

Purification of Delicate Compounds with RediSep Rf Gold® Diol and Cyano Columns

Abstract

Many compounds are difficult to purify because they decompose on the column. An epoxide compound was synthesized and purified with a RediSep Rf Gold Diol and RediSep Rf Gold Cyano column. The epoxide makes an excellent model for other unstable compounds as epoxides commonly decompose on silica gel. Unstable compounds are often purified using a series of liquid-liquid extractions. Purifying such compounds on a column where the amount of solvent used and evaporation is reduced is desirable.

The RediSep Rf Gold Diol and RediSep Rf Gold Cyano columns are useful for purifying delicate compounds because they are less active than silica gel. They are both run as normal phase columns; normal phase solvents usually have a lower boiling point than reverse phase solvents. Using lower boiling solvents decreases the heat necessary to evaporate the solvents and reduces evaporation time after purification, thus reducing the time fragile compounds are exposed to heat.

Experimental and Results

Synthesis of *Trans*-anisole oxide

Trans-anisole oxide was prepared according to a published procedure¹. *Trans*-anethole (*p*-Methoxy-*trans*- β -methylstyrene, 0.50 g, 3.4 mmol) was dissolved in 10 ml dichloromethane. This solution was then added to 10% aqueous Na₂CO₃ (20 ml) in an ice bath. A solution of *m*-chloroperoxybenzoic acid (1.4 g, 5.7 mmol dissolved in 20 ml dichloromethane) was added next at a rate 0.5 ml/min with vigorous stirring to the *trans*-anethole mixture. After the addition, the mixture was allowed to stir for an additional 20 minutes.

The organic layer was separated and washed with 10% Na₂CO₃ (5x25 ml). The organic layer was dried over Na₂SO₄ and evaporated to dryness (45 °C bath temperature) to obtain a clear oil (0.5567 g). This mixture was used for the purification on a RediSep Rf Gold Diol column. The reaction used for the RediSep Rf Gold Cyano column yielded 0.5712 g of oil.

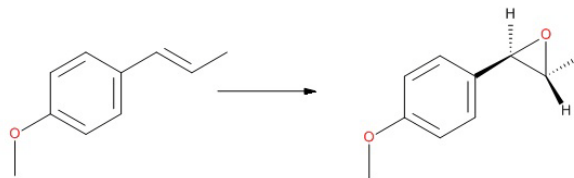


Figure 1: Synthesis of *trans*-anisole oxide

Purification on RediSep Rf Gold Diol

A reusable diol solid load cartridge was made by filling a 5 g “empty” solid load cartridge (PN 69-3873-235) with 2.5 g bulk diol media. The reaction mixture was dissolved in dichloromethane and placed in the diol solid load cartridge. The use of diol media in the solid load cartridge provided a compatible media for elution for the chromatography. The dichloromethane was evaporated by placing the solid load cartridge on the CombiFlash® Rf+ (PN 68-5230-021) instrument and blowing air through the cartridge with the air-purge feature via manual control. As illustrated in Chromatography Application Notes 88² and 89³, loading the sample on a solid load cartridge improves resolution. The diol packing ensures a compatible adsorption surface and minimized compound decomposition.

The mixture was eluted with a hexane-ethyl acetate gradient (Figure 2) using a 50 g RediSep Rf Gold Diol column (PN 69-2203-517). Fractions were collected at 280 nm and evaporated into tared flasks at 45 °C.

1. Centko, R.S.; Mohan, R.S. The Discovery-Oriented Approach to Organic Chemistry. 4. Epoxidation of *p*-Methoxy-*trans*- β -methylstyrene. *J. Chem. Ed.* 2001, 74(1), 77-79.

2. [Loading.pdf](http://www.isco.com/WebProductFiles/Applications/101/Application_Notes/AN88_C18_Flash_Column>Loading.pdf retrieved 21 June 2014.
3. <a href=) retrieved 21 June 2014.

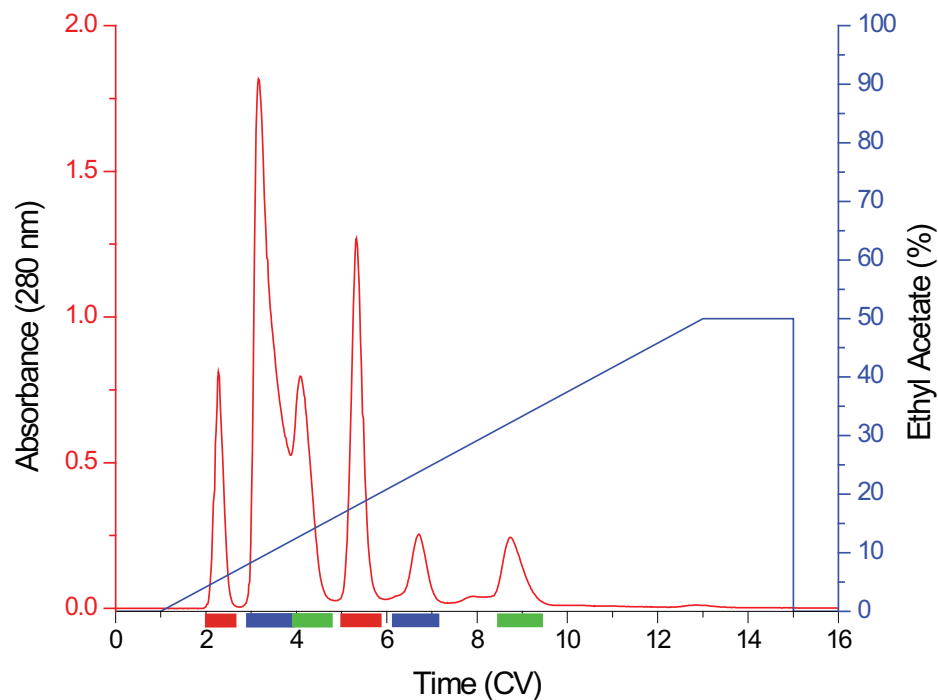


Figure 2: Purification of *trans*-anisole oxide with RediSep Rf Gold Diol column

Table 1: Compound Recovery

Fraction	Recovered Mass (g)
1	0.0549
2	0.2766
3	0.1030
4	0.0139
5	0.0136
6	0.0543
Total:	0.5163

The desired reaction product eluted in fractions 2 and 3. The compound recovery in these fractions was 0.3796 g, or 68% reaction yield, compound identity was verified by NMR and comparison with the spectra reported in Reference 1.

Purification on RediSep Rf Gold Cyano

A reusable cyano solid load cartridge was made by filling a 5 g “empty” solid load cartridge (PN 69-3873-235) with 2.5 g bulk cyano media. The reaction mixture was dissolved in dichloromethane and placed in the cyano solid load cartridge. The dichloromethane was evaporated by placing the solid load cartridge on the CombiFlash[®] Rf+ (PN 68-5230-021) system and blowing air through the cartridge with the air-purge feature via manual control. The cyano solid load cartridge ensures

a compatible adsorption surface and minimizes compound decomposition. The mixture was eluted with a hexane-ethyl acetate gradient (Figure 3) using a 50 g RediSep Rf Gold Cyano column (PN 69-2203-497). Fractions were collected at 280 nm and evaporated into tared flasks at 45 °C.

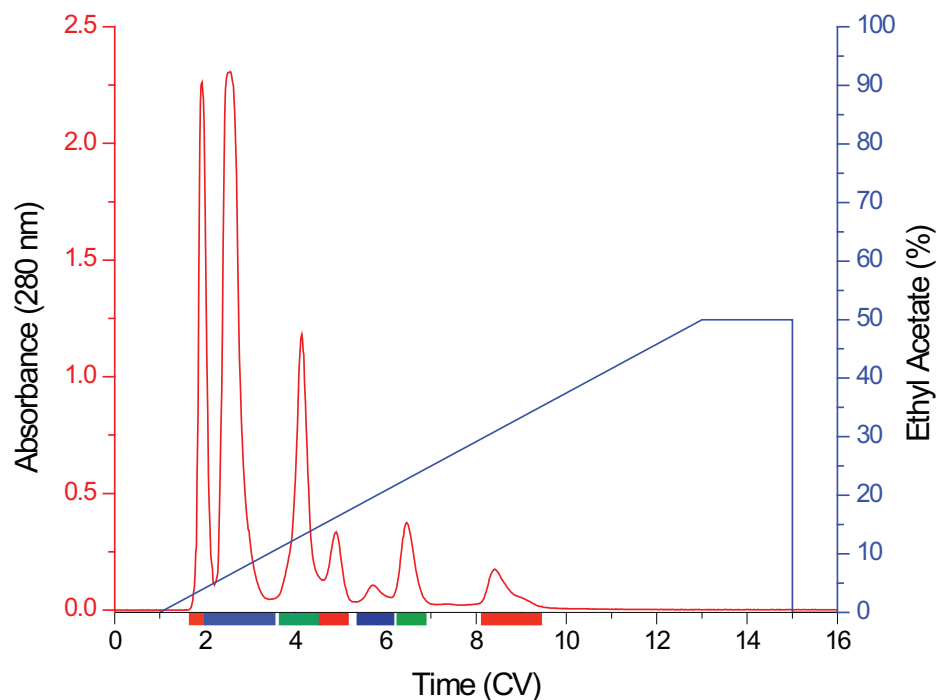


Figure 3: Purification of *trans*-anisole oxide with a RediSep Rf Gold Cyano column

Table 2: Compound Recovery

Fraction	Recovered Mass (g)
1	0.0575
2	0.3012
3	0.421
4	0.0107
5	0.0076
6	0.0510
7	0.0187
Total:	0.4888

The desired reaction product eluted in fraction 2. The compound recovery in this fraction was 0.3012 g, or 55% reaction yield, verified by NMR; the PMR spectrum matched that from Reference 1.

Conclusion

RediSep Rf Gold Diol and RediSep Rf Gold Cyano columns provide viable alternative methods for the purification of delicate compounds, such as epoxides, that often decompose on silica gel. Acidic silanols on the chromatographic media likely open the epoxide to

form an ester that irreversibly binds to the silica. No material was found to elute from silica. The cyano and diol groups are bonded to the silica media which protects the compound by preventing reaction of the epoxide with acidic silanol groups while providing a surface with the required selectivity to purify the mixture running as normal phase columns. The use of low-boiling normal phase solvents allows rapid evaporation of fractions at a moderate temperature compared to reverse phase solvents, further reducing the stress on fragile compounds.

Teledyne Isco

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

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