ELSEVIER

Journal of Chromatography A 819 (1998) 155–159

JOURNAL OF CHROMATOGRAPHY A

# Application of gas chromatography–Fourier transform infrared spectrometry to the analysis of amphetamine analogues

I. Dirinck, E. Meyer, J. Van Bocxlaer, W. Lambert, A. De Leenheer*

*Laboratorium voor Toxicologie, Universiteit Gent, Harelbekestraat 72, B-9000 Ghent, Belgium*

**Abstract**

Capillary gas chromatography coupled with Fourier transform infrared detection (GC–FT-IR) was successfully applied to the analysis of amphetamine-like compounds in judicial exhibits. With light pipe GC–FT-IR, unique vapor-phase infrared spectra were generated allowing the unambiguous differentiation between closely related amphetamines. The obtained vapor-phase spectra were submitted to a spectral search on a laboratory-made vapor-phase FT-IR library. Several amphetamine analogues have been identified in confiscated powders and tablets using this approach. 

*Keywords:* Detection; Infrared spectrometry; Amphetamines

## 1. Introduction

Amphetamine (β-phenylisopropylamine) is the basic molecule of the amphetamines, a group of structurally related compounds with stimulating and mood-modifying properties. Despite overwhelming evidence of their dangerous effects, amphetamines remain significant drugs of abuse and addiction. So-called designer drugs are widespread drugs of abuse among recreational drug users. Therefore, many of these phenethylamines have become controlled substances. Consequently, clandestine laboratories are producing new, closely related substances to circumvent drug legislation.

Unambiguous identification of these amphetamines is essential for the successful prosecution of these designer drug cases in a court of law. Although GC–MS spectra often yield complementary information for structure elucidation, identification of underivatized amphetamines with GC–MS alone can be difficult due to the very similar mass spectral fragmentation patterns of the analogues [1]. Gas chromatography–Fourier transform infrared spectrometry (GC–FT-IR), however, is the most powerful hyphenated technique in the fingerprinting of isomeric structures and the identification of functional groups. With light pipe GC–FT-IR unique vapor-phase infrared spectra are generated allowing unequivocal differentiation between closely related structures.

This light pipe interface is the most conventional interface between a GC and a FT-IR spectrometer. Each column eluate is measured in real time in a narrow, gold-coated tube at high temperature [2]. Recent developments in FT-IR interfaces have resulted in the use of low temperature sample storage interfaces such as matrix isolation (MI) and direct deposition (DD) interfaces. With GC–MI-FT-IR the column eluate is trapped in an argon matrix on a moving reflective surface at cryogenic temperatures [3]. The DD interface deposits the GC eluate directly to a moving, low temperature and transparent Zn–Se

*Corresponding author.

0021-9673/98/$19.00 
PII: S0021-9673(98)00524-X

window [4]. With both of the latter interfaces, the sensitivity increases 1–2 orders of magnitude in comparison with the conventional light pipe interface [5]. An additional advantage is the applicability of commercial FT-IR libraries containing infrared spectra from KBr disks, since the cryogenic infrared spectra are very similar to condensed-phase infrared spectra. Light pipe GC–FT-IR generates vapor-phase infrared spectra which differ from KBr disk spectra and are therefore often not represented in commercial FT-IR libraries. This explains the importance of a self-made library for our application. Nevertheless, light pipe technology has the advantage of simplicity and robustness.

In this paper we report on a screening method for amphetamine-like compounds in confiscated powders and tablets using capillary GC–FT-IR with the light pipe interface. Apart from some instrumental considerations, unequivocal identification and quantification will be discussed.

## 2. Experimental

### 2.1. Materials and reagents

All solvents were of HPLC-grade purity and were from Merck (Darmstadt, Germany). Methanolic 4 *M* HCl was obtained from Alltech (Deerfield, IL, USA), heptafluorobutyric anhydride (HFBA) from Macherey & Nagel (Düren, Germany), 1-phenyl-2-propanone (P-2-P) from Acros Organics (Geel, Belgium), *n*-propylamine and sodium cyanoborohydride from Sigma (St. Louis, MO, USA). Universal Quick-Seal glass press-fit column splitters and deactivated fused-silica columns of different I.D. (0.15 or 0.32 mm) were obtained from Chrompack (Middelburg, Netherlands). Reference standards of the amphetamines and other toxicologically relevant substances were available from the standards collection at the Laboratory of Toxicology (University of Ghent, Belgium). The internal standard (I.S.) N-*n*-propylamphetamine·HCl was synthesized by reductive amination of 1-phenyl-2-propanone using *n*-propylamine and sodium cyanoborohydride as reductant [6]. Stock solutions of 1.0 mg/ml of all reference standards were prepared in methanol. The judicial exhibits were provided after confiscation by law enforcement authorities on the Belgian drug market.

### 2.2. Instrumentation

A Perkin-Elmer (Buckinghamshire, UK) Autosystem GC with flame ionization detection system (FID) was interfaced with a light pipe GC–IR System 2000 and connected to a FT-IR System 2000 with a mid infrared source and a medium band liquid nitrogen-cooled mercury cadmium telluride (MCT) detector. The programmed temperature vaporization (PTV) CIS 3 injector from Gerstel (Brielle, Netherlands) was used in the splitless mode and programmed from 40°C (0.2 min) to 100°C at a rate of 12°C/s, and from 100°C (1.5 min) to 300°C (5 min) at 2°C/s. Aliquots of 2 μl were injected. Temperature-programmed separations were carried out on a Hewlett-Packard (Palo Alto, CA, USA) Ultra-1 methylsilicone capillary column (25 m×0.32 mm I.D., 0.52 μm film thickness). Conditions were as follows: 60°C (0.2 min) to 110°C at 30°C/min, from 110°C (1.5 min) to 150°C at 5°C/min, and from 150 to 300°C at 30°C/min. The carrier gas was helium at a flow-rate of 1.8 ml/min. The analytical column outlet stretched into the light pipe inlet. Helium carrier gas was added as make-up gas at a flow-rate of 1.8 ml/min at the connection between the capillary column and the light pipe. The gold-coated light pipe (12 cm×1 mm I.D.) was heated at a constant temperature of 270°C.

### 2.3. FT-IR parameters

Real time spectra were obtained by addition of two scans, with a spectral resolution of 8 $cm^{-1}$ and 32 background scans. The scan range was from 4000 to 580 $cm^{-1}$. Chromatograms were calculated by the Gram–Schmidt vector orthogonalization method [7]. Reconstruction was performed using 10 basis vectors throughout the run. Baseline correction was performed on the reconstructed Gram–Schmidt chromatogram (GS) and low-noise vapor-phase infrared spectra were generated after coaddition.

### 2.4. Infrared spectral vapor-phase FT-IR library

Methanolic stock solutions (1.0 mg/ml) of the

reference standards were injected into the GC–FT-IR system to obtain reference vapor-phase infrared spectra which were stored in a computer-based library after normalization.

### 2.5. Sample pretreatment

The confiscated powders and tablets were weighed and homogenized in a small mortar. For qualitative analysis, methanolic solutions were prepared of approximately 10 mg of each exhibit in 50 μl methanol. For quantitative analysis, methanolic solutions were prepared of approximately 10 mg of each exhibit in 1.0 ml methanol. The solutions were vortexed for 1 min and centrifuged for 10 min at 1120 *g*. For quantitative analysis, an aliquot of this supernatant was further derivatized with HFBA before injection into the GC–FT-IR system.

### 2.6. Quantitation

A 50-μl aliquot of the I.S. stock solution (1.0 mg/ml) was added to a 50-μl aliquot of the methanolic solution of each exhibit. This mixture was then evaporated to dryness under nitrogen. At the end of the evaporation step, 25 μl of 4 *M* methanolic HCl was added to prevent the loss of the volatile amphetamines [8]. The obtained residue was dissolved in a mixture of 100 μl ethyl acetate and 100 μl HFBA and allowed to react for 20 min at 70°C. After cooling, the excess of HFBA was evaporated under nitrogen and the samples were redissolved in 50 μl of ethyl acetate. Calibration samples prepared in methanol were taken throughout the derivatization procedure in a manner similar to that used for the exhibits.

## 3. Results and discussion

GC–FT-IR analysis generates Gram–Schmidt (GS) total reconstructed chromatograms with unique vapor-phase infrared spectral data. The application of this technique in our laboratory is predominantly directed towards identification of amphetamine analogues in illicit drug samples, although quantification is also performed when required.

As the commercial FT-IR software was initially not suited for quantitation, multiple detection was evaluated. For this purpose, a flame ionization detector (FID) was coupled with the FT-IR detector. A serial configuration was compared with a parallel configuration of both detectors (Fig. 1). Glass press-fit column splitters were used as splitter devices to obtain a parallel configuration. Split ratios were chosen in function of the difference in sensitivity of the FID and FT-IR detector. They were varied by changing the length ($L$) and/or the inner diameter (I.D.) of the split capillary lines. The length of the deactivated fused-silica line to the FID system was changed between 0.15 and 1.7 m, while the length of the split capillary line to the FT-IR detector remained constant at 0.62 m. The I.D. of the split capillary line to the FID was restricted to 0.15 mm which resulted in an adequate split ratio. The optimized parallel configuration was as follows: split capillary line to FID: $L=0.15$ m and I.D.$=0.15$ mm; split capillary line to FT-IR detector: $L=0.62$ m and I.D.$=0.32$

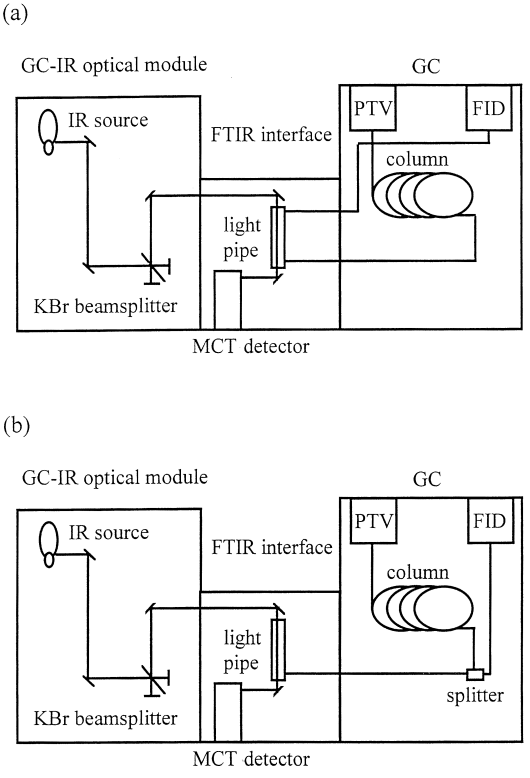


Fig. 1. Schematic diagram of the serial (a) and parallel (b) GC–FT-IR–FID configuration.

mm. The influence of different light pipe make-up flows on FT-IR sensitivity and peak width was also evaluated. Make-up flows were varied from 0 to 4 ml/min. The optimal make-up flow was 1.8 ml/min. Unfortunately, both configurations have severe limitations, precluding their routine use. The parallel configuration was abandoned because of an inferior FT-IR sensitivity. With the serial configuration, unacceptable peak tailing was observed in the FID chromatogram, preventing accurate quantitation. The main reason for this lies in the high I.D. of the light pipe. This results in a decrease of the average linear velocity and consequently distortion of the peaks. Increasing the make-up flow resulted in a steep decline in FT-IR sensitivity. Therefore, a software program was developed in-house that permitted quantitation on the GS total reconstructed chromatogram. When chromatograms are reconstructed using the GS vector orthogonalization method, the infrared spectrometer is a true GC detector measuring the integrated total infrared absorbance (TIRA) of the effluent. This method provides accurate quantitative information as the total infrared absorbance of all absorption peaks can be measured directly from the GS total reconstructed chromatogram [7].

During sample preparation, potential losses of highly volatile amphetamines were systematically avoided by addition of methanolic HCl during evaporation. For quantitative analysis HFBA derivatization was necessary to further improve chromatographic peak shape and enhance FT-IR sensitivity. HFB-derivatives display increased infrared sensitivity due to the presence of fluorine and the carbonyl functional group, which are both strong infrared absorbers.

Unequivocal identification of the amphetamines was accomplished by a spectral search on a laboratory-made computer-based vapor-phase FT-IR library, which contains to date 147 reference vapor-phase infrared spectra of commercially available amphetamines, as well as several in-house synthesized amphetamine analogues and other toxicologically relevant substances.

Using the developed GC–FT-IR method, commonly encountered illicit amphetamines were identified in approximately 200 judicial exhibits. Fig. 2 shows a GS total reconstructed chromatogram of a representative exhibit with the vapor-phase infrared

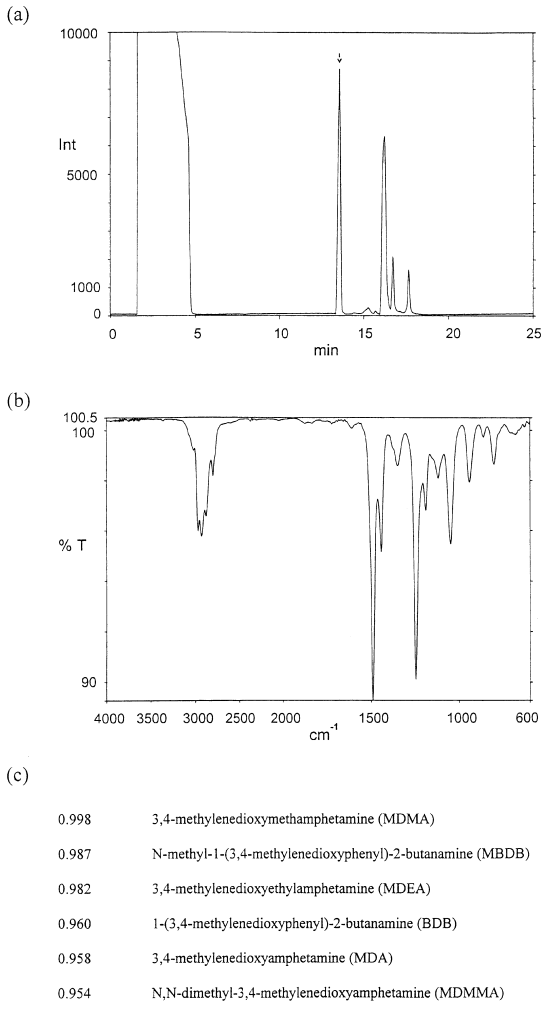


Fig. 2. (a) Gram–Schmidt total reconstructed chromatogram with (b) vapor-phase infrared spectrum of the peak marked with an arrow. (c) Result of the spectral search of this peak on the laboratory-made vapor-phase FT-IR library with best match for 3,4-methylenedioxymethamphetamine (MDMA). Hit quality indices of several amphetamine analogues indicate the best correlation (0.998) of the vapor phase FT-IR spectrum of the arrow marked peak with the one of an MMDA standard.

spectrum of the main component and the computer-based spectral search on the laboratory-made vapor-phase FT-IR library. Moreover, four amphetamine analogues were also identified for the first time in Belgium: α-phenylethylamine [9], 4-bromo-2,5-dimethoxyphenylethylamine (2C-B) [10], N-methyl-1-(3,4- methylenedioxyphenyl)-2-butanamine (MBDB) [11] and N-methyl-α-phenylethylamine. These com-

Table 1
GC–FT-IR data of major components in illicit powders and tablets

| Exhibit type | Component (concentration in %) |
|---|---|
| P | AMPH (12) CAF (51) |
| P | AMPH (71) |
| P | AMPH (1.5) |
| T | MDMA (1.5) MDEA (31) CAF (18) |
| T | MDMA (22) MDEA (26) |
| T | 2C-B (17) |

Abbreviations: P, powder; T, tablet; AMPH, amphetamine; CAF, caffeine; MDMA, 3,4-methylenedioxymethamphetamine; MDEA, 3,4-methylenedioxyethylamphetamine; 2C-B, 4-bromo-2,5-dimethoxyphenylethylamine.

pounds are not listed as controlled substances in the Belgian drug legislation to date.

Quantitative data were obtained after HFBA derivatization. Calibration graphs were prepared and weighted linear regression was performed. Some of the quantitative findings are presented in Table 1.

The presence of precursors, impurities, by-products and adulterants in the analyzed powders and tablets is important in proving the synthetic pathway and confirming the identity of different seized samples. For example, in many samples of amphetamine, trace amounts of 1-phenyl-2-propanone (P-2-P), an important precursor, were demonstrated [6]. The synthetic route by which illicit compounds are synthesized in basement chemistry laboratories can be determined by complete analysis and characterization of the samples.

## 4. Conclusion

The GC–FT-IR technique presented is able to identify and quantify different amphetamine analogues in illicit powders and tablets. Recently, several legally noncontrolled amphetamines were identified using this approach, indicating some possible new trends on the Belgian drug scene.

## Acknowledgements

E. Meyer acknowledges her postdoctoral researcher position at the Fund for Scientific Research Flanders. This work was supported by the Fund for Medical Scientific Research through grant 9.0024.92.

## References

[1] K.S. Kalasinsky, B. Levine, M.L. Smith, J. Anal. Toxicol. 16 (1992) 332.
[2] K. Krishnan, R. Curbelo, P. Chiha, R.C. Nooman, J. Chromatogr. Sci. 17 (1979) 413.
[3] G.T. Reedy, D.G. Ettinger, J.F. Schneider, S. Bourne, Anal. Chem. 57 (1985) 1602.
[4] S. Bourne, A.M. Hoeffner, Y.-L. Norton, P.R. Griffths, Anal. Chem. 62 (1990) 2448.
[5] J. Auger, S. Ferary, J. Chromatogr. A 683 (1994) 87.
[6] C.R. Clark, J. DeRuiter, F.T. Noggle, J. Chromatogr. Sci. 30 (1992) 399.
[7] J.A. de Haseth, T.L. Isenhour, Anal. Chem. 49 (1977) 1977.
[8] K. Pfleger, H.H. Maurer, A. Weber, Mass Spectral and GC Data of Drugs, Poisons, Pesticides, Pollutants and their Metabolites, Part I, VCH, Weinheim, 1992.
[9] E. Meyer, J.F. Van Bocxlaer, W.E. Lambert, L. Thienpont, A.P. De Leenheer, J. Anal. Toxicol. 20 (1996) 116.
[10] J. DeRuiter, C.R. Clark, F.T. Noggle, J. Chromatogr. Sci. 33 (1995) 583.
[11] C.R. Clark, J. DeRuiter, F.T. Noggle, J. Chromatogr. Sci. 34 (1996) 230.