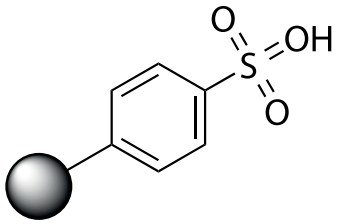
Biotage® MP-TsOH

Resin-bound Acid



Key Facts

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

Specifications

Chemical Name:	Macroporous polystyrene sulfonic acid (0.5% inorganic antistatic agent)
Resin Type:	Macroporous poly(styrene-co-divinylbenzene)
Application:	Scavenging and catch-and-release of amines, acid catalysis
Scavenging Conditions:	Approx. 2–3 equivalents of resin relative to amine, 0.5–1 h, 20 °C
Compatible Solvents:	DCM (3.0 mL/g), THF (3.1 mL/g), DMF (3.1 mL/g), MeOH (3.05 mL/g)
Storage:	Cool, dry location

MP-TsOH resin is a sulfonated macroporous polystyrene resin that is a resin-bound equivalent of p-toluenesulfonic acid (TsOH). The resin may be used as an equivalent to the strong cation-exchange resin, Amberlyst A-15 (Rohm and Haas).[1–4] MP-TsOH has been optimized for use as a bound reagent or scavenger resin for the synthesis of small molecules. The sulfonic acid groups in MP-TsOH are readily accessible for removal of basic compounds (e.g. primary, secondary, and tertiary amines) by quartenary salt formation. In addition, MP-TsOH does not contain dark leachable impurities derived from over-oxidation of the polystyrene backbone observed in higher loading sulfonic acid resins.[5]

Representative amine scavenging examples in batch as a function of time are provided in Table 1. MP-TsOH provides a useful alternative to quenching reactions with aqueous or soluble organic acids.

Other Applications

In Mitsunobu, Suzuki and Heck reactions, it is often challenging to isolate pure products from the byproducts such as triphenylphosphine oxide and palladium. MP-TsOH columns can be used to purify these products when they contain a basic functional group. The reaction mixture is applied to the column and the product is retained by MP-TsOH. The byproducts can be easily removed with a methanol or DCM wash step. The product can then be released by eluting with 2 M ammonia in methanol.

MP-TsOH may also be used in cartridge applications to perform Catch-and-Release of amine derivatives in analogy to silica-derived SCX columns.[6–8]

Catch-and-Release Purification of Amines

The procedure for isolating amines using MP-TsOH in columns is known as catch-and-release and is detailed below. When a solution containing an amine is passed through a MP-TsOH column the amine is retained or “caught” by the resin. Non-basic impurities are not retained and are further removed by washing the column with an organic solvent, such as DCM, THF or methanol. 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 trifluoro-acetate) are exchanged onto the resin and are released as the free amine during the ammonia/methanol wash.

Biotage®

Catch-and-Release Procedure

1. Column Pre-conditioning

Wash the column with DCM, methanol or THF (4 mL/g resin).

2. Sample Loading

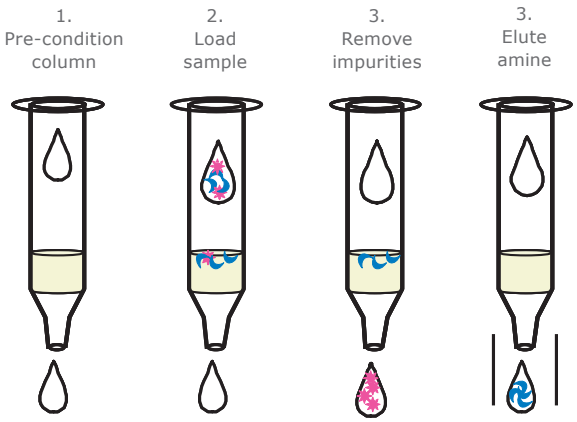
Load the amine sample or reaction mixture onto column under gravity and discard the eluent.

3. Wash Impurity

Remove the non-basic impurities by washing with DCM (3 x 3 mL/g resin). Discard the wash.

4. Amine Elution

Elute basic amines with a solution of ammonia in methanol (2 M, 4 mL/g resin). Evaluate the use of 4 M ammonia/methanol solution (2 mL/g resin) to improve elution efficiency and reduce elution volume. Collect the eluent. Wash with methanol (2 x 4 mL/g resin) for complete recovery of the amine.



Schematic showing catch-and-release of amines using MP-TsOH columns

Amine	MP-TsOH (equivalent)	% Scavenged	
		20 min	1 h
Propylamine	3	100	100
3-(morpholino) propylamine	3	100	100
Aniline	3	100	100
Nitroaniline	3	75	96
2-Aminothiazole	3	100	100

Table 1. Amine removal by MP-TsOH (batch mode).

Amine	MP-TsOH (equivalent)	% Scavenged (5 min)
Propylamine	5	100
3-(morpholino)propylamine	5	100
Aniline	5	100
2-Aminothiazole	5	98

Table 2. Amine removal by MP-TsOH (cartridge mode).

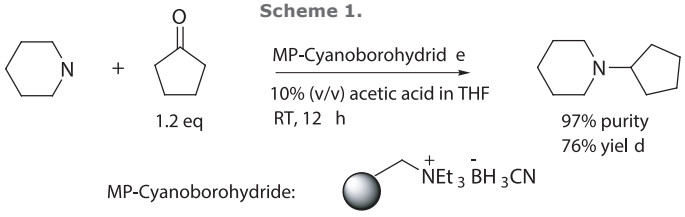
We have found catch-and-release purification of amines with MP-TsOH columns to be effective in retaining amines with a wide range of basicity, including N-methylmorpholine, aniline, aminothiazole, and nitroaniline. Full retention of weakly basic amines such as nitroaniline was achieved when DCM was used as the solvent, however, retention is less efficient in THF or DMF. The use of greater than three equivalents of resin is recommended for weakly basic amines in these solvents.

Application in Reductive Amination Reactions

The reductive amination of carbonyl compounds is widely used in amine synthesis. MP-TsOH(columns can be used to simplify the purification process following this type of reaction. When using this approach, the stoichiometry of the reaction is usually adjusted towards excess carbonyl compound (10–20%) to drive the reaction to completion. It is therefore best suited for reactions where product over-alkylation is not an issue. The catch-and-release purification approach is particularly useful when used in conjunction with a bound reducing agent, such as MP-Cyanoborohydride.

An example of this approach is provided by the synthesis of N-cyclopentylpiperidine (Scheme 1). Reductive amination of 1.2 equivalents of cyclopentanone with 1 equivalent of piperidine was carried out with MP-Cyanoborohydride in 10% (v/v) acetic acid/THF. On completion, the reaction mixture was filtered and the filtrate passed through a conditioned MP-TsOH(column to retain the amine product. The excess carbonyl compound and its reduced product passed directly through the column, with an additional DCM wash removing any remaining non-basic impurities. The free amine was “released” with ammonia/methanol to afford the product in 76% yield and 97% purity. In addition to product purification, the process serves to exchange the product solution from acetic acid/THF to a more volatile ammonia/methanol solution.

Scheme 1.



Ordering Information

Part Number	Quantity
800498	3 g
800461	10 g
800462	25 g
800463	100 g
800464	1000 g

References

1. Flynn, D. L.; Crich, J. Z.; Devraj, R. V.; Hockerman, S. L.; Parlow, J. J.; South, M. S. Woodard, S. S. *J. Am. Chem. Soc.* 1997, 119, 4874.
2. Gayo, L. M.; Suto, M. J. *Tetrahedron Lett.* 1997, 38, 513.
3. Parlow, J. J.; Flynn, D. L. *Tetrahedron* 1998, 54, 4013.
4. Suto, M. J.; Gayo-Fung, L. M.; Palanki, M. S. S.; Sullivan, R. *Tetrahedron* 1998, 54, 4141.
5. Stahlbush, J. R.; Strom, R. M.; Byers, R. G.; Henry, J. B.; Skelly, N. E. *Prediction and Identification of Leachables from Cation Exchange Resins*, Presented at the 48th Annual Meeting International Water Conference, Pittsburgh, PA Nov. 1987, IWC-87-10.
6. Siegel, M. G.; Hahn, P. J.; Dressman, B. A.; Fritz, J. E.; Grunwell, J. R.; Kaldor, S. W. *Tetrahedron Lett.* 1997, 38, 3357.
7. Shuker, A. J.; Siegel, M. G.; Matthews, D. P.; Weigel, L. O. *Tetrahedron Lett.* 1997, 38, 6149.
8. Lawrence, M. R.; Biller, S. A.; Fryszman, O. M.; Poss, M. A. *Synthesis* 1997, 553.
9. Part Number 800477-0050-C.

bsi. ISO 9001 Quality Management FM 31206 ISO 14001 Environmental Management EMS 640981

Biotage holds certification for both ISO9001 Quality Management and ISO14001 Environmental Management.

EUROPE
Main Office: +46 18 565900
Toll Free: +800 18 565710
Fax: +46 18 591922
Order Tel: +46 18 565710
Order Fax: +46 18 565705
order@biotage.com
Support Tel: +46 18 56 59 11
Support Fax: + 46 18 56 57 11
eu-1-pointsupport@biotage.com

NORTH & LATIN AMERICA
Main Office: +1 704 654 4900
Toll Free: +1 800 446 4752
Fax: +1 704 654 4917
Order Tel: +1 704 654 4900
Order Fax: +1 434 296 8217
ordermailbox@biotage.com
Support Tel: +1 800 446 4752
Outside US: +1 704 654 4900
us-1-pointsupport@biotage.com

JAPAN
Tel: +81 3 5627 3123
Fax: +81 3 5627 3121
jp_order@biotage.com
jp-1-pointsupport@biotage.com

CHINA
Tel: +86 21 2898 6655
Fax: +86 21 2898 6153
cn_order@biotage.com
cn-1-pointsupport@biotage.com

To locate a distributor, please visit our website www.biotage.com

Part Number: PPS398.V.1

Biotage®