Tech note

Analysis of cathinone samples encountered on the black market using GC-IR

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Introduction

Cathinones, also commonly referred to as “bath salts”, are a large compound class belonging to the family of new psychoactive substances (NPS). Due to their stimulant effects, they are often sold as alternatives to common recreational drugs [1]. Cathinones have been detected as adulterants or substitutes in common recreational drugs, e.g., MDMA-tablets (“ecstasy”) [2]. The substance class of cathinones is characterized by a vast diversity of structurally closely related compounds, including constitutional isomers. Depending on the regulatory framework regarding narcotics, it might be that some constitutional isomers are classified differently from other cathinones. Ultimately, this means that forensic laboratories require analytical methods for court-proof annotation of the exact isomeric structure of cathinones. In the context of chemical analysis of drug samples, information on the exact chemical structure is essential as well, as pharmacologic effects can differ between constitutional isomers.

When using mass spectrometry, structural isomers are often not distinguishable because they can result in similar retention times and mass fragmentation patterns. In such cases infrared (IR) spectroscopy has proven highly valuable, as for instance substitution at different positions on aromatic rings results in distinct IR adsorption patterns [3]. Common IR techniques such as attenuated total reflection Fourier transform IR spectroscopy (ATR-FTIR), or near-IR spectroscopy (NIRS) are well suited in cases where pure compounds are analyzed. However, mixtures are frequently encountered when analyzing recreational drugs. Drugs encountered on the black market often contain cutting agents, adulterants, and/or, in cases of tablets, additional tablet fillers and various excipients. This limits the reliability of the analytical results obtained by direct IR methodologies. These issues could be overcome when IR spectroscopy is hyphenated to a chromatographic technique, for instance gas chromatography (GC).

We demonstrate the unique strengths of GC-IR for the analysis of the important drug class of cathinones, on the structural isomers 3-methylmethcathinone (metaphedrone; 3-MMC) and 4-methylmethcathinone (mephedrone; 4-MMC) as well as 3-chloromethcathinone (clophedrone, 3-CMC) and 4-chloromethcathinone (clephedrone; 4-CMC) (see Figure 1).

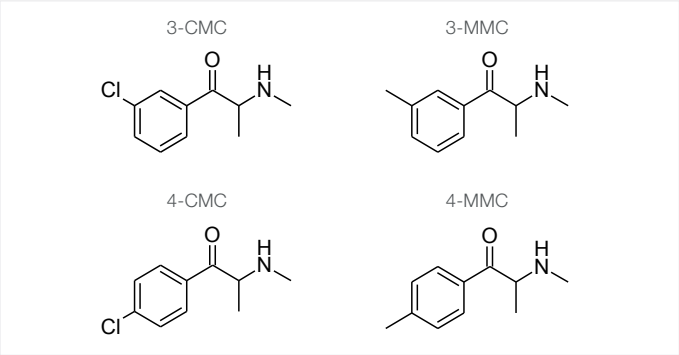

Figure 1. Chemical structures of the investigated cathinones.

Experimental

Samples, comprised of powders and tablets (Figure 2), were analyzed at the Department of Forensic Toxicology and Chemistry, Institute of Forensic Medicine of the University Basel. Between 1–2 mg of pure reference standards and 10 mg of homogenized black market samples were weighed and dissolved in 1 mL 0.5 M NaOH, thereby generating the free base of the drugs. The samples were extracted using 1 mL of ethyl acetate. GC-IR analyses were conducted using a Thermo Scientific Trace 1310 gas chromatograph hyphenated to a Thermo Scientific™ Nicolet™ iS50 FTIR Spectrometer. The FTIR system was equipped with a iS50 GC-IR module, running with a liquid nitrogen cooled MCT-A detector. An OPTIMA 5 MS GC column (30 m x 0.25 mm, 0.25 µm film thickness) purchased from Macherey Nagel (Oensingen, Switzerland) was used for prior separation of the compounds. The GC system was configured with a split/splitless injector kept at 280° C and operated in splitless mode with an injection volume of 1 µL. Helium was used as carrier gas at a flow rate of 1.5 mL/min. The GC temperature program started at 90° C held for 1 minute followed by a 45° C/min ramp to the final temperature of 270° C. This temperature was held for 5 minutes, resulting in a total run time of 17.4 min. The transfer line and flow cell of the GC-IR module were heated to 270° C and 280° C, respectively. Series files were generated at 4 scans per second at 8 cm^{-1} resolution. The background was measured before every sample injection (100 scans). Data analysis was conducted in the Thermo Scientific™ OMNIC™ Software via library searches against an in-house library. The library was generated using certified reference material obtained from Lipomed (Arlesheim, Switzerland) or kindly provided by the Zurich Forensic Science Institute (Zurich, Switzerland). In addition, the TBI GC IR gas phase library obtained from Thermo Fisher Scientific[4] was used.

Figure 2. Picture of sample 4.

	Appearance	Result	Match
Sample 1	White powder	4-CMC	98.46
Sample 2	White powder	4-MMC	99.61
Sample 3	White powder	3-MMC	98.92
Sample 4	Yellow tablet	4-MMC MDMA	97.17 99.02

Table 1. Summary of the analysis results.

Results and Discussion

Results for all investigated samples are summarized in Table 1. GC-IR enabled the unequivocal distinction of the investigated cathinones, demonstrated by high match factors (>97) for definite identification. The high distinguishing power of IR spectroscopy is well seen when comparing the reference spectra of 3-CMC and 4-CMC depicted in Figure 2 and 3-MMC and 4-MMC shown in Figure 3.

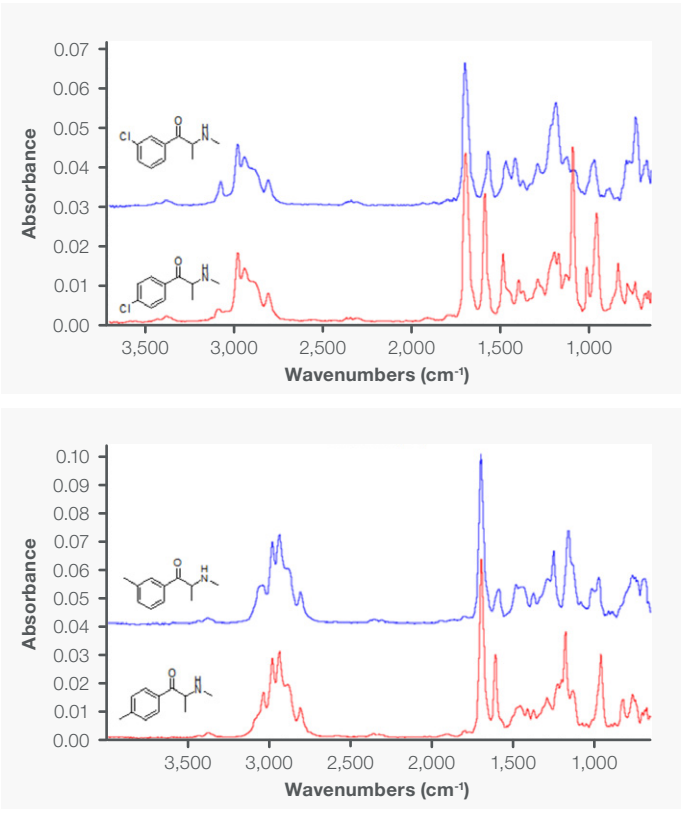

Figure 3. IR Spectra of the 3-CMC and 4-CMC (top) and 3-MMC and 4-MMC (bottom).

The white powder of Sample 1 contained 3-CMC. For Samples 2 and 3 the detected cathinones were 4-MMC and 3-MMC, respectively. Finally, the GC-IR analysis of sample 4, although resembling common ecstasy tablets, revealed a mixture of 4-MMC and MDMA. Mixtures of compounds often hinder correct compound annotation when using direct IR-methodologies, compromising the reliability of results.

As seen with the tablet of Sample 3, GC-IR enabled the reliable, fast, and easy detection of both 4-MMC and MDMA. Both compounds presented distinct peaks in the Gram-Schmidt profile. Use of the command GC Identify in the Mercury GC analysis software resulted in fully automatic annotation of 4-MMC and MDMA (Figure 4), therefore eliminating subjective data interpretation.

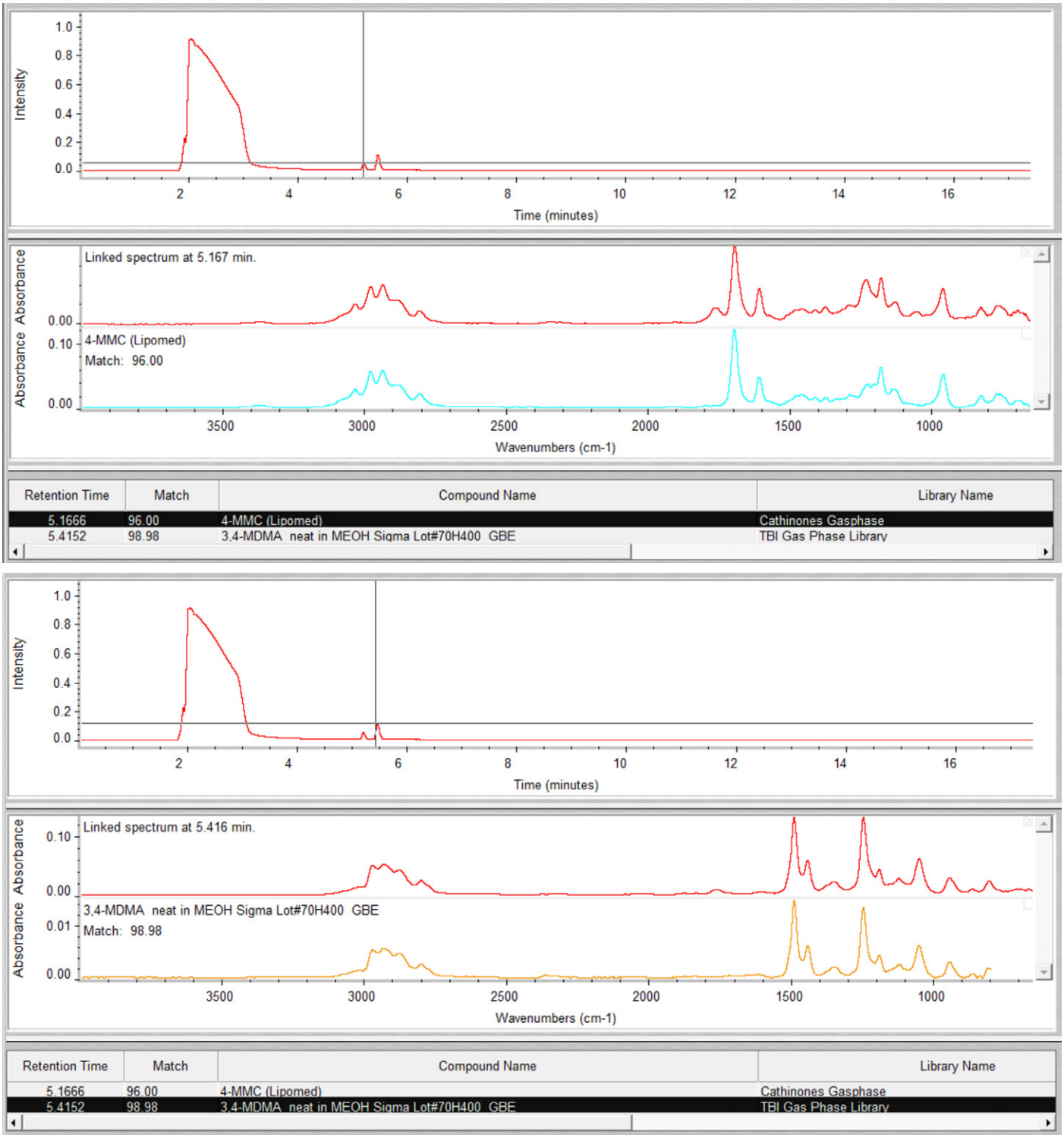

Figure 4. Results from the automated OMNIC Mercury GC data analysis for sample 4.

Conclusion

Cathinones keep emerging on the recreational drug market, requiring reliable methods for unequivocal and fast identification of constitutional isomers of this compound class in the forensic context. The use of the GC-IR module by Thermo Fisher Scientific enabled the easy, reliable, and fast detection of cathinones in drug samples encountered on the black market. Besides pure powders, more challenging samples such as compound mixtures and tablets were also successfully analyzed. Finally, data handling and interpretation was found to be straightforward when applying the Mercury GC analysis software.

References

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