

RediSep[®] SCX column

Purification of high pKa organic compounds with a multipurpose scavenger.

Case Study 1

Mikael Mahler, Veronica Thomason

Teledyne Isco, Inc.

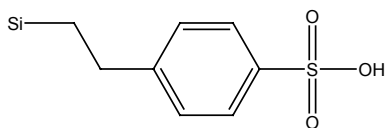
Overview

Purifying organic compounds holding inherent basic properties (*e.g.* amines or nitrogen-containing heterocycles) present technical challenges when using normal phase silica flash chromatography.

This application describes how Teledyne Isco's RediSep SCX column can be used as a practical and efficient tool for the selective isolation of either basic or non-basic compounds from a crude reaction mixture containing both. Use of the RediSep SCX column as a crude reaction mixture clean-up tool among other possible applications is also discussed.

Background

The SCX (Strong Cation Exchange) media is a silica-bound tosic acid:

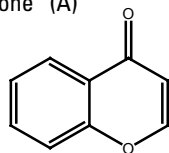


The strong acidity of this media induces the full retention of any compounds with basic properties subjected through a RediSep SCX column. This intrinsic media property can be exploited several ways.

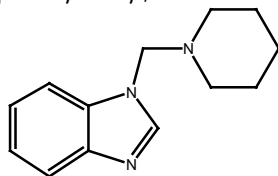
Results and Discussion

The separation of a mixture of chromone and a benzimidazole derivative was investigated.

Chromone (A)



1-(1-piperidinylmethyl)-1H-benzimidazole (B)



Flash chromatography of the mixture on a normal phase RediSep column showed release of the two products (Figure 1).

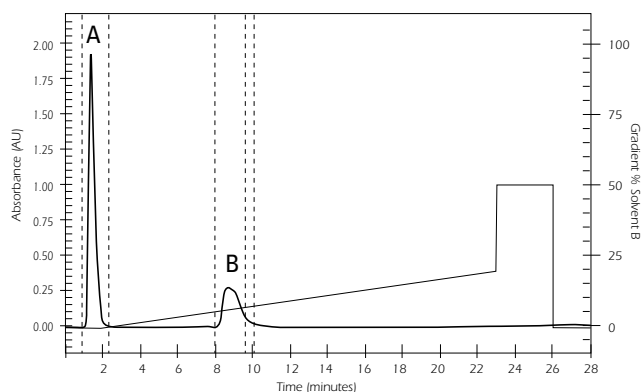


Figure 1: Chromatogram of normal phase column
Elution with dichloromethane/methanol

The use of a RediSep SCX column showed total retention of the benzimidazole derivative onto the column and release of the chromone (Figure 2).

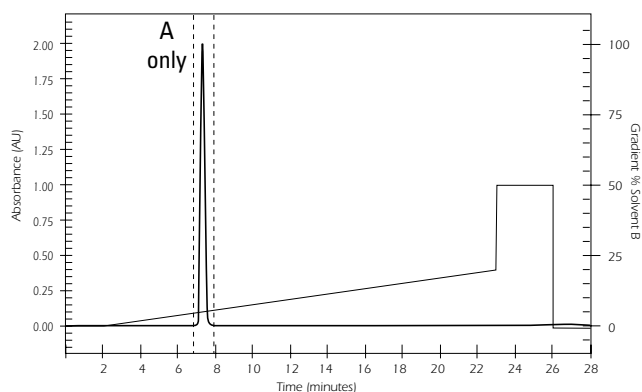


Figure 2: Chromatogram of SCX column
Elution with dichloromethane/methanol

This isolation of the basic compound, while allowing one or more organic compounds holding neutral properties to migrate freely through the column, demonstrates that the column can be effective as a clean up tool.

If the eluant from the SCX column contains multiple compounds holding neutral properties that require further purification, column stacking can be an option. Stacking an SCX column on top of a normal phase column (Figure 3) would first strip the compounds holding basic properties, and then separate the remaining neutral compounds. A solvent system should be selected to provide satisfactory resolution on normal phase silica.

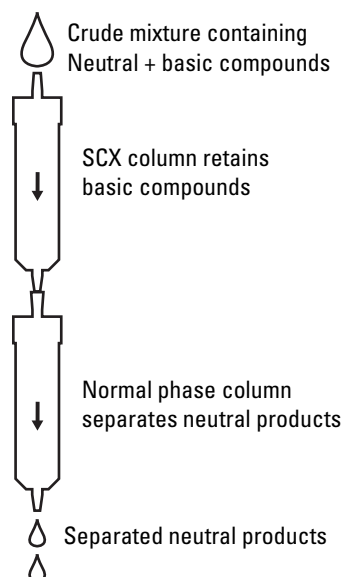


Figure 3: Stacked columns of different media as a purification tactic

RediSep columns' Luer-lok[®] fittings and Teledyne Isco's Column Stacker offer a convenient solution for column stacking.

Conversely, the SCX column also represents a practical tool for the isolation of desired compounds holding basic properties. In this case, the contaminants would be the neutral compounds which would be immediately released then discarded by the SCX column run.

The compounds holding basic properties retained by the SCX column are liberated by injecting 8 column volumes of a 5% ammonia in methanol solution. This solution can be directly injected through the column with a syringe flush. In this case, the SCX column works as a catch and release process.

The RediSep column not only scavenges compounds holding basic properties such as amine or nitrogen-containing heterocycles, it can also retain borohydrides, nickel, and silver species.

The RediSep SCX column media will not degrade when using common protic or aprotic organic solvents. It is reusable if regenerated after each use with 5 column volumes of a solution of 1M HCl in acetonitrile.

Experimental

Table 1: Method Parameters and Results

Instrumentation:	Isco CombiFlash [®] Companion [™] 4x	
Columns	4g Normal Phase RediSep 5g SCX RediSep	
Sample Loading Method	45 mg pre-loaded on celite (J.T. Baker celite 503)	
Wavelength	254 nm	
Mobile phase:	Solvent A: Hexane	Solvent B: Ethyl Acetate
Flow Rate:	18 mL/minute	
Equilibration Volume:	3 column volumes	
Gradient:	% Solvent B	CV
	0	Initial
	0	2.0
	20	21.0
	50	0.0
	50	3.0
	0	0.0
	0	1.0
Recovery yields:	chromone product (A): 99%	benzimidazole product (B): 99%

Conclusion

The RediSep SCX column is a multi-purpose scavenger column which can be used for the separation and isolation of either high pKa compounds or neutral compounds. It can also be used as a scavenger for some metal containing species.

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Teledyne Isco, Inc.

P.O. Box 82531, Lincoln, Nebraska, 68501 USA
Toll-free: (800) 228-4373 • Phone: (402) 464-0231 • Fax: (402) 465-3091
E-mail: info@isco.com

