New GC-MS Assay for Amphetamine and Methamphetamine

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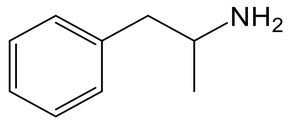
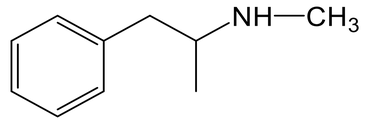
Introduction

Amphetamine and Methamphetamine are central nervous system stimulants and schedule II controlled substances at the federal level [1]. The analysis of of these drugs in crime labs represents about 30% of all drug exhibits in the US [2]. Confirmatory and quantitative analysis is typically performed by gas chromatographic (GC) analysis [3]. The highly polar nature of the drugs in both the salt and free base forms cause strong interactions with surfaces such as the inlet and stationary phase in the GC; these interactions are problematic, especially for quantitation. Our laboratory recently developed a method to attenuate this surface interaction that resulted in improved chromatographic behavior and detector response by mass spectrometry (MS). We have established that derivatization of the basic nitrogen with alkanoic anhydrides enhances the sensitivity of the assay significantly.



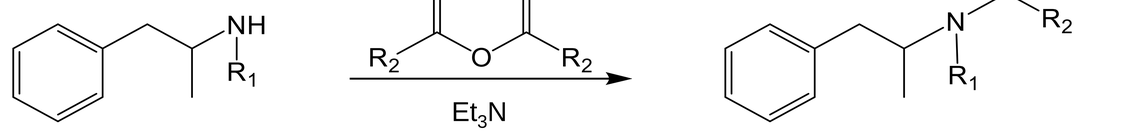
Amphetamine



Methamphetamine

Objectives

The purpose of this project was to apply a quantitative method recently developed in our lab for several non-controlled substances to two controlled substances. Amphetamine and Methamphetamine free base were derivatized with several alkanoic anhydrides and analyzed by GC-MS in full scan mode using a C_{24} internal standard.



Amph/Meth free base (R_1 = H, CH_3)

Amph/Meth amides (R_2 = $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$)

Experimental

Sample Preparation: Amphetamine and Methamphetamine salts were purchased from Restek as DEA exempt solutions in methanol (1.0 mg/mL). 1.0 mL aliquots were evaporated to dryness. The residues were taken up in 1.0 mL of $CHCl_3$ and washed with 1N NaOH to produce the free bases (dissolved in $CHCl_3$). Two additional $CHCl_3$ extractions of the NaOH solution were performed. The combined extracts were dried through a cotton-plugged Pasteur pipet into a 10.0 mL volumetric flask and diluted to the mark with $CHCl_3$. The amides were formed on-column with the addition of alkanoic anhydrides and triethylamine.

Analytical Conditions: Agilent GC-MS Model 7890A/5975C, fitted with a ZB-5 column, 30 m x 0.25 mm i.d. x 0.25 mcm film (Amphetamine) or a HP-1 column, 30 m x 0.32 mm i.d. x 0.25 mcm film (Methamphetamine), 1.0 mcL injection volume, split ratio = 5:1, septum purge = 3.0 mL/min, He carrier gas, constant flow = 1.0 mL/min., oven program: 60° C (2.0 min. hold), 30° C/min to 320° C (6 min. hold), total run time = 13.667 min., EI at 70 eV, full scan 40-550 daltons, inlet 275° C, MS transfer line 280° C, MS source 230° C, MS quad 150° C.

Results

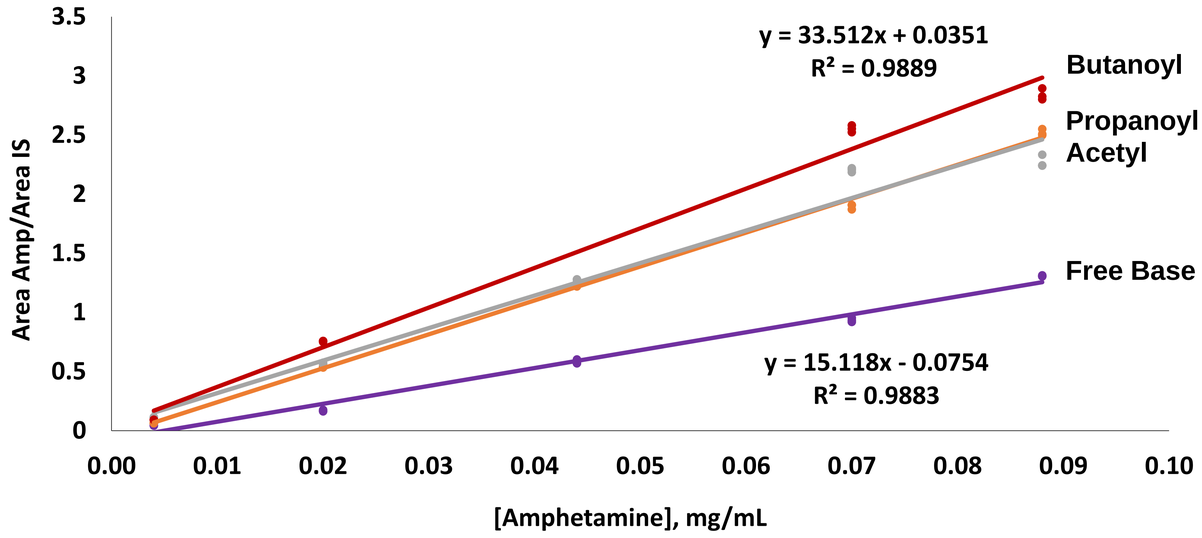


Figure 1: MS Full Scan Response for $Area_{Amph}/Area_{IS}$ vs [Amphetamine]

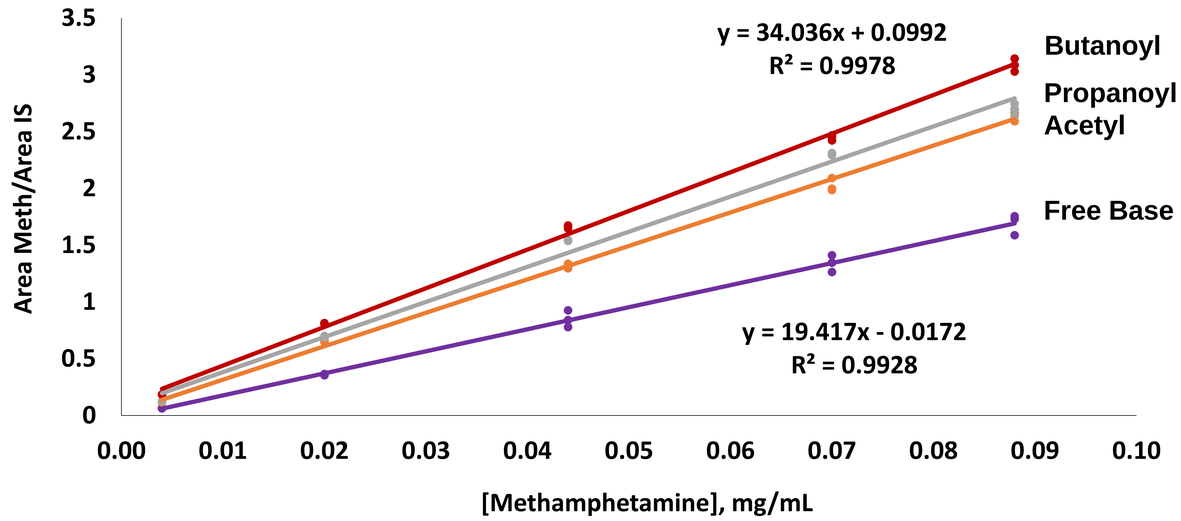


Figure 2: MS Full Scan Response for $Area_{Meth}/Area_{IS}$ vs [Methamphetamine]

Conclusions

- Derivatization with alkanoic anhydrides enhanced the full scan MS response significantly compared to the free bases (Fig. 1,2). Also, sensitivity increased with increasing size of the derivatizing group (base < acetyl < propanoyl < butanoyl).
- Calibration curves were linear in the range of 0.0880 to 0.00400 mg/mL.
- We are grateful to Loyola University Chicago for support of this research project.

References

[1] Controlled Substances Act, Section 812, 21 U.S.C., §801, Title 21 Code of Federal Regulations, Part 1300-end, https://www.deadiversion.usdoj.gov/21cfr/cfr/1300/1300_01.htm

[2] National Forensic Laboratory Information System (NFLIS) 2019 Annual Drug Report, pp 7, https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS-Drug-AR2019.pdf

[3] Quantitation of Methamphetamine by GC-LTM Column Module, Method #DEA 103L, Validated Quantitative Methods, https://www.dea.gov/documents/2021/01/08/ summary-validated-methods-0