

ISOLUTE® Si-TsOH (SCX-3)

Scavenger/Reagent

Specifications**Chemical Name:**

Silica Ethylbenzene sulfonic acid
(Si-TsOH; Si-Tsolic acid; SCX-3)

Solid-Support Type: Silica

Typical Capacity: 0.6 mmol/g

Size: 60 μm

Appearance: Free flowing off-white powder

Application:

Scavenger of amine, Catch and Release,
Acid catalyst/reagent, Metal scavenger
(e.g. Ni and Ag.)

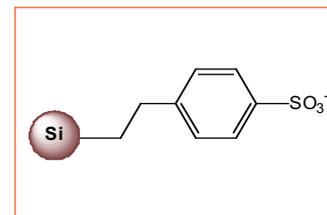
Typical conditions:

Stir crude reaction mixture with 2-4 equivalents
for 1 h and filter.

Compatible Solvents: Methanol (MeOH),
Dichloromethane (DCM), Acetonitrile (MeCN),
Acetone, Ethyl Acetate (EtOAc),
N,N-Dimethylformamide (DMF),
Dimethylsulfoxide (DMSO)

Storage: Cool (4 °C), dry location

ISOLUTE® Si-TsOH (SCX-3) is the bound equivalent of p-toluene sulfonic acid with a $\text{pK}_a < 1$. Similar to ISOLUTE propylsulfonic acid (SCX-2)¹, it can be used to (a) scavenge amines and other bases such as anilines and borohydrides (b) as an acid catalyst in reactions or (c) as a replacement for aqueous or organic acids in quenching reactions.



ISOLUTE Si-TsOH is stable to microwave heating and has been reported² as an excellent replacement to p-TsOH in both thermal and microwave assisted acid catalyzed reaction (Scheme 1).



Scheme 1. Synthesis of 1,5-Diarylpiperazines using Si-TsOH as an acidic reagent.

The advantage of using Si-TsOH was that no work-up was necessary. The crude reaction mixture was evaporated to dryness and the resulting free flowing solid was purified directly by flash column chromatography. The advantage of using Si-TsOH was that no work-up was necessary.

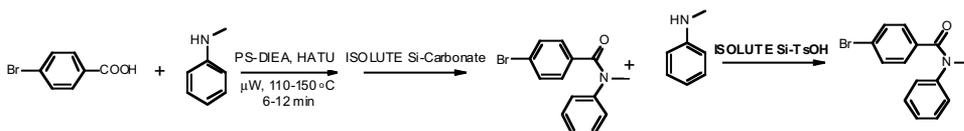
Applications**Catch and Release Purification of Amines**

ISOLUTE Si-TsOH is a strong cation exchanger (SCX) for the "Catch and Release" purification of amines. When a solution containing an amine is passed through a Si-TsOH (SCX-3) column the amine is retained or "caught" by the SCX-3. Non-basic impurities are not retained and are further removed by washing the column with an organic solvent, such as methanol, acetonitrile or THF. The product is subsequently "released" from the column by elution with a solution of ammonia in methanol. Amine salts of weak conjugate acids (e.g. acetate and trifluoroacetate) are exchanged onto the silica and are released as the free amine during the ammonia/methanol wash.

SCX-3 columns can be used successfully to isolate amines from solutions of DMF. After complete removal of the DMF using DCM or methanol, the retained amine is eluted with an ammonia/methanol solution. The amine is then isolated by removal of the volatile ammonia/methanol solution by evaporation. The slower sample flow rate exhibited by certain viscous solvents including DMF and DMSO can be improved by increasing the vacuum, applying positive pressure to the column, or diluting with a less viscous solvent.

Application in amidation reactions

ISOLUTE Si-TsOH columns can be used to simplify the purification process following amide coupling reactions. In the event of incomplete conversion the unreacted amines can be removed by filtering the reaction mixture through a short column of ISOLUTE Si-TsOH. An example of this approach is provided in Scheme 1.³ Amide coupling of p-bromobenzoic acid with N-methyl aniline was carried out with PS-DIEA⁴ and HATU in acetonitrile. On completion, the reaction mixture was filtered and the filtrate passed through a conditioned ISOLUTE Si-Carbonate column⁵ to remove the unreacted acid and HATU. The resulting filtrate, consisting of the amide product and unreacted amine, was passed through a column of ISOLUTE Si-TsOH. Unreacted aniline was retained on the column providing pure product in the filtrate.



Scheme 1.

Scavenging of basic impurities

ISOLUTE Si-TsOH columns, similar to MP-TsOH⁶, can also be used to scavenge basic impurities and thereby purify reaction mixtures. Passing a reaction mixture through an ISOLUTE Si-TsOH column will result in removal of all basic components in the mixture. If additional selectivity is required, the use of a more selective scavenger resin is recommended, for example, PS-Isocyanate⁷ (for removal of primary and secondary amines), or PS-Benzaldehyde⁸ (for selective removal of primary amines). An alternative approach to selectivity enhancement is the use of derivatization purification techniques in conjunction with silica based strong cation exchange columns ISOLUTE SCX-2.

ISOLUTE is a trademark of Argonaut Technologies, now a BIOTAGE company.

References

- 1 ISOLUTE Si-Propylsulfonic acid (SCX-2): Part Numbers 9532-0010 (10g); 9532-0025 (25g); 9532-0100 (100g); 9532-0500 (500g); 9532-1000 (1000g)
- 2 Humphries, P. S. and Finefield, J. M. *Tetrahedron Lett.* 2006, 47, 2443-2446
- 3 Ghassemi, S. *MEDI* 46, ORGN 302, ACS Atlanta 2006
- 4 PS-DIEA: Part Numbers 800494 (3g); 800279 (10g), 800280 (2 g), 800281 (100g); 800312 (1000g)
- 5 ISOLUTE Si-Carbonate: Part Numbers 9510-0010 (10g), 9510-0025 (25g), 9510-0100 (100g), 9510-0500 (500g), 9510-1000 (1000g); 510-0050-B (SPE; 500mg/3mL); 510-0100-C (SPE; 1g/6 mL); 510-0200-C (2g/6 mL); 510-0050-BG (SPE tab-less; 500mg/3mL); 510-0100-CG (SPE tab-less; 1g/6mL); 510-0200-CG (SPE tab-less; 2g/6mL)
- 6 MP-TsOH(65): Part Numbers 800477-0010-BG (SPE tab-less, 100mg/3 mL); 800477-0025-CG (SPE tab-less; 250mg/6mL); 800477-0050-CG (SPE tab-less; 500mg/6mL)
- 7 PS-Isocyanate: Part Numbers 800495 (3g); 800260 (10g), 800261 (25g), 800262 (100g); 800311 (1000g)
- 8 PS-Benzaldehyde: Part Numbers 800502 (3g); 800360 (10g), 800361 (25g), 800362 (100g); 800363 (1000g)
- 9 Request Technical Note TN128 Increasing the Selectivity of Silica Based Cation Exchange Sorbents for the Purification of Reaction Mixtures Using Derivatization Purification Techniques.

Ordering Information

Part Number	Quantity
9537-0010	10 g
9537-0025	25 g
9537-0100	100 g
9537-0500	500 g
9537-1000	1000 g

Also available in SPE Column and Array plate formats.

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