Introduction

The analysis of low volatility impurities in a solid matrix can pose a significant method development challenge. A trace level detection method can take weeks to develop. Since FT-MRR spectra are measured at ideal pressures of 1-3 mTorr, this highly selective spectroscopic technique can be used for gas phase detections of low volatility species without chromatography. We present a method for detecting acetaminophen (Fig. 1) at 0.015% by mass in the highly efficient sublimation and transfer method. We quantitatively measured acetaminophen in a mixture at 0.008% with sublimation and transfer a mixture at 0.015% with sublimation and transfer.

What is FT-MRR

FT-MRR is ideal for addressing the challenge of low volatility analysis, even in the gas phase because optimum pressure ranges for FT-MRR spectroscopy are 1-100 mTorr.

Acetamide

Acetamide is an ideal candidate for FT-MRR detection.

Challenge

1. Reference measurement: High volatility impurities dominate the spectrum, so purification is needed for a reference measurement.
2. Impurity analysis: adsorption effects diminish sample transfer efficiency, and contribute to chemical crossovers.

What is FT-MRR

FT-MRR is an excellent tool for high-dynamic range complex mixtures analysis. FT-MRR can detect acetaminophen without a reference library measurement. It is structurally and spectrally described to the measurement. We effectively purified a sample of 0.5% acetaminophen by sublimation followed by flow transfer with N2. We measured a liquid nitrogen temperature of 77K. Sublimation followed by flow transfer with N2 is ideal for efficient transfer and effective impurity analysis.

Procedure

A) Reference Spectrum
1. 50mg Acetaminophen vacuum purified by sublimation in Synthware 50ml High Vacuum Glass Tube and condensation of step.
2. The purified crystals were heated to 65°C and transferred to the spectrometer with a heated transfer line (50°C, 55°C, 65°C, and 75°C).
3. The sample was heated to 144°C (melting point of Acetaminophen). Inset below is narrow pressure scans. The sample was heated to 144°C.

B) Sampling Method
1. A sample of 0.5% acetamide spiked into acetaminophen was prepared. 50 mg of acetaminophen and 35 mg of acetamide was sublimated at 200°C.
2. The sample was heated to 70°C, 80°C, and 90°C.

Results: Reference Spectrum

Figure 3: Evaluation of flow rate and sample transfer pressure relationship that is required for a detection. With experimental data, the flow rate is optimal at a flow rate of 0.5-1.0 mTorr. This resonates with the high-dynamic range capability of routine use.

Results: Sampling Method

Figure 4: Static spectrum taken on BrightSpec One 260 GHz spectrometer of 50mg of 0.5% Acetaminophen and spiked acetaminophen mixture used for transfer efficiency experiments.

Conclusions and Implications

- Sublimation followed by flow transfer with N2 effectively purifies acetaminophen, sublimating 99.8% of acetaminophen.
- Loop transfer sampling method reproduces acetaminophen signals (±0.02mV) between 344 and 80°C trials.
- Without chromatography, a real mixture produces distinguishable FT-MRR spectra for fast qualitative and quantitative analysis.

Future Work

- Continued characterization of sampling methods for efficient transfer of low volatility organic solids.