Acetone as an Alternative to Ethyl Acetate

in Flash Chromatography

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Chromatography Application Note AN20

Abstract

Ethyl acetate is one of the most commonly used solvents in flash chromatography. It is readily available and easy to remove by rotary evaporation. However, ethyl acetate adsorbs in the wavelength range of 200 to 235 nm, a region where many compounds also absorb UV light. Acetone is presented as an alternative to ethyl acetate for these compounds. Acetone is slightly more polar than ethyl acetate, allowing for faster elution of some compounds.

Reasons for Using Acetone

Useful with gradients separating compounds absorbing at short wavelengths

The main reason for using acetone as a flash solvent is that it does not absorb at short wavelengths. As seen in Figure 1, acetone does not absorb at wavelengths shorter than 220 nm, while ethyl acetate absorbs in this range. This makes acetone useful for gradient flash chromatography of compounds that absorb at 220 nm or less.

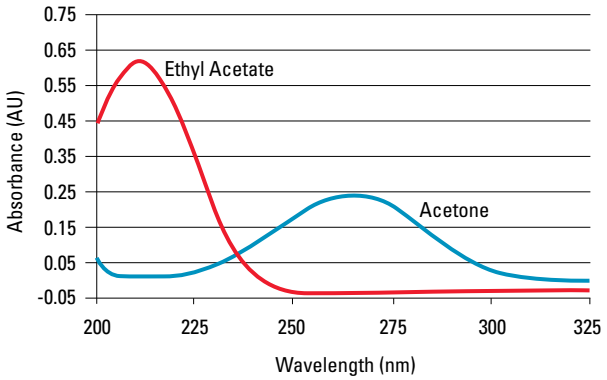
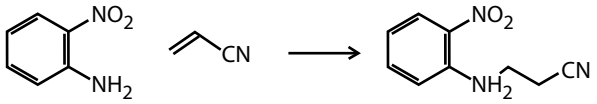


Figure 1: UV spectra of acetone and ethyl acetate
Ethyl acetate shows "end absorption"

The commonly used ethyl acetate has "end absorption" (absorbance near 200 nm, typically the end of a UV detector's range), so compounds with similar absorption are difficult to detect at low wavelengths using this solvent.

The synthesis and purification of 3-(2-nitrophenylamino)propionitrile provides an example of the use of acetone for purification.



To a round bottomed flask, p-nitroaniline (25.084 g) dissolved in absolute ethanol (125 mL) was added. The reaction mixture was heated to 80 °C and Triton B (3.8 mL) was added. To the stirring reaction mixture was added acrylonitrile (35 mL) and stirred at 80 °C for 24 hours. The mixture was evaporated on a rotary evaporator to elute a brown oil.

The oil was dissolved in 40 mL of ethyl acetate. Activated charcoal (1.6 g) was added to the solution followed by filtration. Heptanes (50 mL) were added and heated to boiling, then allowed to cool. After 2 days, dark brown crystals were collected to yield 6.3 g of pure product, 3-(2-nitrophenylamino)propionitrile.

A 30 mg sample consisting of 50:50 p-nitroaniline and 3-(2-nitrophenylamino)propionitrile was separated using the parameters in Table 1.

Table 1: Method parameters for purification of p-nitroaniline and 3-(2-nitrophenylamino)propionitrile

Instrumentation:	Teledyne ISCO Combi*Flash*®		
Column	40 g Redi*Sep*®		
Sample Loading Method	Liquid Injection		
Wavelength	210 nm		
Mobile phase:	Solvent A: Hexane		Solvent B: Acetone
Flow Rate:	30 mL/minute		
Equilibration Volume:	3 column volumes		
Gradient:	% Solvent B	CV (segment length)	Time (segment length)
	10	Initial	Initial
	10	5.0	2.8
	40	10.0	6.0
	40	≈3.0	2.0
	10	0.0	0.0
	10	≈1.0	1.0

Alternatively, the crystallization step could be avoided simply by adsorbing the reaction mixture onto silica gel and running the mixture on a Redi*Sep* column. For example, a 330 g column would easily take 1/6 of the reaction mixture. Even if six runs were required, a day would be saved and the yield would be higher since 3-(2-nitrophenylamino)propionitrile is still left in the supernatant solution from the crystallization.

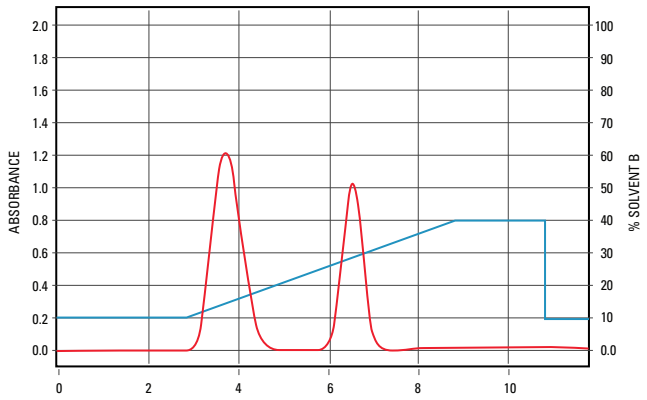


Figure 2: Gradient elution of p-nitroaniline and 3-(2-nitrophenylamino) propionitrile with detection at 210 nm

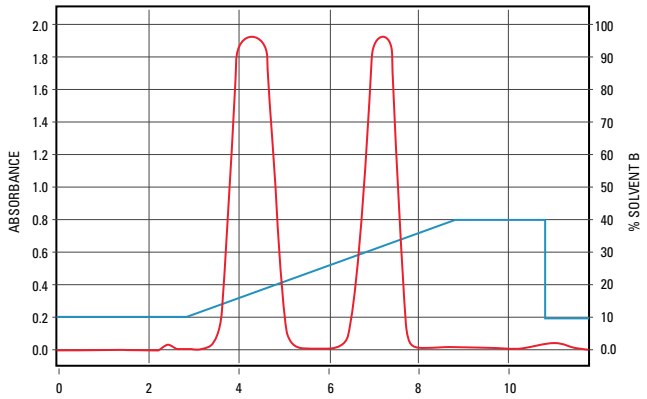


Figure 3: Gradient elution of p-nitroaniline and 3-(2-nitrophenylamino) propionitrile with detection at 210 nm and higher sample loading

Since acetone is more polar than ethyl acetate, acetone will cause the compounds to elute more quickly and shorten your run time while conserving solvent.

Acetone can cost about half the price of ethyl acetate, resulting in significant monetary savings.

Natural products

Hexane/acetone is commonly used to purify natural products. It can be used in high concentrations (up to 100%), while methanol is commonly believed to dissolve silica gel. Acetone also makes a useful mid-polar solvent.

Using a Combi*Flash* allows users to run a hexane/acetone gradient with an easy switch to methanol to elute compounds with a wide range of polarity in a single run. The Combi*Flash* systems have up to four solvent inlets, allowing for easy solvent switching.

Caveats

Acetone does have some drawbacks. First, acetone easily picks up water from the air. Therefore, acetone should be capped when not in use. When developing TLC plates, use fresh acetone.

Second, acetone absorbs UV light with wavelengths longer than 220 nm. For this reason, it is not useful for detectors that operate only at 254 nm.

Conclusion

Acetone can be used in place of ethyl acetate for compounds that show absorption at wavelengths below 220 nm and are not UV active at 254 nm. Acetone is a cheaper alternative to ethyl acetate.

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