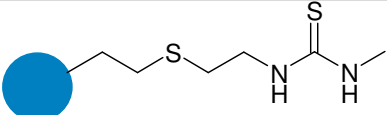
- For compound purification in Medicinal Chemistry, typically from 50 mg to 500 mg scale; for single compounds or focused arrays
- Range of size options available : 1 g scavenger (6 mL volume), 2 g scavenger (15 mL), 5 g scavenger (20 mL), 10 g scavenger (75 mL)
- Silica : particle size 35-70 μm ; pore size 60Å
- Also available as loose powders for slurry applications
- Weak anion exchange products SEAd & SPA5d available

Material	Code	Function
	POH1d	Cation Exchange (pKa ~2)
	STMAAd	Cation Exchange (pKa ~4)
	SEAd	Weak Anion Exchange
	SPA5d	Weak Anion Exchange



Additional Organic Scavenger Cartridges Available

- For compound purification in Medicinal Chemistry, typically from 50 mg to 500 mg scale; for single compounds or focused arrays
- Range of size options available : 1 g scavenger (6 mL volume) or 10 g scavenger (75 mL)
- Silica : particle size 35-70 μm ; pore size 60 \AA

Material	Code	Scavenges
	SPM32d	Electrophiles
	SEAd	Electrophiles Weak Anions
	SPA5d	Electrophiles Weak Anions
	MTCd	Electrophiles

