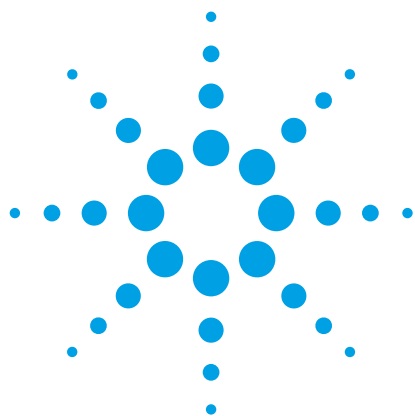




Streamline Purification of Organic Synthesis Mixture

Technical Overview

Rapidly Scrub Water-Soluble Impurities, Reagents, and Byproducts with Chem Elut and Hydromatrix

- Select from a family of formats to fit your reaction scale
- Increase throughput with parallel processing
- Eliminate emulsion formation and improve reproducibility with gravity-flow cartridges

Purification of synthesis mixtures is easy and fast with Agilent brand diatomaceous earth products for liquid/liquid extraction. This high-purity support improves purification compared to traditional liquid/liquid extraction by eliminating emulsion formation and improving purification reproducibility. Diatomaceous earth is packed into many convenient formats, including Combilute 96-well plates, Chem Elut cartridges, or is available in bulk as Hydromatrix. Purification on reaction scales from microplates to process synthesis has never been easier!



Agilent Technologies

General Method

Following is a general method for scrubbing impurities from organic reaction mixtures.

1. Load aqueous buffer using the volume guidelines from Table 1. Use gravity flow. Note: Buffer will adsorb onto the packing material rather than flow through the cartridge. Allow 3-5 minutes for complete adsorption to take place.

To scrub: amines, imidazoles, azoles, and other bases
Add: 1N HCl or other acids

To scrub: thiochlorides, sulfonic acids, HBr, m-CPBA, and other acids
Add: 1M NaOH, Na₂CO₃, or other bases
2. Apply water-immiscible organic synthesis mixture. Use gravity flow. Typical solvents include dichloro-methane, chloroform, ethyl acetate, butanol, hexanol, butyl acetate, and toluene.
3. Collect purified mixture as it passes through sorbent bed. Mixture is now scrubbed of water-soluble components and ready for concentration or additional purification.

Choosing the right purification product

Table 1. Choosing the right product is as simple as selecting the format based on reaction mixture volume. Then, select the conditioning buffer based on the General Method guidelines, and apply the volume indicated above.

Agilent product	Typical reaction mixture volume	Maximum buffer volume
Combilute: 96-well plates with Hydromatrix material	2 mL or less	500 µL
Chem Elut: pre-packed cartridges with Hydromatrix material	5-500 mL	0.3-300 mL
Hydromatrix Bulk Sorbent: high capacity, extra-clean diatomaceous earth	>500 mL	2 mL/g

Improve Purification with Hydromatrix and Chem Elut

Small-scale parallel synthesis mixture purification

96-well Combilute is routinely used to rapidly purify small-scale synthesis libraries – 96 reactions at once. Following is a typical procedure for purifying an amide library by scrubbing excess amines [1].

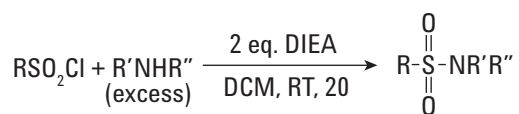
1. Apply 500 µL 1M HCl to each well of a Combilute 96-well purification plate under gravity flow only.
2. Wait 3-5 minutes for aqueous acid to adsorb.
3. Place Combilute on top of a clean 2 mL 96-well collection plate. Apply up to 2 mL organic synthesis mixture in water-immiscible solvent under gravity flow. Collect purified reaction mixture as it drips into collection plate.

Intermediate-scale synthesis mixture purification

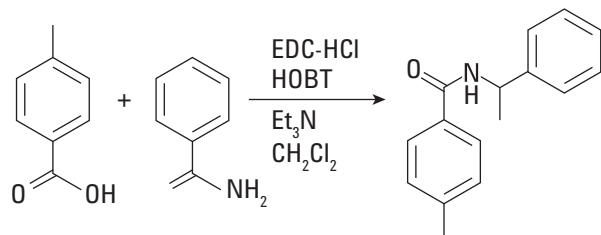
Chem Elut cartridges are ideal for scrubbing water-soluble impurities in milligram quantities. The gravity flow cartridge minimizes extraction variations and eliminates emulsions that occur with standard liquid/liquid extraction methods. Chem Elut 3 mL cartridges treated with 2M H₂SO₄ were used to work up the parallel solution-phase sulfonamide synthesis providing quantitative yields of 99% [2].

Large-scale purification of multiple components

Acid-treated and base-treated Hydromatrix can be combined in two layers in a large glass column to remove both acidic and basic components in a single purification. Such an approach is used to scrub unreacted starting materials from the amide synthesis performed on a multigram scale affording >95% yields [3].



Remove impurities and byproducts from a wide variety of reaction types such as in this sulfonamide synthesis.



Achieve efficient purifications and eliminate the unwieldy shaking necessary for standard liquid/liquid extractions.

References

1. This is a typical method. For variations, see also Peng, S.E., *et al.* Anal. Chem., 72, 2000, 261-266; and Breitenbucher, J.G., *et al.* Tetrahedron Letters, 39, 1998, 1295-1298.
2. Tamanaha, L.L., Porco, J.A., Synthesis & Purification Letters, 1998, #3.
3. Albany Molecular Research, Inc. Technical Report: Volume 4, Number 17, <http://www.albmolecular.com/features/tekreps/vol04/no17>

Ordering information

Part number	Description	Units/package
65401507	Combilute 96-well plate, 200 mg Hydromatrix per well	1
12198001	Chem Elut, 0.3 mL aqueous capacity	100
12198002	Chem Elut, 1 mL aqueous capacity	100
12198003	Chem Elut, 3 mL aqueous capacity	100
12198004	Chem Elut, 3 mL aqueous capacity, buffered to pH 4.5	100
12198005	Chem Elut, 3 mL aqueous capacity, buffered to pH 9	100
12198006	Chem Elut, 5 mL aqueous capacity	100
12198007	Chem Elut, 10 mL aqueous capacity	100
12198008	Chem Elut, 20 mL aqueous capacity	100
12198009	Chem Elut, 50 mL aqueous capacity	50
12198010	Chem Elut, 100 mL aqueous capacity	25
198003	Hydromatrix, 1 kg	1 kg
198004	Hydromatrix, 4 kg	4 kg

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© Agilent Technologies, Inc., 2012
Printed in the USA
May 1, 2012
SI-2501



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