

Development of an Identification and Derivatization Method for Synthetic Cathinones by GC-MS

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Abstract

Synthetic cathinones have become increasingly popular over the past decade. The synthetic cathinones Mephedrone, Methyone, and MDPV have been placed into Schedule I of the Controlled Substances Act based on the Analog Act, which was created to allow substances to be scheduled based on similarities to an already scheduled compound. Several synthetic cathinones have positional isomers, which produce ambiguous mass spectra. Derivatization has been proven useful for producing mass spectra with differences that allow for differentiation of similar compounds. Synthetic cathinone standards were derivatized with three perfluoroacyl derivatizing agents to determine their ability to differentiate positional isomers within a mixture. Compounds containing a primary or secondary nitrogen readily derivatized; while compounds containing a tertiary nitrogen were not able to be derivatized. When placed into mixtures, the positional isomers were distinguishable. Future studies include the determination of a method to derivatize synthetic cathinones containing a tertiary nitrogen.

Introduction

- Synthetic cathinones, commonly found in substances referred to as bath salts, have stimulant and psychoactive properties similar to amphetamine and cocaine.
- Structures are chemically altered to circumvent legislation.
- Mass spectra of the positional isomers are near identical and cannot be individualized.
- Due to the legal ramifications associated with synthetic cathinones, often with minor structural variations, identification of the exact structure is imperative.
- Perfluoroacyl anhydrides have been used to differentiate between compounds with similar mass spectra.
- Trifluoroacetic anhydride (TFAA), heptafluorobutyric anhydride (HFBA), and pentafluoropropionic anhydride (PFPA) are common perfluoroacyl derivatizing agents and were used in this research.
- Perfluoro acyl anhydrides bond with nitrogen atoms contained within synthetic cathinones.
- The effects of the derivatizing agents on each compound and several mixtures of multiple cathinones were compared to determine which agent performed the best for each compound.
- The best overall derivatizing agent was determined by examining the GC retention times, the amount of breakdown products present, and mass spectra.

Materials

Cathinones: 2-Methylmethcathinone, 3-Methylmethcathinone, Mephedrone, 2-Methoxymethcathinone, 3-Methoxymethcathinone, Methedrone, 2,3-Methylenedioxy-methcathinone, Methyone, 2-Fluoromethcathinone, 3-Fluoromethcathinone, 4-Fluoromethcathinone

Reagents: Methanol, Ethyl Acetate, Trifluoroacetic anhydride (TFAA), Heptafluorobutyric anhydride (HFBA), Pentafluoropropionic anhydride (PFPA), Pyridine

Methods

Standard Solutions

- Approximately 1 mg standard was dissolved in 300 μ L methanol in a GC vial insert

Derivatizations

- Approximately 1 mg standard dissolved in 25 μ L ethyl acetate in a GC vial
- 100 μ L TFAA, HFBA, or PFPA added to vial
- Vial capped; sit for 15 minutes at room temperature
- Solution transferred to open vial and evaporated on a hot plate on low
- Residue was reconstituted with 300 μ L ethyl acetate, placed in GC vial insert, and capped

Instrumentation

Agilent Technologies© 6890 GC- 5973 MS

Table 1: Column Temperature Program

Rate	Starting Temperature	Final Temperature	Hold Time	Final Time
-	140 °C	140 °C	6.1 min	6.1 min
20 °C/min	140 °C	200 °C	0.0 min	9.1 min
40 °C/min	200 °C	300 °C	14.1 min	25.7 min

Table 2: Gas Chromatography-Mass Spectrometry Parameters

Carrier Gas	Helium
Flow Rate	0.6 mL/min
Split Ratio	20:1; 35:1; 50:1
Injector Temperature	250 °C
Transfer Line Temperature	290 °C
Solvent Delay	0.42 min
Ionization Voltage	70 eV
Mass Range	40 – 550 m/z

Results

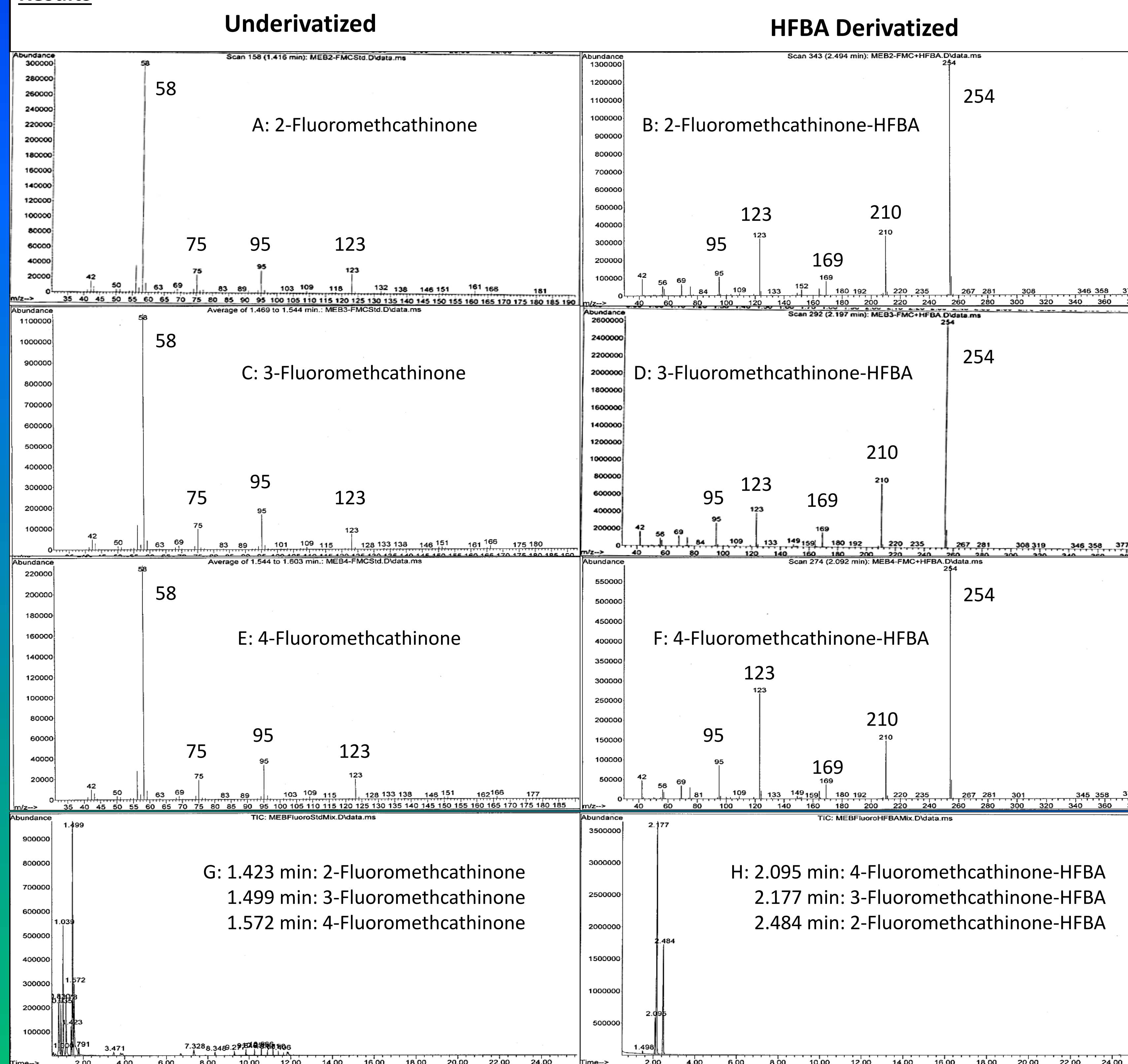


Figure 1: Mass Spectra and Chromatogram Results for Fluoromethcathinones. A: 2-Fluoromethcathinone; B: 2-Fluoromethcathinone-HFBA; C: 3-Fluoromethcathinone; D: 3-Fluoromethcathinone-HFBA; E: 4-Fluoromethcathinone; F: 4-Fluoromethcathinone-HFBA; G: Fluoromethcathinone Standard Mix; H: Fluoromethcathinone HFBA Mix.

Discussion

- HFBA was the best overall derivatizing agent for the synthetic cathinone positional isomers (Table 2)
- HFBA was the best derivatizing agent for the Fluoromethcathinones and Methoxymethcathinones
- Methylmethcathinones were difficult to differentiate due to:
 - Fragmentation resulting in a stable tropylium ion
 - Methyl groups on benzene ring are not very electronegative
- HFBA was able to provide some differentiation among the Methylmethcathinones
 - The mass spectrum of 3-Methylmethcathinone was differentiated from the mass spectra of 2-Methylmethcathinone and Mephedrone
- PFPA was the best derivatizing agent for the Methylenedioxy-methcathinones
 - 2,3-Methylenedioxy-methcathinone and 3,4-Methylenedioxy-methcathinone produced individual ions with PFPA
 - HFBA was able to differentiate the mass spectra, but did not provide individual ions

Table 3: Perfluoroacyl Derivatizing Agent Results on Synthetic Cathinone Positional Isomer Groups

Positional Isomer Group	TFAA	HFBA	PFPA
Fluoro-methcathinones	Co-elution in a mixture; prevented breakdown; differentiated MS	Compounds resolved in a mixture; prevented breakdown; differentiated MS	Compounds resolved in a mixture; some breakdown observed; differentiated MS
Methoxy-methcathinones	Compounds not fully resolved in a mixture; prevented breakdown; differentiated MS	Compounds resolved in a mixture; prevented breakdown; differentiated MS	Compounds resolved in a mixture; some breakdown observed; differentiated MS
Methyl-Methcathinones	Co-elution in a mixture; prevented breakdown; slight differences in MS	Compounds resolved in a mixture; some breakdown observed; 3-MMC MS easily distinguished, slight difference between 2-MMC and Mephedrone MS	Co-elution in a mixture; some breakdown observed; 3-MMC MS easily distinguished, slight difference between 2-MMC and Mephedrone MS
Methylenedioxy-methcathinones	Compounds resolved in a mixture; some breakdown observed; differentiated MS	Compounds resolved in a mixture; some breakdown observed; differentiated MS	Compounds resolved in a mixture; some breakdown observed; differentiated MS with ions observed at 119 m/z for 2,3-MDMC and 121 m/z for Methyone

Conclusions & Future Work

The mass spectra of 11 synthetic cathinones were compared to one another before and after derivatization with TFAA, HFBA, and PFPA. HFBA derivatization allowed for differentiation between the mass spectra of positional isomers better than TFAA or PFPA, overall. PFPA was more successful than HFBA or TFAA for the derivatization of the Methylenedioxy-methcathinones isomers. When choosing between the three derivatizing agents studied, HFBA provided the best overall results as it was successful in differentiating all of the positional isomers. Future studies will include reproduction of the current results, analysis of more complex cathinone mixtures, and development of a derivatization method for compounds containing tertiary nitrogens.

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