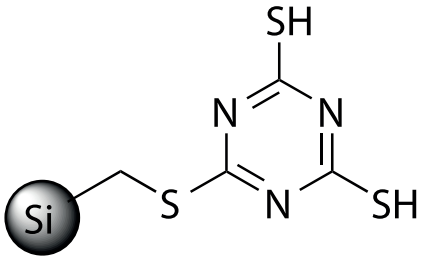
ISOLUTE® Si-TMT

Metal Scavenger



Key Facts

Stoichometric | Shelf Life | Capacity (mmol/g) | BSE/TSE | Scalable | Particle Size (µm) | Thermally & Mechanically Stable | Good Laboratory Practice | Bulk Density (g/L)

Specifications

Chemical Name:	2,4,6-trimercaptotriazine silica
Solid-Support Type:	Silica
Applications:	Metal Scavenging
Typical Scavenging Conditions:	3-5 equiv. ISOLUTE Si-TMT, 30 min, room temperature; fixed bed or batch format
Compatible Solvents:	Water, Acetonitrile (MeCN), methanol, Dimethylsulfoxide (DMSO), Dichloromethane (DCM), tetrahydrofuran (THF), N,N-Dimethylformamide (DMF), Dioxane
Storage:	Cool, dry location

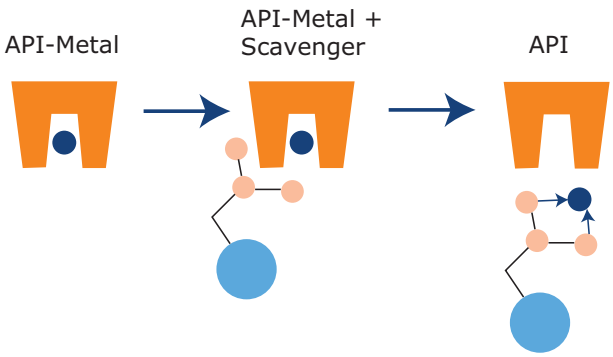


Figure 1. Metal Scavenging

Palladium-catalyzed reactions are very popular in organic synthesis. Some of the most widely practiced examples include Suzuki-Miyaura cross coupling reactions, Heck reactions, Buchwald aminations, Wacker-type oxidation, hydrogenation, allylation, reductive deallylation and indole formation.

Despite the widespread use of these palladium-mediated reactions, removal of residual palladium during workup and product isolation remains a major problem.

Reducing the palladium content to the low parts per million (ppm) levels, as is required for active pharmaceutical ingredients, is particularly challenging. Biotage has developed a portfolio of scavenging products designed to remove these transition metal impurities. ISOLUTE® Si-TMT (along with MP-TMT, our polymeric resin variant) are some of the most powerful generic use metal scavengers available.

ISOLUTE® Si-TMT is the silica bound equivalent of 2,4,6-trimercaptotriazine (TMT). Si-TMT has been shown to efficiently scavenge residual palladium from palladium-catalyzed reactions. The function group in Si-TMT is attached to a bioanalytical grade silica platform, thus the use of this material does not introduce impurities to the reaction system. There are numerous advantages of functionalized Isolute Silica.

Solvent Independent

Like MP-TMT, Si-TMT neither shrinks nor swells in solvent, which makes it ideal for limited volume development reactors (e.g. microwave vials, 96 well plates and SPE columns).

Fast Kinetics

The functional groups are on the surface and in pores of the silica, (similar to highly cross-linked macroporous polystyrene, MP-TMT) so the rate of reaction is not controlled by diffusion as with traditional 1% cross linked PS-gels.

Biotage®

Simplified Workflow

Si-TMT can be added to a reaction in "batch mode" and stirred in traditional ways, or as a fixed bed in a cartridge. Si-TMT is stable at room temperature and under atmospheric conditions.

Si-TMT was applied successfully in a one-pass scavenging of palladium acetate (Figure 2), dichlorobis(triphenylphosphine) palladium (II) (DCB) (Figure 3) and tetrakis(triphenylphosphine) palladium (0) (KIS) (Figure 4) using MP-TMT from Biotage, Si-Thiol from Biotage, and a commercially available alternative supported thiourea scavenger.

Thermally and Mechanically Stable

Most silica based products, can withstand temperatures over 200 °C for short periods of time. They are also stable to mechanical agitation and can be used in conjunction with both magnetic and mechanical stirring.

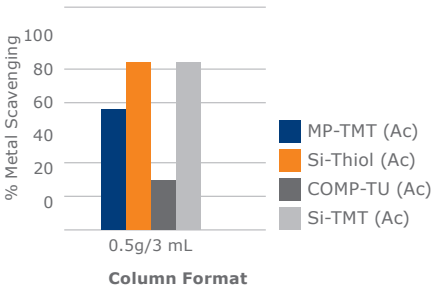


Figure 2. Palladium acetate scavenging efficiency using Si-TMT in column format in comparison with popular solid supported scavengers.

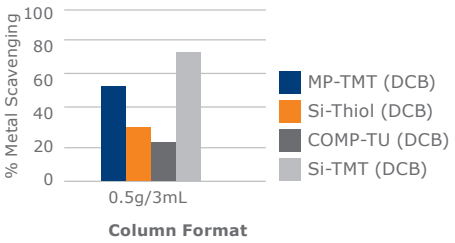


Figure 3. Dichlorobis (triphenylphosphine)-palladium (II) (DCB) scavenging efficiency using Si-TMT in column format in comparison with popular solid supported scavengers.

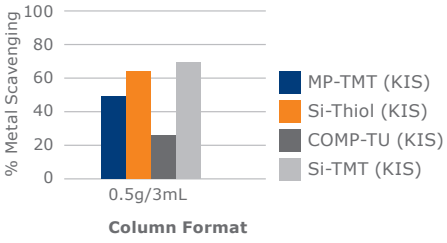


Figure 4. Tetrakis (triphenylphosphine)-palladium (0) (KIS) scavenging efficiency using Si-TMT in column format in comparison with popular solid supported scavengers.

Conclusions

Si-TMT, Si-Thiol and MP-TMT were effective at removing palladium. Even in column format MP-TMT was able to remove palladium under one pass flow through conditions, however the Silica scavengers Si-Thiol and Si-TMT were far more effective. Si-Thiol is an excellent workhorse metal scavenger, applicable in a wide variety of cases, but the powerful combination of optimum particle size and metal-ligand binding affinity made Si-TMT the clear winner in these cases.

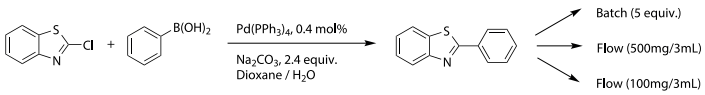
Easy to Use and Handle

Silica is easy to weigh and handle. These products do not stick to glassware when dried and also do not require extensive washing for high product recovery.

Application

Suzuki Coupling

A Suzuki coupling was performed (Scheme 1) and scavenging experiments were performed on the mother liquids in both batch and flow mode. The results, as shown in Table 1 show that Si-TMT is more efficient in scavenging palladium residues than other silica based metal scavengers.



Scheme 1. Suzuki coupling.

Scavenger	Batch Studies (5 equiv.)	Flow (Cartridge) Scavenging	
		500 mg/3 mL	100 mg/3 mL
Si-Thiol (Competitor S)	82%	91%	45%
Si-TMT (Biotage)	>99%	>99%	95%

Table 1. Results of metal scavenging experiments following reaction shown in Scheme 1. Table shows percentage of reduction of palladium as measured by ICP.

Ordering Information

Part Number	Quantity
9538-0003	3 g
9538-0010	10 g
9538-0025	25 g
9538-0100	100 g
9538-1000	1000 g

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