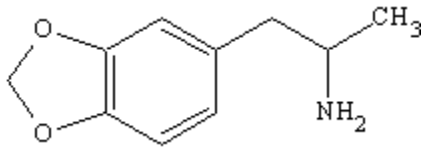
3,4-METHYLENEDIOXYAMPHETAMINE

Latest Revision: August 16, 2005



1. SYNONYMS

CFR: 3,4-Methylenedioxyamphetamine

CAS #: Base: 4764-17-4
Hydrochloride: 6292-91-7

Other Names: 3,4-Methylenedioxy-α-methyl-β-phenethylamine
3,4-Methylenedioxyphenylisopropylamine
alpha-Methyl-1,3-benzodioxole-5-ethanamine
alpha-Methyl-1,3-benzodioxole-5-ethanamine
Tenamfetamine
Adam
Love
EA-1299
MDA

2. CHEMICAL AND PHYSICAL DATA

2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Base	$C_{10}H_{13}NO_2$	179.2	Oil
Hydrochloride	$C_{10}H_{13}NO_2 \cdot HCl$	215.7	187-88

2.2. SOLUBILITY

Form	A	C	E	H	M	W
Base	***	S	S	S	S	I
Hydrochloride	SS	S	I	***	S	S
Sulfate	***	I	I	I	S	***

A = acetone, C = chloroform, E = ether, H = hexane, M = methanol and W = water, VS = very soluble, FS = freely soluble, S = soluble, PS = sparingly soluble, SS = slightly soluble, VSS = very slightly soluble and I = insoluble

3. SCREENING TECHNIQUES

3.1. COLOR TESTS

REAGENT	COLOR PRODUCED
Marquis	Purple to black

3.2. THIN LAYER CHROMATOGRAPHY

Visualization

Acidified potassium permanganate solution

COMPOUND	Relative R_f	
	System TLC 5	System TLC 6
3,4-methylenedioxyethylamphetamine	1.1	1.2
3,4-methylenedioxyamphetamine	1.0	1.0
3,4-methylenedioxydimethylamphetamine	0.9	1.2
3,4-methylenedioxymethamphetamine	0.8	0.6

3.3. GAS CHROMATOGRAPHY

Method MDA-GCS1

Instrument:	Gas Chromatograph operated in split mode with FID
Column:	5% phenyl/95% methyl silicone 30 m x 0.25 mm x 0.25 µm film thickness
Carrier gas:	Hydrogen at 2.0 mL/min
Temperatures:	Injector: 260°C Detector: 270°C Oven program: 1) 90°C initial temperature for 1.0 min 2) Ramp to 295°C at 30°/min 3) Hold final temperature for 2.6 min
Injection Parameters:	Split Ratio = 50:1, 1 µL injected

Samples are to be dissolved in 4:1 chloroform: methanol and filtered.

COMPOUND	RRT	COMPOUND	RRT
amphetamine	0.61	acetaminophen	1.24
methamphetamine	0.67	caffeine	1.34
safrole	0.80	methyl stearate	1.49
C_{14}	0.89	cocaine	1.61
MDA	**1.0 (4.17 min)**	methyl eicosanoate	1.62
MDMA	1.05	tetraphenylethylene	1.78
MDEA	1.09	heroin	1.89
MMDA	1.12		

Method MDA-GCS2

Instrument: Gas Chromatograph operated in split mode with FID

Column: 50% phenyl/50% methyl silicone 30 m x 0.25 mm x 0.25 µm film thickness

Carrier gas: Hydrogen at 2.0 mL/min

Temperatures: Injector: 260°C
Detector: 270°C
Oven program:
1) 90°C initial temperature for 1.0 min
2) Ramp to 295°C at 30°/min
3) Hold final temperature for 2.6 min

Injection Parameters: Split Ratio = 50:1, 1 µL injected

Samples are to be dissolved in 4:1 chloroform: methanol and filtered.

COMPOUND	RRT	COMPOUND	RRT
amphetamine	0.62	acetaminophen	1.31
methamphetamine	0.66	caffeine	1.38
safrole	0.80	methyl stearate	1.30
C_{14}	0.69	cocaine	1.58
MDA	**1.0 (4.84 min)**	methyl eicosanoate	1.41
MDMA	1.03	tetraphenylethylene	1.77
MDEA	1.05	heroin	2.03
MMDA	1.07		

Method MDA-GCS3

Instrument: Gas Chromatograph operated in split mode with FID

Column: 5% phenyl/95% methyl silicone 5 m x 0.25 mm x 0.25µm film thickness

Carrier gas: Hydrogen:
1) Initial pressure of 2.5 psi for 0.10 min
2) Ramp to 5.0 psi at 3.41 psi/min
3) Hold final pressure for 0.77 min

Temperature: Injector: 260°C
Detector: 270°C
Oven program:
1) 90°C initial temperature
2) Ramp to 100°C at 10°C/min
3) Hold final temperature for 0.60 min

Injection Parameters: Split Ratio = 50:1, 1 µL injected
EZFlash Parameters:
1) Time 0 sec = 100°C
2) Time 6 sec = 110°C
3) Time 50 sec = 310°C
4) Time 96 sec = 310°C

Samples are to be dissolved in 4:1 chloroform:methanol and filtered.

COMPOUND	RRT	COMPOUND	RRT
amphetamine	0.73	acetaminophen	1.19
methamphetamine	0.77	caffeine	1.27
safrole	0.85	methyl stearate	1.28
C_{14}	0.92	cocaine	1.50
MDA	**1.0 (4.79 min)**	methyl eicosanoate	1.40
MDMA	1.04	tetraphenylethylene	1.69
MDEA	1.07	heroin	1.88
MMDA	1.08		

Method MDA-GCS4

Instrument: Gas Chromatograph operated in split mode with FID

Column: 1% phenyl/99% methyl silicone 30 m x 0.25 mm x 0.25 µm film thickness

Carrier gas: Hydrogen at 2.0 mL/min

Temperature: Injector: 260°C
Detector: 270°C
Oven program:

1) 90°C initial temperature for 1.0 min
2) Ramp to 295°C at 30°/min
3) Hold final temperature for 2.6 min

Injection Parameters: Split Ratio = 50:1, 1 µL injected

COMPOUND	RRT	COMPOUND	RRT
amphetamine	0.56	acetaminophen	1.27
methamphetamine	1.75	caffeine	1.36
safrole	0.77	methyl stearate	1.63
C_{14}	0.97	cocaine	1.70
MDA	**1.0 (4.1 min)**	methyl eicosanoate	1.78
MDMA	1.06	tetraphenylethylene	1.89
MDEA	1.12	heroin	2.01
MMDA	1.15		

4. SEPARATION TECHNIQUES

5. QUANTITATIVE PROCEDURE

***5.1.* GAS CHROMATOGRAPHY**

Method MDA-GCQ1

Internal Standard Stock Solution:
1.0 mg/mL *n*-butylamphetamine HCl in chloroform.

Standard Solution Preparation:
Prepare a standard solution of MDA HCl at 0.4 mg/mL in chloroform.

Sample Preparation:
Accurately weigh out 50 mg of sample into a 25 mL volumetric flask and dilute with water to the mark. Take a 2 mL aliquot of the solution, add 3 mL of I.S. and 2-3 mL of 0.5 M KOH. Shake. Separate layers and extract twice more with 2-3 mL each time of chloroform. Combine fractions – dry over sodium sulfate and dilute to total volume of 10 mL. Treat the standard in the same fashion as the sample prior to analysis.

Instrument:	Gas Chromatograph operated in split mode with FID
Column:	DB-1, 30 m x 0.25 mm x 0.25 μm film thickness
Carrier gas:	Hydrogen at 1.3 mL/min
Make-Up gas:	Nitrogen at 40.0 mL/min
Temperatures:	Injector: 230°C Detector: 280°C Oven Program: 1) 150°C initial temperature 2 min 2) Ramp to 190°C at 5°C/min 3) Hold final temperature for 1.0 min
Injection Parameters:	Split Ratio = 20:1, 1μL injected
Typical Retention Time:	3,4-MDA: 2.13 min N-Butylamphetamine HCl: 1.89 min
Linear Range:	0.06 mg/mL to 2.0 mg/mL
Repeatability:	RSD less than 2.0%
Correlation Coefficient:	0.9998
Accuracy	Error less than 5%

COMPOUND	RRT	COMPOUND	RRT	COMPOUND	RRT
methylbenzylamine	0.40	salicylamide	0.89	caffeine	2.14
P2P	0.44	methyl paraben	0.89	antipyrine	2.30
amphetamine	0.45	penicillin	0.90	benzphetamine	2.35
nicotinic acid	0.48	phenmetrazine	0.93	diphenhydramine	2.46
phentermine	0.48	MDP-2-P	0.97	aminopyrine	2.60
methamphetamine	0.51	phendimetrazine	0.99	doxylamine	2.66

COMPOUND	RRT	COMPOUND	RRT	COMPOUND	RRT
fenfluramine	0.55	**MDA**	**1.0 (2.13 min)**	phthalic acid	2.82
ethylamphetamine	0.56	MDMA	1.15	palmitic acid	2.82
dimethylamphetamine	0.58	aminorex	1.21	dipyrone	2.89
safrole	0.63	methyl aminorex	1.21	procaine	3.06
salicylic acid	0.64	MDEA	1.30	eicosane	3.07
cathine	0.68	ibuprofen	1.43	dextromethorphan	3.59
phenylpropanolamine	0.68	MBDB	1.45	strychnine	3.65
methcathinone	0.69	hexadecane	1.47	amitriptyline	3.84
nicotinamide	0.71	guaifenesin	1.50	scopolamine	4.27
chlorpheniramine	0.75	acetaminophen	1.55	tetracosane	4.58
chloroephedrine	0.76	MMDA	1.59	chlordiazepoxide	4.96
pseudoephedrine	0.76	phenacetin	1.62	quinine	6.02
ephedrine	0.78	chloromdma	1.71		
butylamphetamine	0.89	methylphenidate	1.87		

5.2. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Method MDA-LCQ1

Standard Solution Preparation:
Accurately weigh and prepare a standard solution of MDA HCl at approximately 1.0 mg/mL using water. Filter with a 0.45-µm filter.

Sample Preparation:
Accurately weigh an amount of sample into a volumetric flask and dilute with water. If necessary dilute the sample so the final concentration approximates the standard concentration or falls within the linear range. Filter sample with a 0.45-µm filter.

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5 µm ODS, 4.0 mm x 125 mm

Detector: UV, 210 nm

Flow: 1.0 mL/min

Injection Volume: 1 µL

Buffer: 4000 mL distilled water, 30 mL phosphoric acid, 10 g sodium hydroxide and 8.0 mL hexylamine at pH 2.5

Mobile Phase: Buffer: acetonitrile 85:15 with gradient to 60:40 over 6 min

Typical Retention Time: 3,4-MDA: 1.63 min

Linear Range: 0.1338 - 4.28 mg/mL

Repeatability: RSD less than 0.2%

Correlation Coefficient: 0.999

Accuracy: Error less than 5%

COMPOUND	RRT
Nicotinamide	0.62
MDA	1.00
MDMA	1.16
MDEA	1.41

Method MDA-LCQ2

Standard Solution Preparation:
Prepare a standard solution of MDA HCl at approximately 0.5 mg/mL using water, buffer, or methanol.

Sample Preparation:
Accurately weigh an amount of sample into an appropriate volumetric or Erlenmeyer flask and dilute so that the final MDA HCl concentration is approximately that of the standard solution.

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5µ Phenomenex Luna, 150 mm x 3.2 mm at 35°C

Detector: UV, 210 nm

Flow: 1.0 mL/min

Injection Volume: 5 µL

Buffer: 4000 mL distilled water, 22.5 mL phosphoric acid, adjust to pH 2.2-2.3 with triethanolamine (approx. 22 mL)

Mobile Phase: Buffer:acetonitrile 90:10

Typical Retention Time: 3,4-MDA: 9.8 min

Linear Range: 0.05 mg/mL - 2 mg/mL

Repeatability: RSD less than 0.5%

Correlation Coefficient: 0.9999

Accuracy: Error less than 5%

COMPOUND	RRT	COMPOUND	RRT
phenylpropanolamine	0.65	methyl aminorex	1.09
methyl benzylamine	0.67	phentermine	1.10
cathine	0.68	chloroephedrine	1.11
doxylamine	0.74	ethylamphetamine	1.13
dipyrone	0.75	MDP-2-P	1.13
ephedrine	0.77	lidocaine	1.15
methcathinone	0.79	caffeine	1.16
pseudoephedrine	0.79	MDEA	1.22
amphetamine	0.90	phenyl-2-naphthalene	1.22
theophylline	0.94	phthalic acid	1.22
methapyrilene	0.96	strychnine	1.23
phenmetrazine	0.96	MMDA	1.26
methamphetamine	0.98	MBDB	1.34
phendimetrazine	0.98	salicylamide	1.37
scopolamine	0.99	acetaminophen	1.39

COMPOUND	RRT	COMPOUND	RRT
MDA	**1.00 (9.8 min)**	chloro-mdma	1.47
quinine	1.03	methylphenidate	1.48
saccharin	1.03	glycerol glycolate	1.59
dimethylamphetamine	1.04	chlorpheniramine	1.67
MDMA	1.08	aspirin	1.95
		chlordiazepoxide	2.01

5.3. CAPILLARY ELECTROPHORESIS

Method MDA-CEQ1

Internal Standard Stock Solution:
0.50 mg/mL *n*-butylamphetamine HCl in 50 mM sodium phosphate at pH 7.0.

Standard Solution Preparation:
Accurately weigh and prepare a standard solution of MDA HCl at approximately 0.8 mg/mL using the internal standard stock solution. Filter with 0.45 micron filter.

Sample Preparation:
Accurately weigh an amount of sample into a volumetric flask and dilute with internal standard stock solution. If necessary, dilute the sample so the final concentration approximates the standard concentration or falls within the linear range. Filter sample with 0.45-micron filter.

Mode:	Cyclodextrin system analysis
Column:	49 cm x 52 µm fused silica capillary
Run Buffer:	10 mM gamma-highly sulfated cyclodextrin in 50 mM sodium phosphate at pH 7.0
Detector:	UV, 210 nm
Voltage:	12 kV
Temperature:	30°C air cooled
Injection:	1 s hydrodynamic at 50 mbar/s
Run Time:	17 min
Rinse Time:	2.0 min
Linear Range:	0.02 - 1.00 mg/mL
Repeatability:	RSD of area less than 1.5%
Correlation Coefficient:	0.999
Accuracy:	Error less than 5%

COMPOUND	RRT	COMPOUND	RRT
d-methamphetamine	0.83	l-pseudoephedrine	1.23
d-ephedrine	0.93	MDMA*	1.25
MDA*	**1.0 (8.83 min)**	l-ephedrine	1.36
cathine	1.06	MDEA*	1.40
l-methamphetamine	1.11	MDMA*	1.48
d-amphetamine	1.18	l-norephedrine	1.65
d-norephedrine	1.18	l-amphetamine	1.68
d-pseudoephedrine	1.21	**MDA***	1.70
		MDEA*	1.86

Method MDA-CEQ2

Internal Standard Stock Solution:
1.0 mg/mL *n*-Butylamphetamine HCl in 3.8 mM phosphate buffer (pH 2.5).

Standard Solution Preparation:
Weigh an appropriate amount of standard MDA HCl into a volumetric flask to obtain a final concentration of approximately 0.08 mg/mL. Pipette an appropriate amount of internal standard solution to obtain a final concentration of 0.1 mg/mL. Dilute to volume with injection solvent. Filter approximately 1.0 mL of solution with regenerated cellulose 0.45 µm 25mm filter into a 2.0 mL glass vial (Agilent part number 5182-0567.) Make sure there are no air bubbles on bottom of glass vial. Cap vial with polypropylene cap (Agilent part number 5182-9697.)

Sample Preparation:
Weigh an appropriate amount of sample into a volumetric flask so that the final phenethylamine concentration is approximately that of the standard solution. Pipette appropriate amount of internal standard solution to obtain a final concentration of 0.1 mg/mL. Dilute to volume with injection solvent. Sonicate for 15 minutes. Filter approximately 1.0 mL of solution with regenerated cellulose 0.45 µm 25mm filter into a 2.0 mL glass vial (Agilent part number 5182-0567.) Make sure there are no air bubbles on bottom of glass vial. Cap vial with polypropylene cap (Agilent part number 5182-9697.)

Mode:	HP 3D instrument operated in CE mode Cyclodextrin system analysis
Column:	50 µm i.d. x 32.2 cm (23.7 cm length to detector)
Run Buffer:	Celixir Reagent B, pH 2.5 (MicroSolv CE)
Detector:	Diode-array
Voltage:	10 kV
Temperature:	15°C
Injection:	50 mbar x 2 s followed by water at 35 mbar
Run Time:	6 min
Rinse Time:	2 min
Linear Range:	0.02 – 1.00 mg/mL
Repeatability:	RSD <1.6%

Correlation Coefficient: 1.0

Accuracy: Error less than 3.2%

COMPOUND	RRT	COMPOUND	RRT
doxylamine	0.765	ephedrine	0.932
chlorpheniramine	0.784	phenylephrine	0.951
quinine	0.804	MDEA	0.961
β-phenethylamine	0.807	ketamine	0.962
chlorquinine	0.812	phenyltoxolamine	0.971
nicotinamide	0.836	***n*-butylamphetamine**	**1.0 (4.6 min)**
amphetamine	0.868	dextromethorphan	1.00
methamphetamine	0.883	lidocaine	1.03
procaine	0.883	benzocaine	1.25
MDA	**0.900**	acetaminophen	2.11
norpseudoephedrine	0.906	caffeine	2.14
MDMA	**0.914**	guaifenesin	2.14
norephedrine	0.917	P2P	2.24
pseudoephedrine	0.919	DMSO (neutral marker)	2.40
tetracaine	0.927	aspirin	2.71

5.4. NUCLEAR MAGNETIC RESONANCE

Method NMR-1-1

Solvents: Deuterium Oxide (D_2O) containing DSS or TSP for 0 PPM reference.

Internal Standard Stock Solution (ISSS): 5 mg/mL Maleic Acid (accurately weighed) in deuterium oxide (D_2O) containing DSS or TSP for 0 ppm reference.

Sample Preparation: Accurately weigh an amount of sample, usually 10-30 mg, into a capped test tube and accurately add a volume, normally 1.0 mL, of the ISSS. Vortex the sample for several seconds. If insolubles are present, add 1.0 mL D_2O (not containing maleic acid or the reference compound), vortex, and sonicate 15 minutes. Vortex the sample and filter if necessary. Place in NMR sample tube.

Instrument:	Varian Mercury 400 MHz with proton detection probe NMR Spectrometer
Pulse Width:	10 µs or 90° (whichever is less)
Spectral Width (SW)	at least containing –3 ppm through 13 ppm
Number of Scans:	multiple of 4 (greater to enhance S/N)
Delay between Pulses:	45 s
Shimming:	automatic gradient shimming of Z1-4 shims
Total run time/sample:	6 min (NT = 4) -14 min (NT = 16)
Uniformity within spectral width:	0.3% RSD (-0.6 to 11.4 PPM)
Run Time:	6 min
Linear Range:	0.6 mg/mL - 67 mg/mL
Repeatability:	<4%
Correlation Coefficient:	1.0
Accuracy:	<3%

6. QUALITATIVE DATA

See spectra on the following pages for Mass Spectrometry, FT-IR, Vapor Phase IR, FT-Raman, and Nuclear Magnetic Resonance.

7. REFERENCES

Coates, J., and Reffner, J., "Visualization of Micro-ATR Infrared Spectroscopy," *Spectroscopy*, Vol. 14, #4, April 1999.

Clarke, E.G.C., *Isolation and Identification of Drugs, 2nd Edition*, The Pharmaceutical Press, 1986.

Galichat, Laurent Y., *Clarke's Analysis of Drugs and Poisons*, Volume 2, p. 1256, Pharmaceutical Press, 2004.

Budavari, S., *The Merck Index, 13th Edition*, Merck and Co., Inc., 2001.

8. ADDITIONAL RESOURCES

Forendex

Wikipedia

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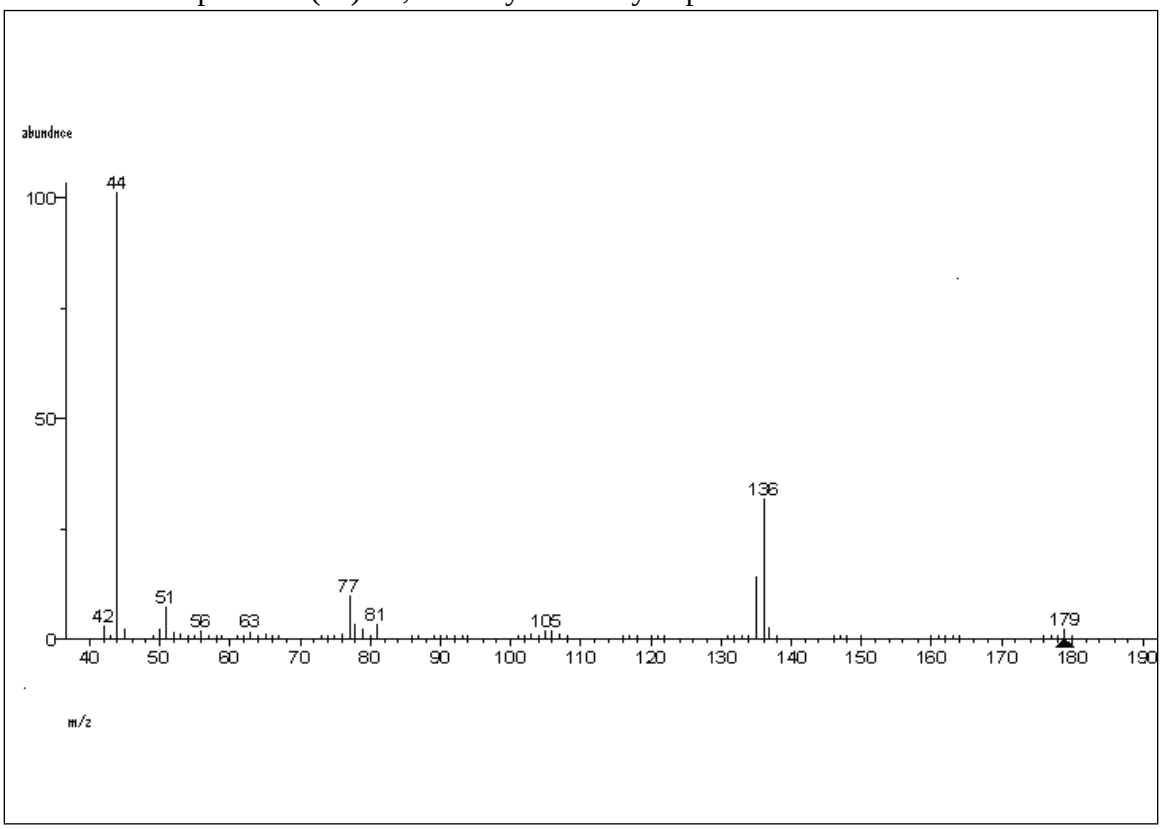
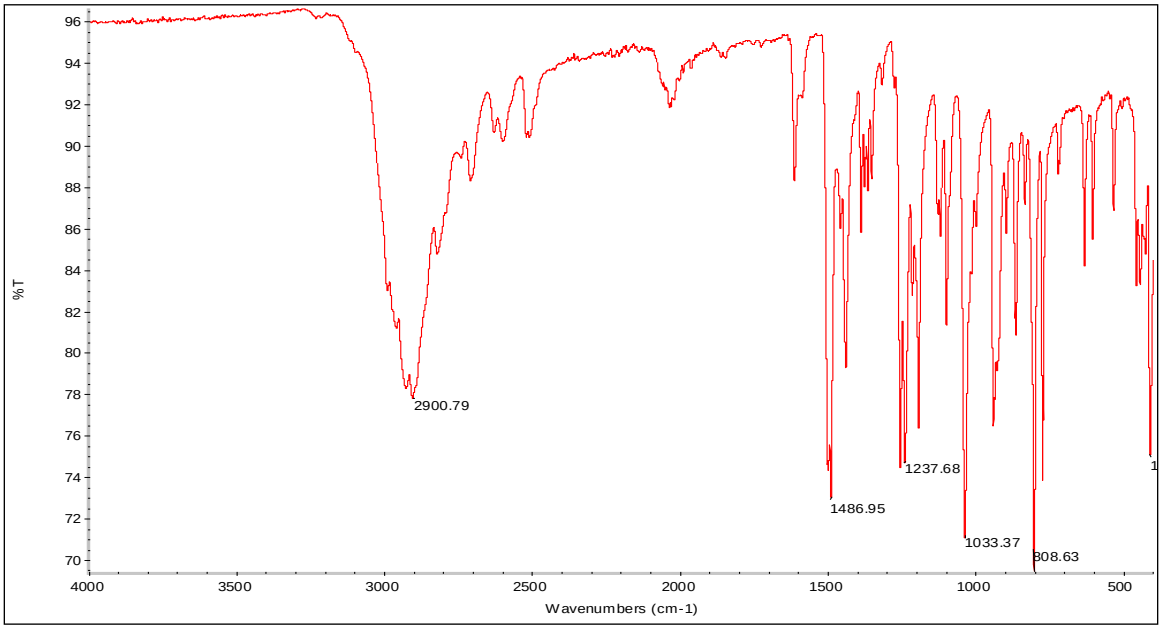
*Optical isomers standards for these compounds were unavailable.
***No Data Available

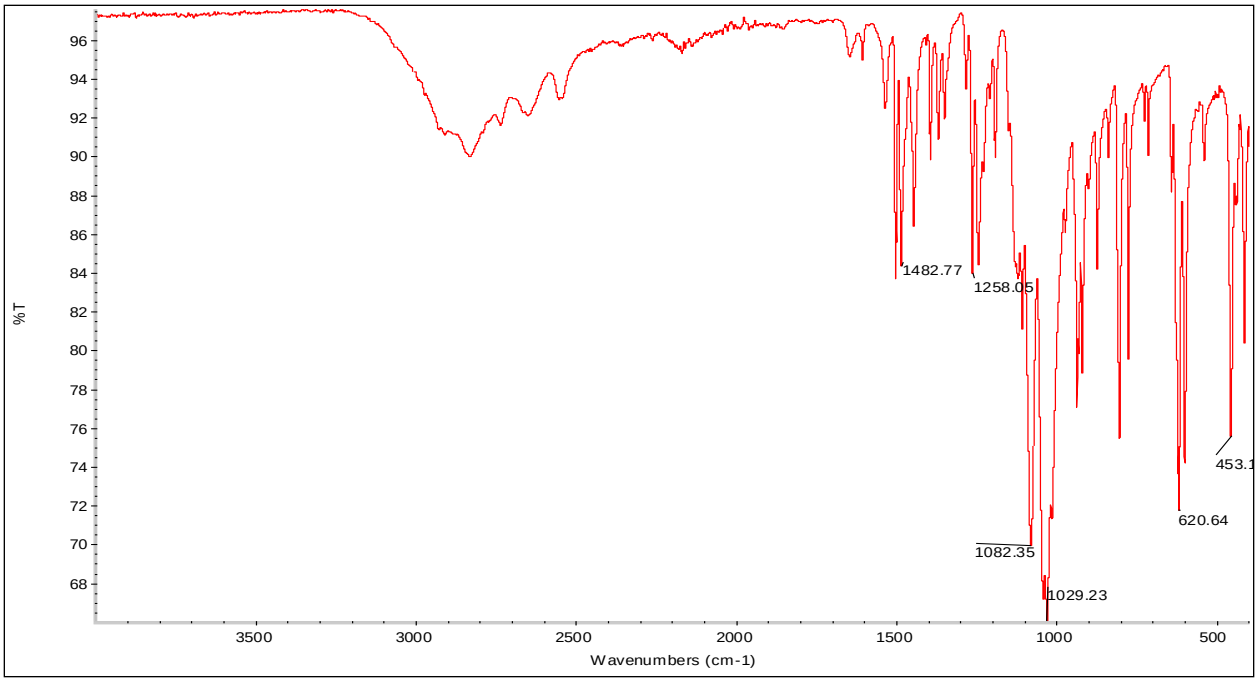
Mass Spectrum (EI): 3,4-Methylenedioxyamphetamine HCl Lot # A150B



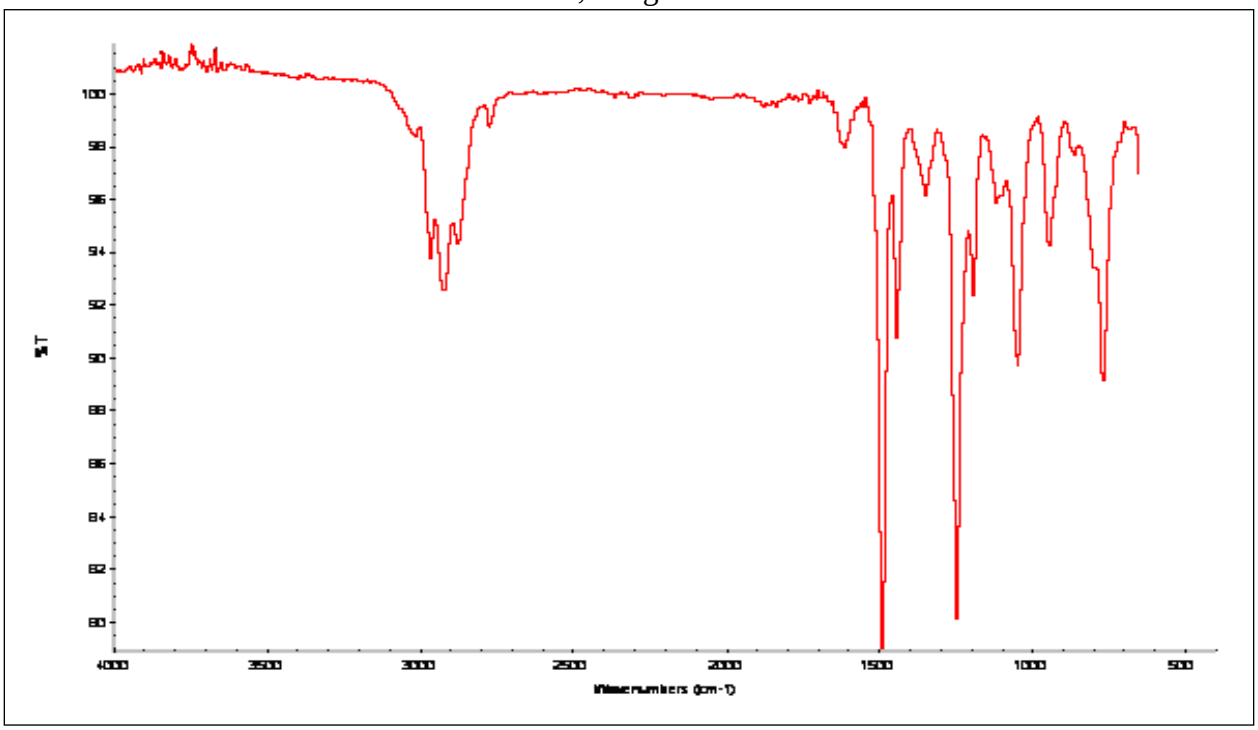
FTIR (One bounce - ATR): 3,4-Methylenedioxyamphetmaine HCl Lot # A150B
4 cm^{-1} resolution, 32 scans



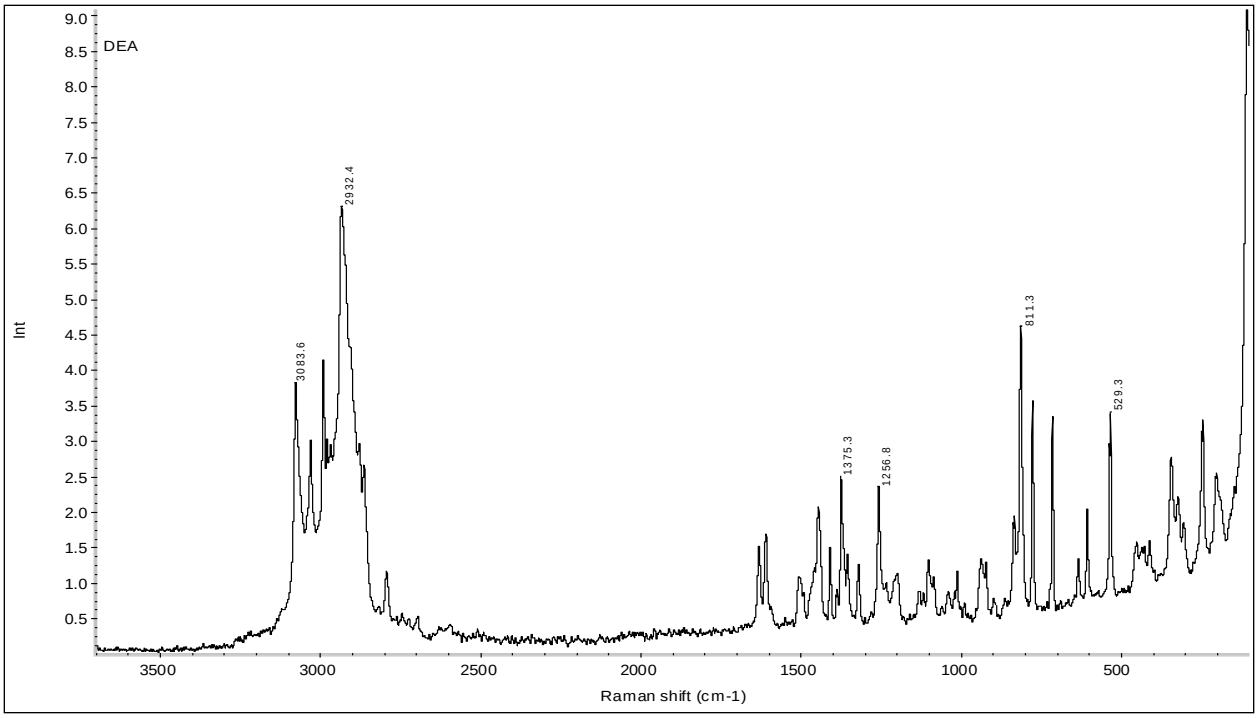
FTIR (One bounce – ATR): 3,4-Methylenedioxyamphetamine sulfate Lot # X-19LDS
4 cm^{-1} resolution, 32 scans



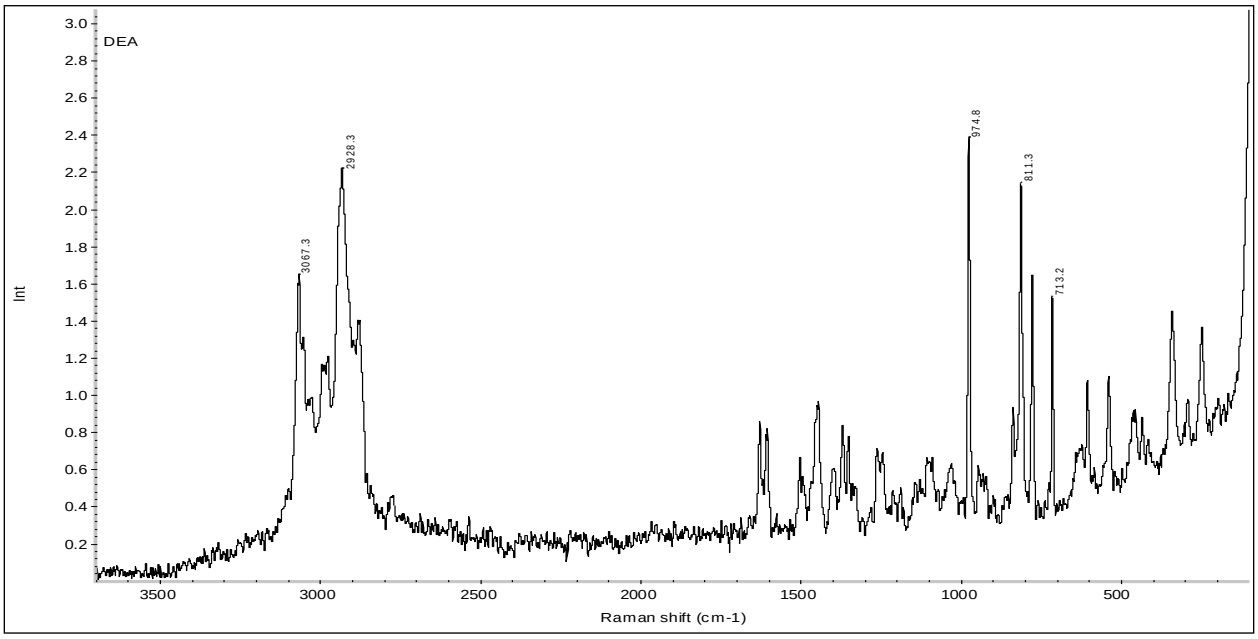
GCIRD: 3,4-Methylenedioxyamphetamine Lot # A150B
4 cm^{-1} resolution, 2 mg/mL in chloroform



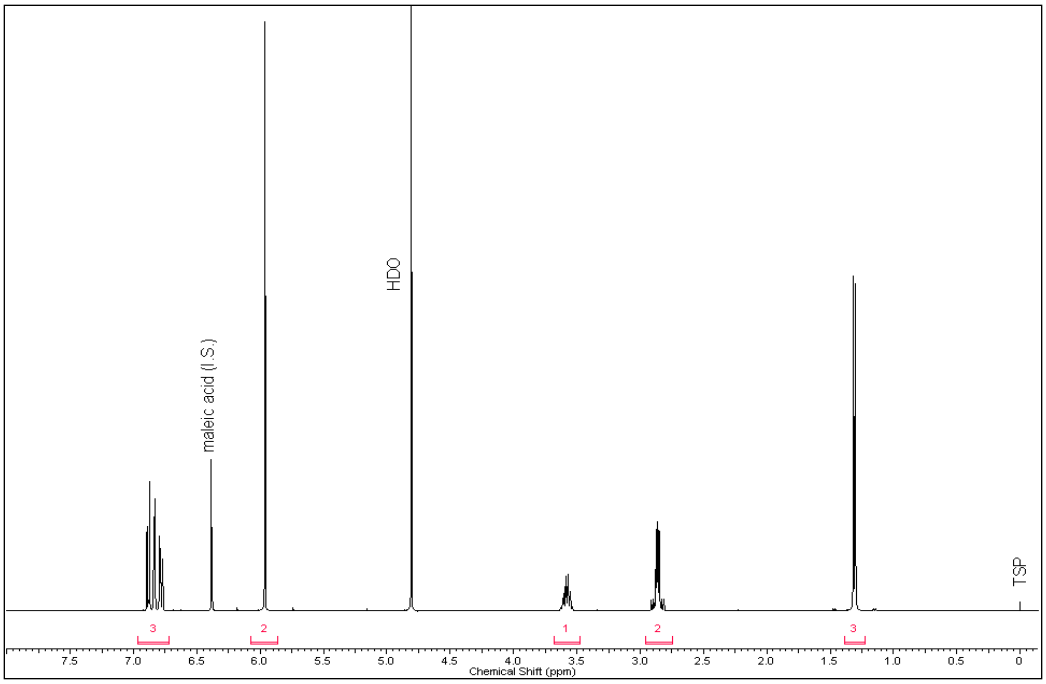
FT-RAMAN: 3,4-Methylenedioxyamphetamine HCl Lot # A150B
4 cm^{-1} resolution, 32 scans



FT-RAMAN: 3,4-Methylenedioxyamphetamine sulfate Lot # X-19-LDS
4 cm^{-1} resolution, 32 scans



^{1}H NMR: 3,4-Methylenedioxyamphetamine HCl Lot # A150B
deuterium oxide, maleic acid as internal standard, 400 MHz



ppm 6.88 (d, J=7.9 Hz, 1 H) 6.83 (d, J=1.4 Hz, 1 H) 6.79 (dd, J=7.9, 1.4 Hz, 1 H) 5.96 (s, 2 H) 3.59 (tq, J=7.2, 6.7 Hz, 1 H) 2.87 (d, J=7.2 Hz, 2 H) 1.32 (d, J=6.7 Hz, 3 H)

^{13}C NMR: 3,4 Methylenedioxyamphetamine HCl Lot #A 150B
deuterium oxide, maleic acid as internal standard