

Highlights

- Static headspace FT-MRR is used to characterize volatile impurities in solutions without chromatography.
- The method provides good linearity and low ppm detection limits.
- Autosampling technology is integrated to perform automated batch runs and remove user variability.

Introduction

Static headspace sampling (SHS) is a simple, robust, and sensitive method for sampling volatile impurities out of solutions. This Application Note describes a method for static headspace sampling integrated with a Fourier Transform Molecular Rotational Resonance (FT-MRR) spectrometer, which circumvents the gas chromatography with a high-resolution spectrometer that can rapidly identify and quantify a wide range of small volatile impurities without spectral interference from each other or from the solvent. Due to the intrinsic specificity of the technique, molecules with similar structures, including isomers, can be distinctly quantified without separation or chemometrics. FT-MRR simplifies the decision-making process for the method development scientist by removing the chromatography step. This note describes the instrumentation and method for automated FT-MRR headspace analysis. The measurement protocol can be software controlled to change the measurement mode from unbiased, fullband spectral analysis, to the more sensitive targeted analysis of specific analytes.

Experimental Methods

The FT-MRR headspace sampling methodology is similar to that for headspace GC, except the FT-MRR instrument requires that low pressure is maintained throughout the transfer path. Rather than the continuous flow of a carrier gas, a vacuum differential is used to transfer vapors to the FT-MRR spectrometer. Air does not interfere with the spectral detection, but it does broaden spectral features and impede ultimate sensitivity. To achieve a quantitative sample transfer, the BrightSpec headspace sampling module incorporates a controlled volume loop transfer system.

The BrightSpec One FT-MRR spectrometer is shown in Fig. 1. This is a benchtop instrument that uses millimeter wave radiation in the 260-290 GHz frequency band to measure pure rotational angular momentum transitions of gas phase molecules. The sampling module (expanded view, right panel) contains the equipment for sample injection, equilibration, and headspace transfer into the FT-MRR instrument. Finally, a PAL-RTC sample prep station is integrated to allow full hands-off automation of the instrument for large batch runs. This autosampler, in addition to mixture preparation, moves headspace vials into the BrightSpec sampling module and injects the solutions for analysis.

The headspace and FT-MRR method parameters are configured through the BrightSpec software interface. For the measurements presented here, the vial is maintained at 50°C, the loop transfer tubing and valves are kept at 80°C, and the spectrometer measurement cell is held at 40°C. The static headspace sampling method consists of evacuation

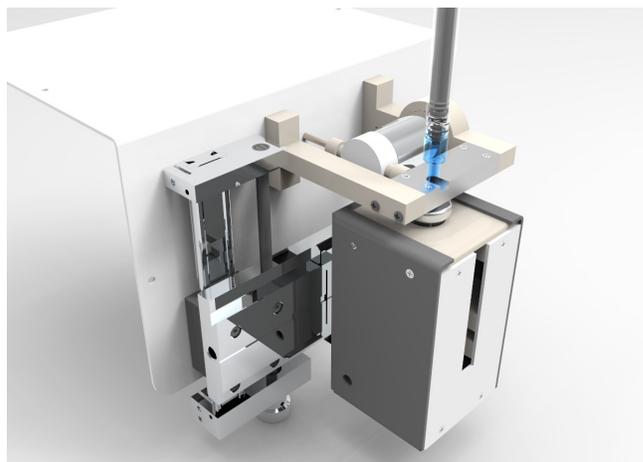
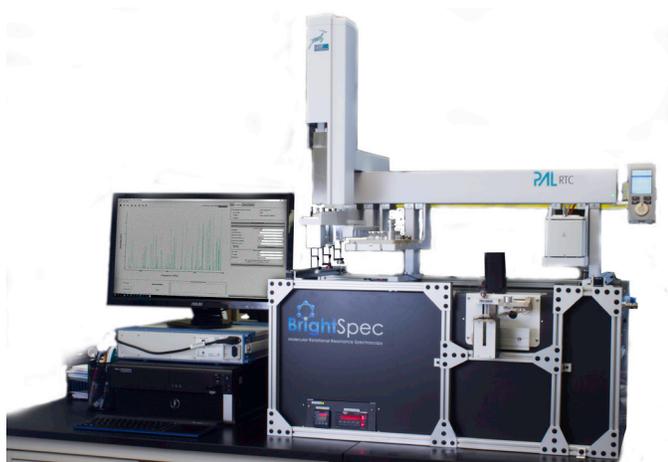


Fig 1: The BrightSpec One FT-MRR spectrometer with headspace sampling and PAL-RTC autosampler integrated. Right: standalone drawing of the headspace module.

and cleaning of a 20 mL headspace vial, injection of the solution, headspace equilibration, and finally loop transfer into the FT-MRR spectrometer. The amount of solution injected into the headspace vial is 1 mL. The total measurement cycle time, which includes a nitrogen flush to clean out the system between measurements as well as each fresh vial as it is introduced to the system, is 18 minutes (with significant potential for future reductions through engineering, as most of this is cleaning and evacuation time). With this method, we observe excellent blank performance and carryover below the method detection limit.

Results

Once the contents of the headspace loop are delivered to the spectrometer vacuum cell, the FT-MRR measurement consists of a series of excitation pulses that are tuned to selectively excite characteristic transitions of each analyte of interest in the sample. Calibration curves for ethanol, methanol, and isopropanol in water across the concentration range 10-100 mg/L are shown in Fig 2. Linear correlation (R^2) is greater than 0.999 and short term RSD is not more than 5%. Variations in the instrumental response from day to day are accounted for through an electronic normalization procedure, so that the instrument signal is directly proportional to the concentration of analyte in a particular matrix. The detection limits for these small alcohols in water are presented in Table 1.

Table 1: Detection limits for small alcohols in water

Analyte	Detection limit (5 sec measurement)
Methanol	0.5 mg/L
Ethanol	1 mg/L
2-Propanol	2 mg/L

Other solvents that are suitable for FT-MRR analysis include *N,N*-dimethylacetamide (DMAC), *N,N*-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO). These solvents, unlike water, do contribute to the total FT-MRR spectrum that is observed, but the spectra are sparse enough that clean features for each analyte can usually be found with little difficulty. Although the headspace partitioning constants are affected by changes in solvent, or other experimental parameters like the vial temperature, the FT-MRR characteristic spectra are defined only by the chemical structure of the analyte and therefore are unaffected by sampling method choices. Method design and optimization is therefore very straightforward.

Conclusions

Static headspace sampling is a simple and powerful way to accomplish sample volatilization (necessary for the FT-MRR analysis) while enhancing the concentrations of volatile components for increased sensitivity. Room temperature FT-MRR, as an alternative to gas chromatography, offers a rapid, quantitative spectroscopy alternative that can resolve multi-component mixtures without need for separation.

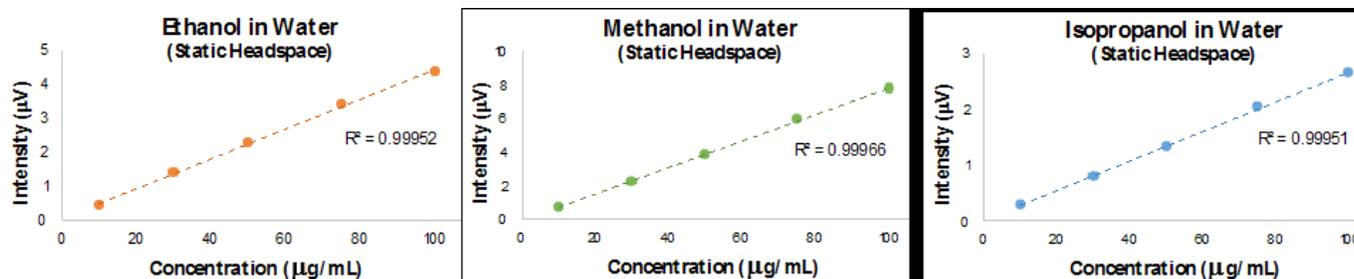


Fig 2: Calibration curves of ethanol, methanol, and isopropanol in water.