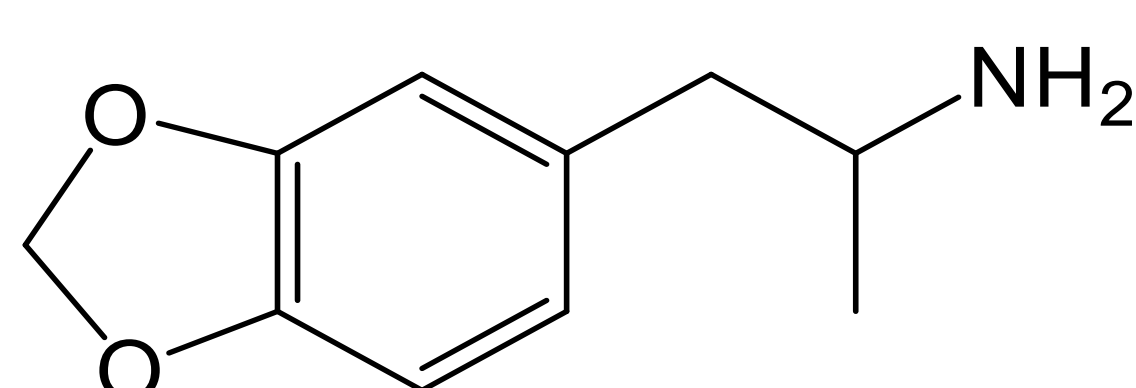
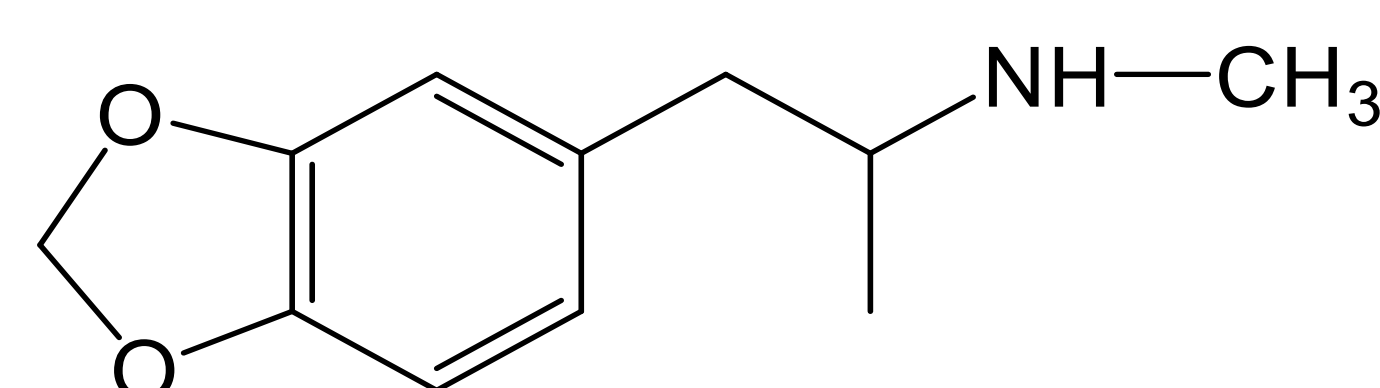


## Introduction

3,4-methylenedioxyamphetamine (MDA) and 3,4-methylenedioxymethamphetamine (MDMA) are central nervous system stimulant/hallucinogens and schedule I controlled substances at the federal level [1]. The analysis of these drugs in crime labs represents about 0.5% of all drug exhibits in the US [2]. Confirmatory and quantitative analysis is typically performed by gas chromatographic (GC) analysis. 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 alkanic anhydrides enhances the sensitivity of the assay significantly.



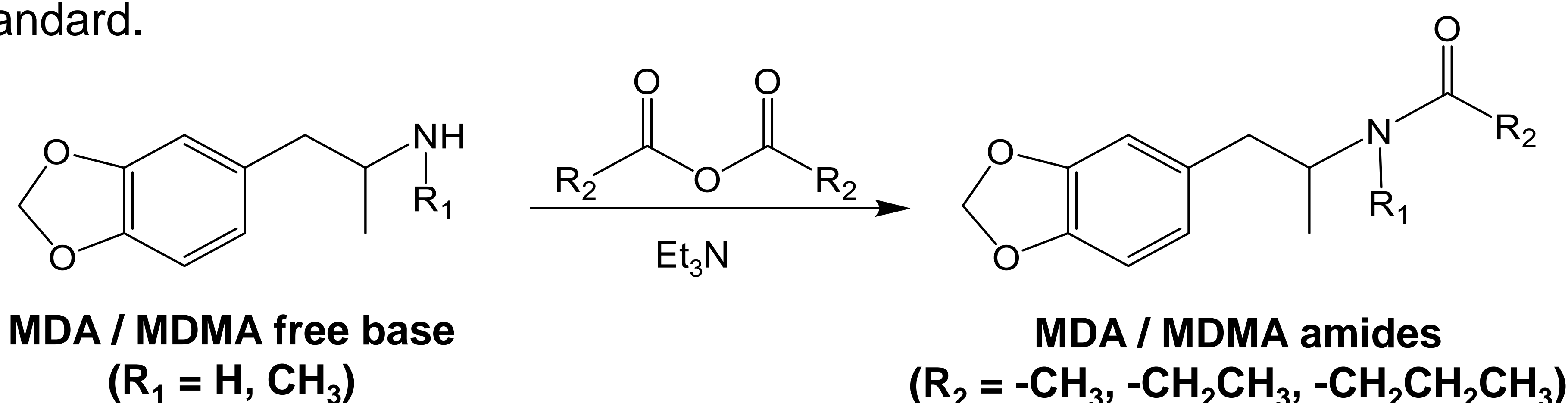
3,4-methylenedioxyamphetamine  
(MDA)



3,4-methylenedioxymethamphetamine  
(MDMA)

## 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. MDA and MDMA free base were derivatized with several alkanic anhydrides and analyzed by GC-MS in full scan mode using a C<sub>24</sub> internal standard.



## Experimental

**Sample Preparation:** MDA and MDMA 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<sub>3</sub> and washed with 1N NaOH to produce the free bases (dissolved in CHCl<sub>3</sub>). Two additional CHCl<sub>3</sub> 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<sub>3</sub>. The amides were formed on-column with the addition of alkanic 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 μm film (MDA) or a HP-1 column, 30 m x 0.32 mm i.d. x 0.25 μm film (MDMA), 1.0 μL 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., inlet 275° C, MS transfer line 280° C, MS source 230° C, MS quad 150° C.

## Results

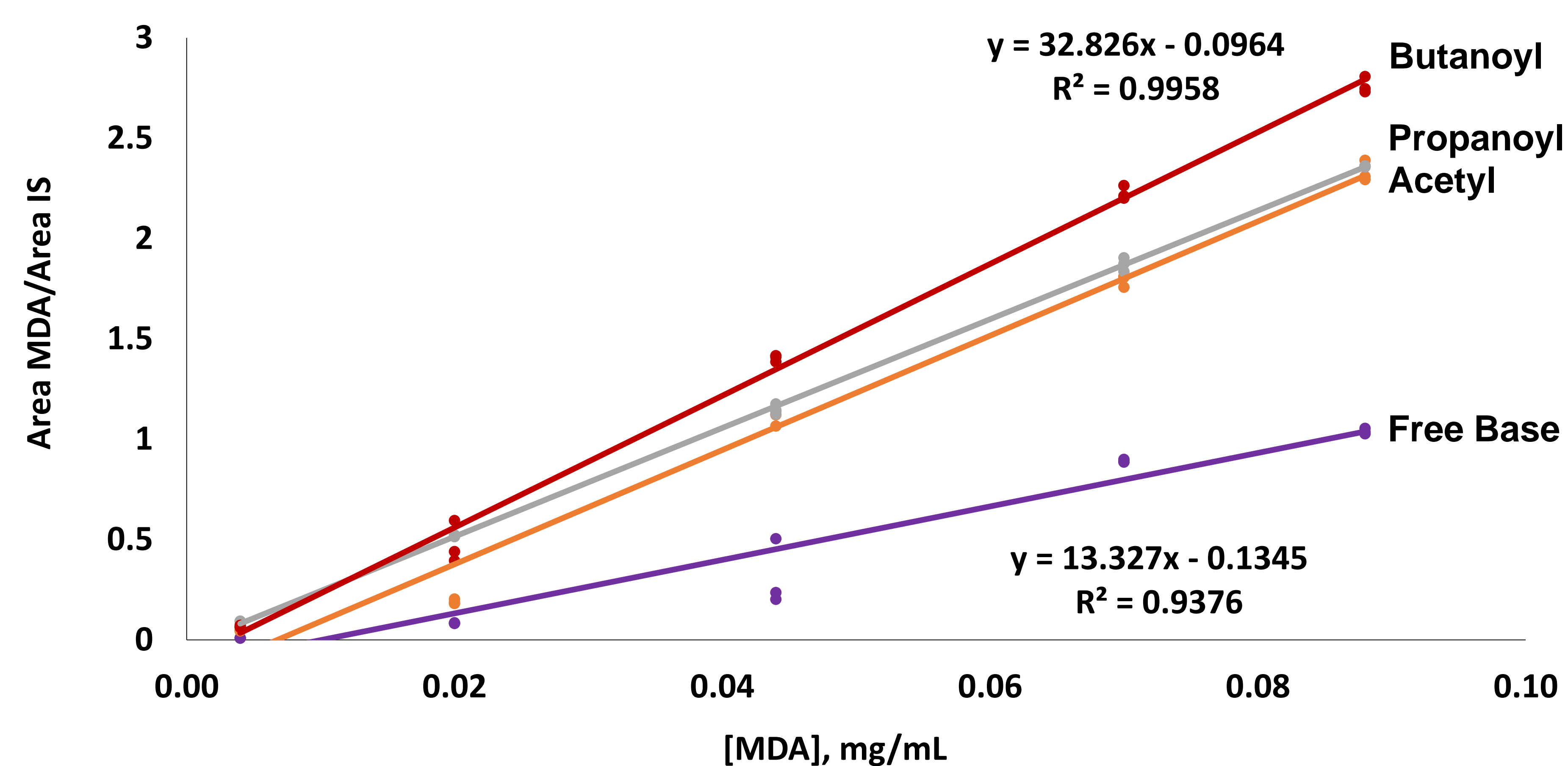


Figure 1: MS Full Scan Response for Area<sub>MDA</sub>/Area<sub>IS</sub> vs [MDA]

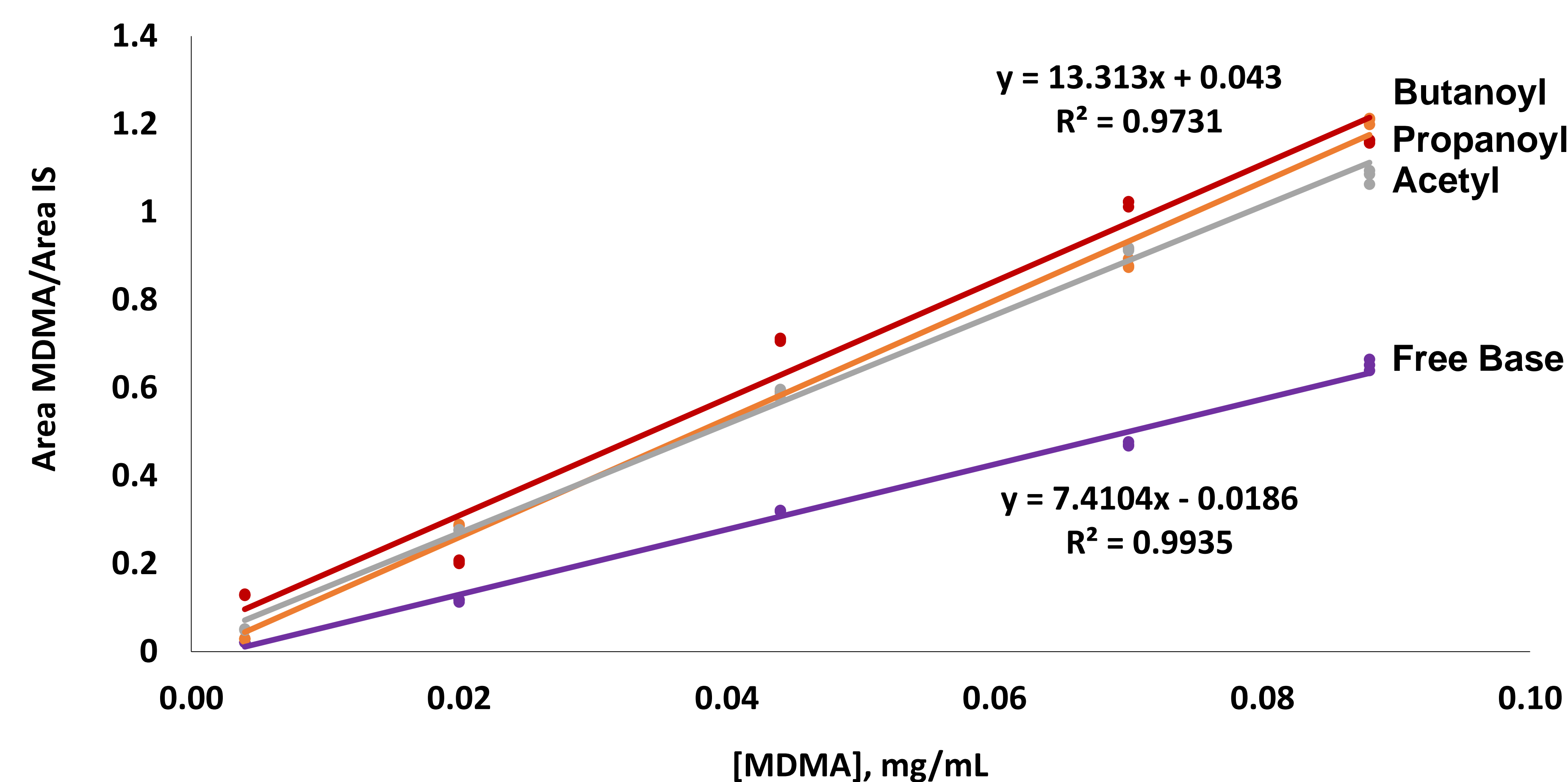


Figure 2: MS Full Scan Response for Area<sub>MDMA</sub>/Area<sub>IS</sub> vs [MDMA]

## Conclusions

- Derivatization with alkanic 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](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>