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Distinguishing the Good and the Bad from the Ugly with GC and FT-IR

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Key Words

- Clandestine Labs
- Ephedrine
- GC-IR
- Hydrocodone
- Meth Labs
- Separation and Identification

Introduction

Drug enforcement agencies are often called upon to investigate clandestine synthesis labs, like the so called "meth labs," where there is a high potential for illegal substances to be present. Usually, there is plenty of sample, although in some cases only traces are present, but almost universally the materials are impure (QC is not a major concern in these labs). Thus, enforcement requires separation and identification of the components of a messy mixture. The court case stemming from the investigation will hinge upon both the identity and quantity of illegal material present, so this is an extremely important consideration.

Clandestine labs have become increasingly sophisticated, being able to synthesize many prescription drugs (like hydrocodone, a key ingredient in Vicodin™) or designer drugs, which typically involve slight chemical modifications of known materials. The class of drugs similar to ephedrine, for instance, includes methamphetamine and pseudoephedrine, one a controlled drug, the other an over-the-counter decongestant. The subtle differences make the need for a rapid, structurally sensitive method of analysis an imperative for effective drug law enforcement.

The most difficult structural difference to determine is stereochemistry – the specific orientation of a chemical species about a single carbon atom. The extreme importance of this became apparent with the drug thalidomide in the 60's. Rotation of the chemical structure about a single bond changed the material from having a desirable, sedative effect (the "R+" form) to having horrific teratogenic effects (the "S-" form). A similar pair in drug enforcement circles is ephedrine and pseudoephedrine, which differ only in the orientation of a side chain on one carbon atom.

The first step in most analyses of these materials is a separation, where individual components are broken out from the mixture (solvent or impurities). Gas or liquid chromatography is commonly used for separation. The now-separated materials are present only in tiny quantities, so very sensitive detectors are needed. Common ones like the flame-ionization detector or the thermal conductivity detector are sensitive, but do not provide any insights into the structure *("something went through, but I don't know what")*. The most common identification tool is a mass spectrometer (MS), which, when coupled to a gas chromatograph (GC), is extremely sensitive and provides excellent identification power, with one major exception in drug analyses.

The MS works by shattering the molecule into components, and then measuring the mass of those components. The fragmentation pattern is reproducible for a given molecule, so the pattern of mass peaks can be used to identify many materials. However, when ephedrine and pseudoephedrine are fragmented, the patterns are identical, as seen in figure 1. As an analogy, when a Lego™ toy is built with ten blocks, specific structures can be built – there are many possible configurations of those ten blocks. However, when broken apart, there is no way to determine which of the structures had been built last. To determine this, one must examine the structure while it is still together.

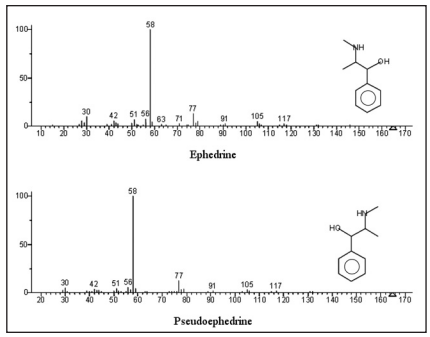


Figure 1: The mass spectrum of ephedrine and pseudoephedrine illustrates the identical mass peak patterns each produce

The combination of GC with FT-IR, shown in figure 2, provides just such a tool. The effluent of the GC column, with the separation complete, is directed onto a light pipe through which IR radiation has been directed. The FT-IR is a powerful gas analyzer, being able to detect trace quantities of gas, so the sensitivity needed to detect the material is present. The IR spectrum detects the structurally-intact form of the drug, and even subtle differences are detectable. Thus, the analysis of suspicious materials containing ephedrine or pseudoephedrine can proceed.

Figure 2: By combining GC and FT-IR, the molecular structure of the components of a mixture can be determined

Experimental

Samples of drug materials containing 0.5 mg per mL of analyte in solvent were prepared under DEA supervision. These included ephedrine, pseudoephedrine, heroin and cocaine.

A Thermo Scientific TRACE™ GC with a 10 meter column (HP-50) and AS-3000 Autosampler was connected to the Thermo Scientific Nicolet™ 6700 FT-IR spectrometer, driven with the Thermo Scientific OMNIC™ and OMNIC Time Series software packages. OMNIC Time Series

software allows collection of Gram-Schmidt reconstructions (GSR; essentially the chromatograms)[1] and the profiling of the data (chemigrams, the time evolution of a particular IR peak). A macro controlled collection in parallel with the autosampler, so sequential samples (up to 105) could be run. Collection of the background spectrum (256 scans) was done during the cooling phase of the GC, so the "dead time" between experiments was minimized.

Results

Figure 3 shows a screen capture from the OMNIC Time Series software for a GC-FTIR run of cocaine. The solvent peak appeared in less than 1 minute, and is off-screen (left). The spectrum resulting from co-adding the spectra in the shaded region in the GSR is shown in the lower window – the signal to noise is excellent. OMNIC Time Series software allows conversion of the data files into waterfall plots or profile plots. The data can be processed (baseline correction, for instance), or exported to an independent OMNIC window. The spectra can then be searched against libraries of spectra; figure 4 shows the matching of this co-add spectrum, with the top two matches being shown.

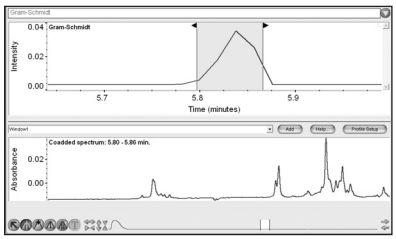


Figure 3: GSR and co-added spectra for cocaine using OMNIC Time Series software

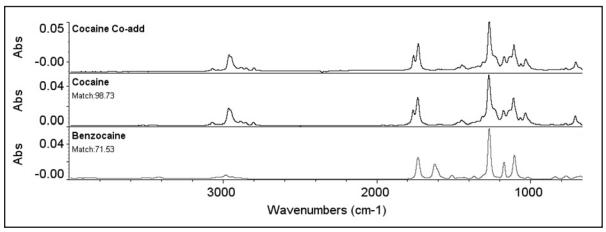


Figure 4: Spectra can be searched against library reference spectra in separate OMNIC software windows

Figure 5 shows the spectra derived by co-adding the signals around the GSR peaks for pseudoephedrine and ephedrine. Both analytes eluted between 3.17 and 3.23 minutes on the short column. As the compounds differ only in stereochemistry, the infrared spectra exhibit many similarities. However, the differences in the fingerprint region around 1100 cm^{-1} allow the two to be discriminated; demonstrating the power of the GC-IR method. The search results are shown in figures 6 and 7; note the hit values were over 90 for both, with the next best hit being lower.

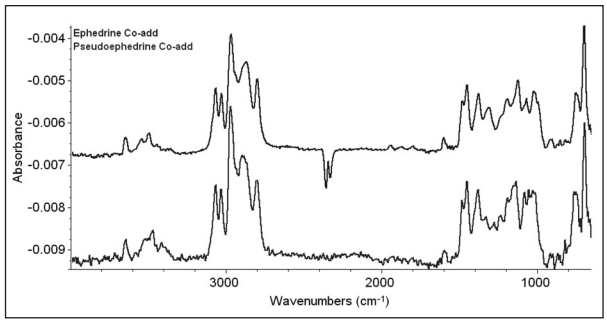
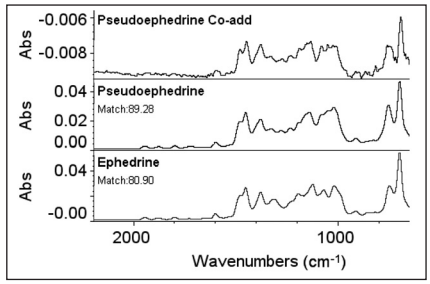


Figure 5: Co-added signals around the GSR peaks for pseudoephedrine and ephedrine

Figure 6: Search results for pseudoephedrine



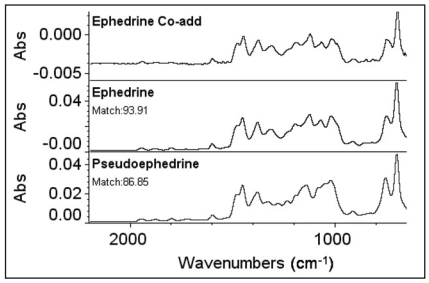


Figure 7: Search results for ephedrine

The closeness of the "incorrect" species is indicative of the degree of similarity between the molecules, but the distance is sufficient to ensure good quality matches will occur.

Conclusions

The GC-FTIR solution from Thermo Fisher Scientific provides not only excellent GC data (chromatograms, in the form of the GSR), but can serve as a stand-alone IR bench. This provides all of the advantages and capabilities of the Thermo Scientific Nicolet™ x700 FT-IR spectrometers, Thermo Scientific Smart Accessories™ (ATR, DRIFTS, etc.), IR microscopy, and Raman to quickly identify gun powder residuals, single crystals, fibers, hit-and-run paint samples, inks from stylograph pens or stamps, and many other Forensic materials.

References

1. Griffiths, P.R.; DeHaseth, J.A. *Fourier Transform Infrared Spectrometry* (Wiley & Sons, 1986), Chapter 18.

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