APPLICATION NOTE

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Benchtop NMR Combined with GC/MS Confirms Identity of Forensic Case Sample

Authors: Dean Antic, Ph.D.,
Thermo Fisher Scientific,
San Jose, CA, USA

WanLi Wei, Senior Engineer,
Institute of Forensic Sciences, Wuxi Public Security Bureau, Wuxi, China

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The benchtop Thermo Scientific™ picoSpin™ 80 ^{1}H NMR spectrometer provides an additional layer of structural identification of drug analogues and precursors, complementing GC/MS analysis. The combination of the two techniques allows for a positive identification of real forensic case samples with high confidence, thereby enhancing the presumptive testing capabilities of illicit drug screening facilities.

Abstract

A forensic case sample of an illicit drug precursor was analyzed by GC/MS and benchtop NMR. The most probable chemical structure from a GC/MS library search, however, conflicts with the spectral features identified by NMR. By interrogating the peak pattern and chemical shifts in the NMR spectra, both experimentally obtained and predicted by Mnova NMR software, the seized sample was identified as a compound with a lower matching score by GC/MS. The combination of the two techniques allows one to discriminate between two possible structural isomers in a real forensic case sample with high confidence.

The case sample demonstrated in this note exemplifies the need for multiple techniques in order to confirm the identity of seized forensic samples, as recommend by SWGDRUG.

Introduction

Illicit drugs identification is a challenge to law enforcement due to the vast assortment of illegal drugs that already exist, and an increasing number of new, “not-yet” illegal analogues of classified drugs appearing on the street. Added to this burden is the identification of clandestine lab chemicals and precursor compounds used in the manufacture of illicit drugs, as well as the excipients used as adulterants to alter street-level drug purity.

Law enforcement has a variety of analytical tools at their disposal, including color tests, Fourier transform infrared (FTIR), gas chromatography/mass spectrometry (GC/MS), Raman spectroscopy and nuclear magnetic resonance spectroscopy (NMR) to aid in characterizing forensic samples and elucidating their structures.

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Since no single technique can provide definitive structure elucidation, the Scientific Working Group for the Analysis of Seized Drugs[1] (SWGDRUG) proposes a combination of analytical techniques be used depending on the nature of the samples and available techniques for analysis. Initial chemical identification of a seized sample includes a color test and FTIR analysis. Molecular weight information is provided by mass spectrometry. When combined with other spectroscopic techniques, including Raman spectroscopy and NMR, a chemical structure can be elucidated. The power of GC/MS, FTIR and Raman is highly dependent upon the databases of reference samples and related compounds. It is, therefore, an arduous endeavor to maintain and update these databases in the face of increasing numbers of novel structural analogues that are appearing.

Seized sample identification methods

Figure 1 shows the GC/MS chromatogram of a sample seized from a clandestine lab. The unknown sample was a clear, highly volatile, and fragrant organic liquid, suspected as a precursor compound used in the production of illicit drugs. The data was acquired using a Thermo Scientific™ ISQ™ QD Single Quadrupole GC-MS system. The main component of the sample has a retention time of 4.38 min (top trace) and the corresponding mass spectrum is shown at the bottom of Figure 1. The main component has a molecular mass of 202 g/mol. In addition, there are a series of fragmentation peaks at m/z 159, 129, 103, 73, and 57. The subsequent library search yielded a high probability match of the sample to 1,1-dibutoxy butane, with its structure shown in Figure 2A.

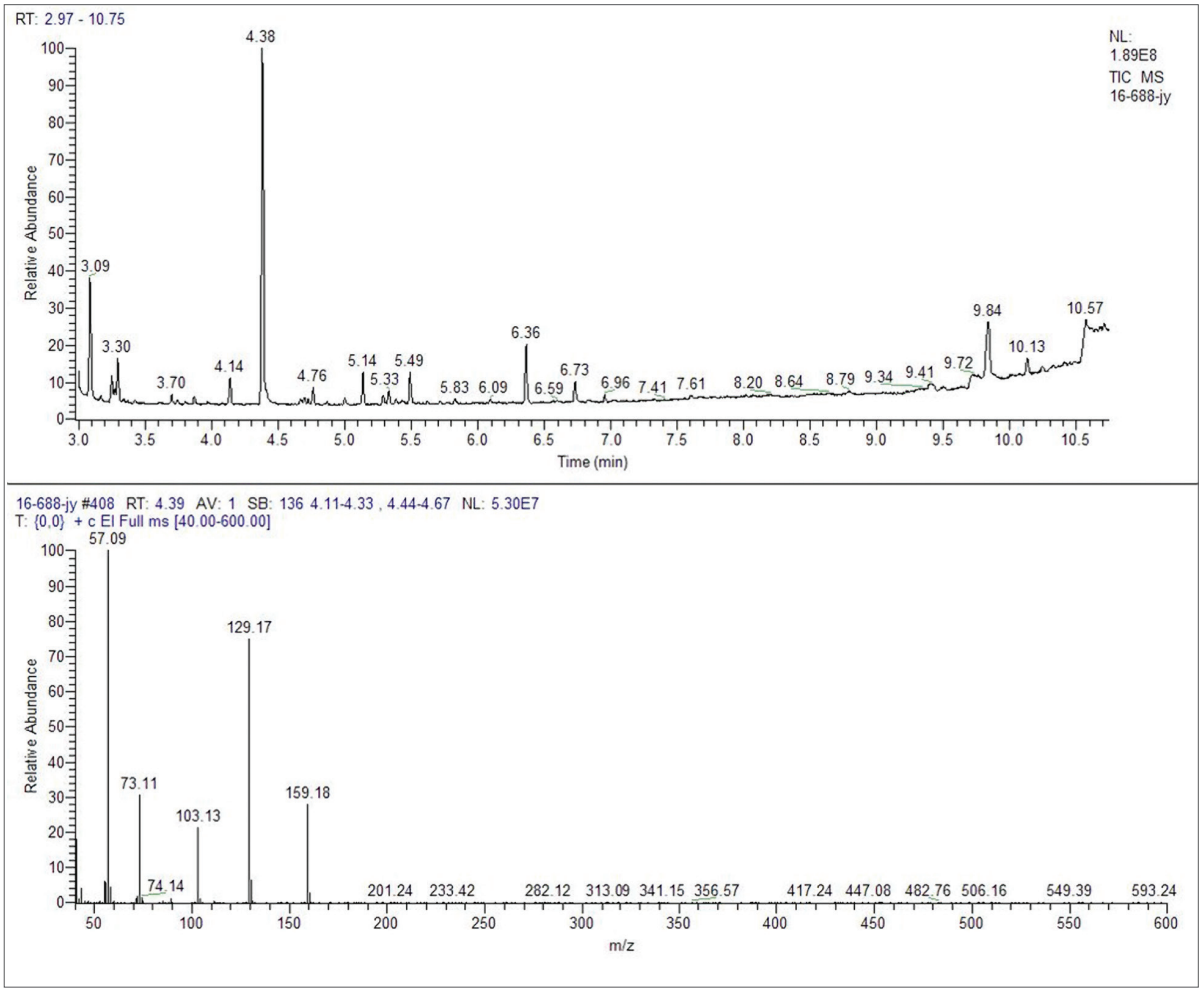

Figure 1
ISQ QD GC-MS chromatogram of unknown liquid (forensic case sample).

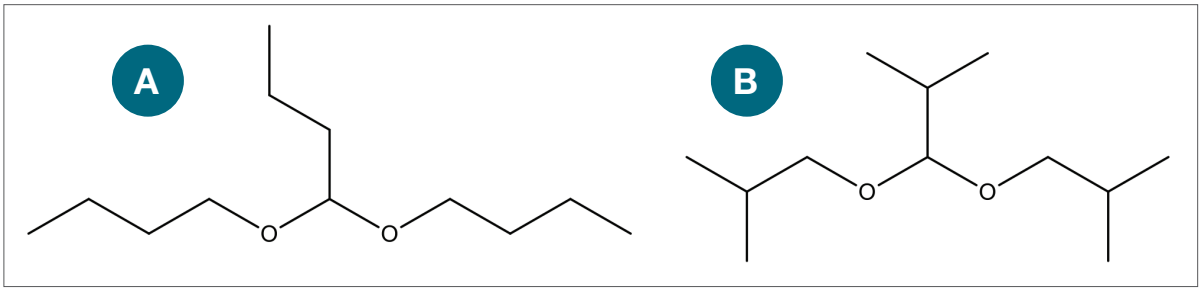

Figure 2
Chemical structures of two isomers; **(A)** 1,1-Dibutoxybutane; and **(B)** 1,1-Diisobutoxy-2-methylpropane.

The sample was further analyzed by a picoSpin 80 ^{1}H NMR spectrometer, an 82 MHz pulsed, Fourier transform ^{1}H NMR permanent magnet instrument, equipped with a capillary cartridge probe. Since the sample was a clear organic liquid, dilution in typical NMR solvents was not required. A small amount of the case sample was placed in a vial, to which a few drops of tetramethylsilane (TMS) was added to reference chemical shifts. The mixture was then directly injected into the NMR spectrometer. The resulting spectrum is shown in Figure 3. Note that the peaks attributed to impurities and TMS are manually labeled gray, whereas the unknown compound peaks are labeled blue.

The spectrum exhibits a distinct pattern of multiplicities characteristic to the isopropyl group: two strong overlapping doublets centered near 0.95 ppm, followed by a more complex series of weaker multiplets between 1 – 2 ppm. In addition, two strong doublets emerge centered at 3.34 and 4.49 ppm, respectively. The pattern of doublets suggests the presence of a single neighboring proton (CH), and the shift to high frequency indicates that the carbon center is attached to an electron withdrawing group. The NMR spectrum also implies structural symmetry of the sample. These suggested structural features, however, conflict with 1,1-dibutoxybutane suggested by the GC/MS library search.

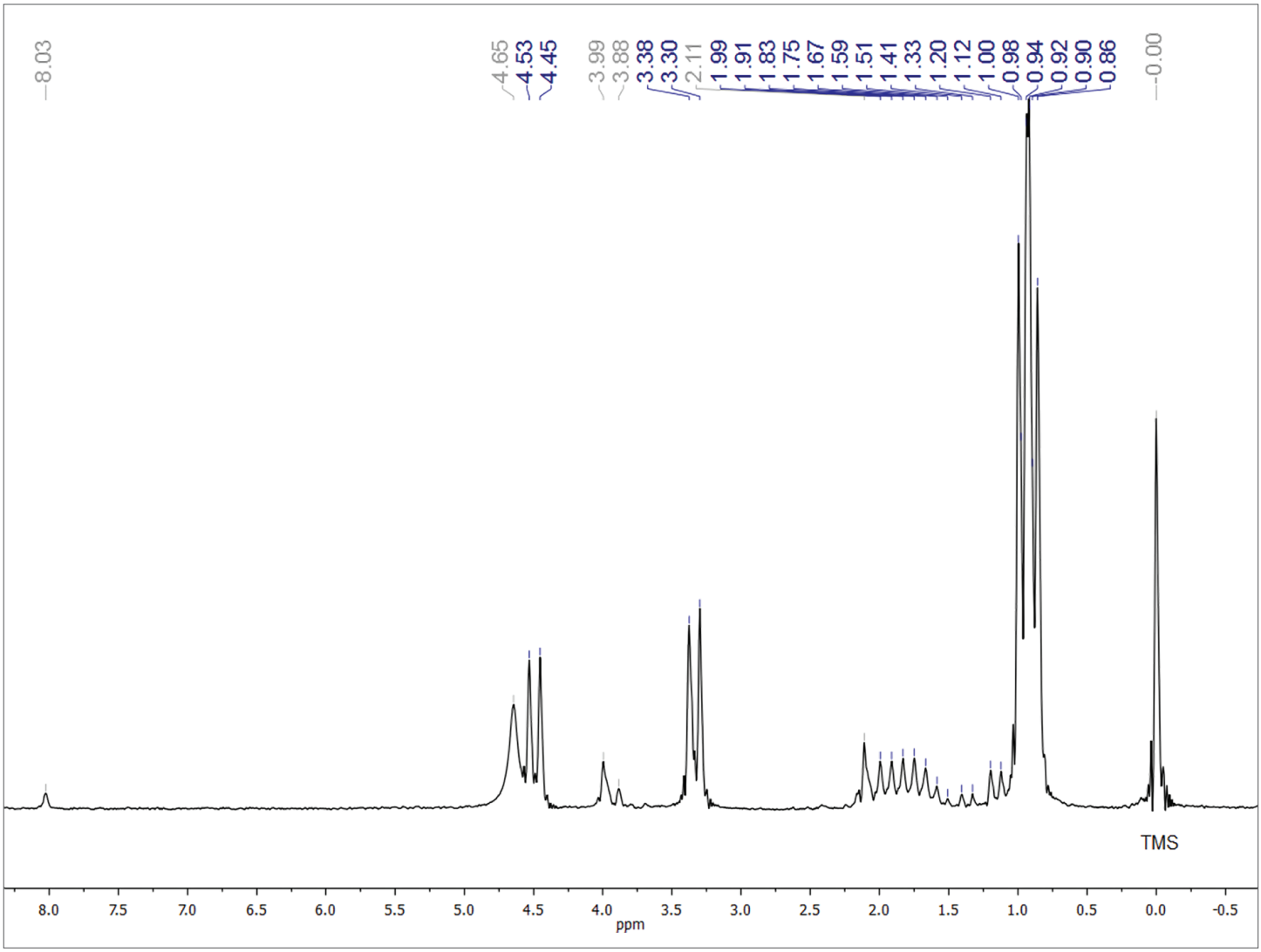

Figure 3

Experimental ^{1}H NMR 82 MHz spectrum of the seized sample. Data was acquired using a 90° pulse and 15 s recycle delay between pulses. The spectrum is an average of 5 co-added scans and processed using the Mnova NMR software suite (Mestrelab Research Inc.).

Figure 4 shows the comparison between the predicted NMR spectrum of 1,1-dibutoxybutane by Mnova software (top) and the experimental ^{1}H NMR spectrum of the seized sample (bottom). There are vast differences between the two spectra, indicating the sample under analysis is not 1,1-dibutoxybutane.

Upon further examination of the compound list from the GC/MS library search, a low probability match compound, 1,1-diisobutoxy-2-methylpropane (Figure 2B), was identified as a strong candidate. The structure possesses all key elements suggested by the experimental NMR spectrum: isopropyl groups, electron withdrawing O atoms, and high symmetry. Figure 5 shows a good agreement between the predicted NMR spectrum of 1,1-diisobutoxy-2-methylpropane (top) and the experimental NMR spectrum of the seized sample (bottom).

The key features of the NMR spectrum are assigned as follows:

- An intense, overlapping set of doublets at 0.9 ppm is due to the terminal methyl's of the isopropyl group ($-CH(CH_3)_2$);
- A broad, weak multiplet between 1 - 2 ppm is due to the methine (CH) coupling to the adjacent CH_3;
- The doublet centered at 3.3 ppm originates from the methylene groups (CH_2) of the 2-methyl propyl moiety. The doublet arises from the coupling to the adjacent CH proton of the isopropyl fragment;
- The doublet at 4.5 ppm belongs to the CH group. It shifts further due to their attachment to two electron withdrawing O atoms. The weaker signal compared to the doublet at 3.3 ppm is due to the presence of only one CH group.

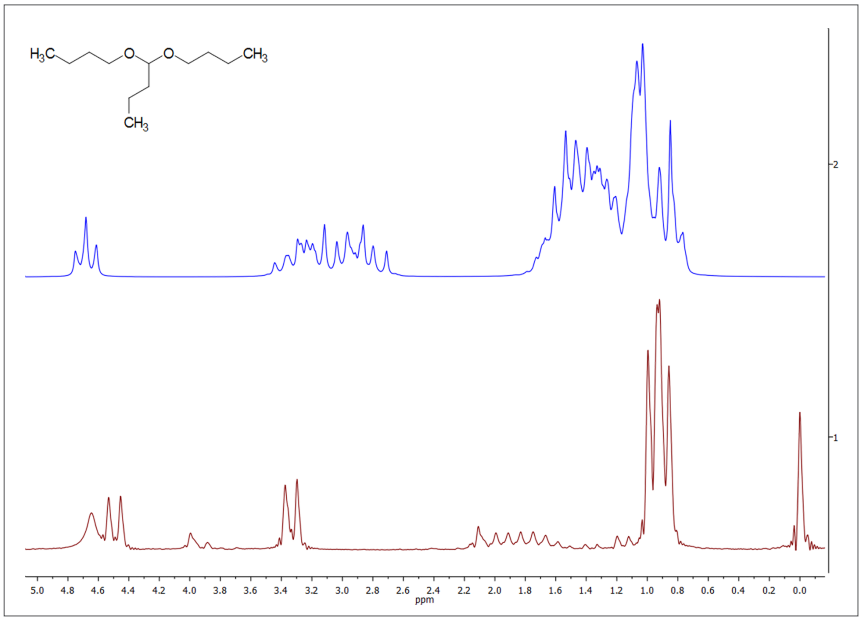

Figure 4
Predicted NMR spectrum of 1,1-dibutoxybutane (top) and experimental ^{1}H NMR 82 MHz spectrum of the seized sample (bottom). The predicted spectrum was generated by using Mnova NMRPredict plugin. Field strength was set at 82 MHz and linewidth value was set at 2.5 Hz.

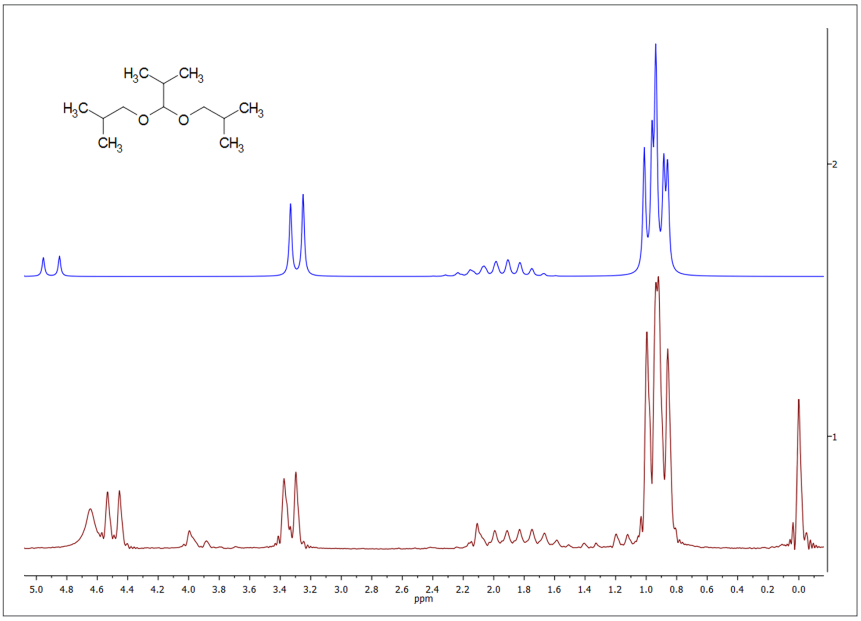

Figure 5
Experimental ^{1}H NMR 82 MHz spectrum of the seized sample and the predicted NMR spectrum of 1,1-diisobutoxy-2-methylpropane generated by Mnova software.

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The GC/MS data in combination with the picoSpin 80 NMR spectrum allows for the positive identification of the seized sample as 1,1-diisobutoxy-2-methylpropane. The compound is a precursor chemical and not a variant structural analogue of known illegal drugs.

Conclusions

In this note we showed how the picoSpin 80 NMR was able to provide additional information by interpreting and predicting the likely structure of a seized sample, complementing those derived from GC/MS analysis. The combination of the two techniques allows for a positive identification of an unknown compound with high confidence. The practices demonstrated in this note conform to the recommendations by SWGDRUG that multiple techniques are required to confirm seized sample identity.

The benchtop picoSpin 80 ^{1}H NMR solution offers structure selectivity and discriminating power needed to provide an additional layer of structural identification of drug analogues and precursors. This compact instrument can be conveniently placed in workspace-limited labs and testing areas, while enhancing the presumptive testing capabilities of illicit drug screening facilities.

Thermo Scientific™ picoSpin™ 80 NMR spectrometer and Thermo Scientific™ ISQ™ QD Single Quadrupole GC/MS System

References

SWGDRUG home page: http://www.swgdrug.org/ (accessed Jun 17, 2016).

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