## Trifluoroacetyl Derivatization of Amphetamine, Methamphetamine, MDMA and Other Controlled Substances with Similar Mass Spectra

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### Abstract

For the identification of a controlled substance, mass spectrometry is the most commonly used method. However, there are some cases where the controlled substance shares a similar mass spectrum with a drug of a lower scheduling or a compound that is not even considered to be a controlled substance, such as methamphetamine and phenetermine. Here, it is proposed that the derivatization of these compounds will create mass spectra that are sufficiently different enough to make a positive identification. Controlled substance standards were derivatized with trifluoroacetic anhydride and analyzed with a GC-MS, resulting in unique, identifiable spectra for each standard.

### Introduction

- Amphetamine and other amphetamine-related designer drugs share similar mass spectra
- Scientific Working Group for the Analysis of Seized Drugs (SWGDrug) recommends at least one other separate form of analysis be used to identify a controlled substance
- Small or publicly funded labs might not have sufficient funds to obtain the instrumentation to conduct a second analytical procedure
- Some designer drugs have similar gas chromatographic retention times
- Derivatization of the drugs could lead to improved GC properties and formation of unique and discriminating mass spectral fragment ions
- Derivatization provides a second category A test according to SWGDrug guidelines
- Trifluoroacetic anhydride (TFAA) used to replace the active hydrogen on the primary and secondary amines of the amphetamine and amphetamine-related designer drugs with a perfluoroacyl group
- Supplemental experiment was conducted, mixing several controlled substances commonly found combined with each other in street drugs

### Controlled Substances

- Amphetamine
- Methamphetamine
- MDMMA
- MDMA
- Ketamine
- Phentermine
- DOM
- Fenfluramine

### Methods

#### Standard Solutions
- Dissolve 2 mg drug standard in 1.5 mL chloroform
- Add a drop of base
- Analyze with GC-MS

#### Derivatized Solutions
- Dissolve 2 mg drug standard in 1.5 mL chloroform
- Add 200 µL TFAA and 100 µL pyridine
- Let react for 15 minutes at room temperature
- Add equal volume NaOH, vortex, let separate
- Transfer chloroform layer to GC vial
- Analyze with GC-MS

#### Mixed Solution
- Dissolve 1 mg of each of following drug standards in 1.5 mL chloroform
- Amphetamine, methamphetamine, MDMA, MDEA, ketamine
- Add 500 µL TFAA and 200 µL pyridine
- Let react for 15 minutes at room temperature
- Add equal volume NaOH, vortex, let separate
- Transfer chloroform layer to GC vial
- Analyze with GC-MS

### Results

#### Without Derivatization

#### TFA Derivatives

### GC-MS of Mixed Solution

<table>
<thead>
<tr>
<th>Key</th>
<th>Drug</th>
<th>Ion(μs) - m/z *</th>
<th>RT - min</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Amp-TFA</td>
<td>118, 140, 91</td>
<td>5.32</td>
</tr>
<tr>
<td>B</td>
<td>Meth-TFA</td>
<td>154, 118, 110</td>
<td>6.67</td>
</tr>
<tr>
<td>C</td>
<td>MDA-TFA</td>
<td>135, 162</td>
<td>9.37</td>
</tr>
<tr>
<td>D</td>
<td>MDEA-TFA</td>
<td>168, 162, 140, 135</td>
<td>10.77</td>
</tr>
<tr>
<td>E</td>
<td>Ketamine-TFA</td>
<td>110, 125, 152, 270</td>
<td>11.89</td>
</tr>
</tbody>
</table>

* Qualifier ions; quant. ions underlined

### Conclusions

This study showed that derivatization is a viable method to produce a unique, identifiable mass spectra for a controlled substance, that the derivatization process can be conducted at room temperature, and that the same technique can be applied to a drug mixture. Future studies will be conducted looking at different derivatizing agents, controlled substances, and chromatographic conditions. Quantifying as well as qualifying controlled substances via derivatization will also be researched.

### Acknowledgements

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### References