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FSC 630 Forensic Science Internship

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The Validation of a GC-IR and GC-MS and GC-IR Analysis of Methcathinone Analogs

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Abstract:

Gas chromatography-infrared spectroscopy (GC-IR) has been shown to be an important method in the analysis of drugs with similar structures such as the phenethylamines. These drugs have nearly identical mass spectra making identification difficult. GC-IR analysis can differentiate between these compounds. The validation study was performed using nineteen drugs. Each drug was analyzed at least ten times to demonstrate reproducibility. Comparison to reference spectra was performed (when available) to ensure accuracy. Linearity studies were also performed for each drug by changing the amount of sample injected into the system.

Methcathinone is a Schedule 1 psychoactive stimulant, structurally similar to methamphetamine. Many analogs with only minor structural variations have been produced to circumvent the criteria described by the legal system. Currently, only three of these analogs have been placed into Schedule 1 of the Controlled Substances by the DEA: methylone, mephedrone (4-methylmethcathinone) and methylenedioxypyrovalerone (MDPV). With the use of methcathinone analogs on the rise and the unclear scheduling, laboratories are tasked with correctly identifying them.

Like the phenethylamines, methcathinone analysis by GC-MS is problematic due to similar mass spectra for positional isomers. Mass spectra can provide information about what type of structural analog may be present in a forensic sample, but cannot reliably differentiate between positional isomers. GC-IR analysis could potentially distinguish between these isomers.

Twenty-one methcathinone analogs were analyzed via GC-MS and GC-IR. Only two methcathinone analogs had IR spectra that were more similar than the resulting mass spectra. The analogs analyzed include: methylmethcathinone, fluoromethcathinone,

methoxymethcathinone, methyl-α-pyrrolidinopropiophenone, methylenedioxymethcathinone, butylone, pentedrone, 3,4-methylenedioxy-α-PPP, MDPV, α-PPP, 3,4-dimethylmethcathinone and 4-methoxy-α-PPP. Future studies should be conducted to analyze a wider range of methcathinone analogs to aid drug analysts in identification of an increasingly popular family of drugs.

Introduction:

Gas chromatography-mass spectrometry (GC-MS) is the gold standard for forensic drug analysis. As the popularity of designer drugs increases, GC-MS analysis is becoming a less useful tool for drug identification. Many designer drugs have minor structural changes resulting in multiple drugs having similar mass spectra. GC-IR has been shown to be able to differentiate between these designer drugs without the need to chemically modify the drug before analysis. GC-IR is a valuable instrument because it provides a GC retention time with an IR identification. Numerous studies have demonstrated the successful analysis of drugs via GC-IR [1-2]. This study was performed to demonstrate the ability of GC-IR to identify compounds of similar structure and provide a validation method.

The rise in popularity of designer drugs has resulted in increased use of methcathinone [3-6]. Methcathinone is a schedule 1 drug under The United States' Controlled Substances Act which has led to the production of many methcathinone analogs that fall outside of current regulations [4]. Only three of these analogs have been placed into schedule 1 of the Controlled Substances Act by the DEA. All of these analogs contain the basic methcathinone structure, but are modified in one of three regions: the alkyl side chain, the amino group or the aromatic ring [4]. Methcathinone analogs are altered in such a way to avoid scheduling without a significant change in the pharmacological effects. These modifications cause problems for drug analysts

because each compound must be properly identified to determine if they actually are a controlled substance. Many methcathinone analogs have been analyzed via GC-MS [3-6], but few have been analyzed via GC-IR [7]. This study was performed to demonstrate that GC-MS analysis cannot be the sole method of identification for analysis of samples containing methcathinones and to provide reference spectra for many methcathinone analogs via GC-IR analysis.

Methods and Materials:

Samples

Nineteen drug standards (phenethylamines and antihistamines) were provided by the West Virginia State Police Drug Lab and were purchased from Sigma (St. Louis, MO), Fisher Scientific (Waltham, MA) and Toronto Research Chemical (Toronto, Ontario. Canada). Twenty-one methcathinone standards were purchased from Cayman Chemical (Ann Arbor, MI). Figure 1 shows the structures for the methcathinone analogs.

Sample preparation: Most samples were dissolved in chloroform. Samples that had low solubility in chloroform were dissolved in 5% NaOH and then extracted with chloroform. The concentrations of the phenethylamines and antihistamine standards ranged from 2 mg/mL to 16 mg/mL. The concentrations of the methcathinone standards ranged from 1 mg/mL to 3 mg/mL.

Gas Chromatography – Flame Ionization Detector

Gas Chromatography – Flame Ionization Detection was performed using an Agilent (Santa Clara, CA) 6890N GC.

The oven temperature was: Initial temperature 115 °C, ramped to 290 °C at 20.00 °C/min (hold for 4.00 minutes), Post Run: 50°C. The injection port was kept at 225 °C and injections were

performed in splitless mode. The carrier gas was helium at a flow of 2.0 mL/min. The column used was an HP-1 methyl siloxane capillary column (30.0 m x 320 μm x 1.00 μm nominal).

Infrared Spectroscopy

The infrared spectrum was acquired using a Thermo Scientific (Waltham, MA) Nicolet 6700 FTIR. The IR was connected to the GC via a Thermo Scientific GC/IR Interface. The infrared spectra were obtained using 16 scans in the range of 4000-650 cm^{-1} with a resolution of 8-16 cm^{-1}. The aperture was set to 150. The infrared detector flow cell and transfer line temperatures were 280 °C

Gas Chromatography-Mass Spectrometry

The GC-MS study was performed on an Agilent Technologies 7890A gas chromatograph coupled with an Agilent 5975C mass selective detector. The mass range analyzed was 40 to 500. The inlet temperature was 250 °C. The temperature program was: 70 °C for 2.00 minutes then ramped to 270.00 °C at a rate of 20.00 (°C/min).

Validation Study

A study to determine the best IR settings was performed using a fresh pseudoephedrine standard. The study analyzed the pseudoephedrine standard nine times while changing the aperture, the number of scans, and the resolution.

The rest of the standards were analyzed on the GC-FID/IR at least once to determine if a spectrum could be obtained. The spectrum obtained from each standard was compared to a reference spectrum when one was available. The standards were analyzed at least ten times to ensure the analysis was reproducible.

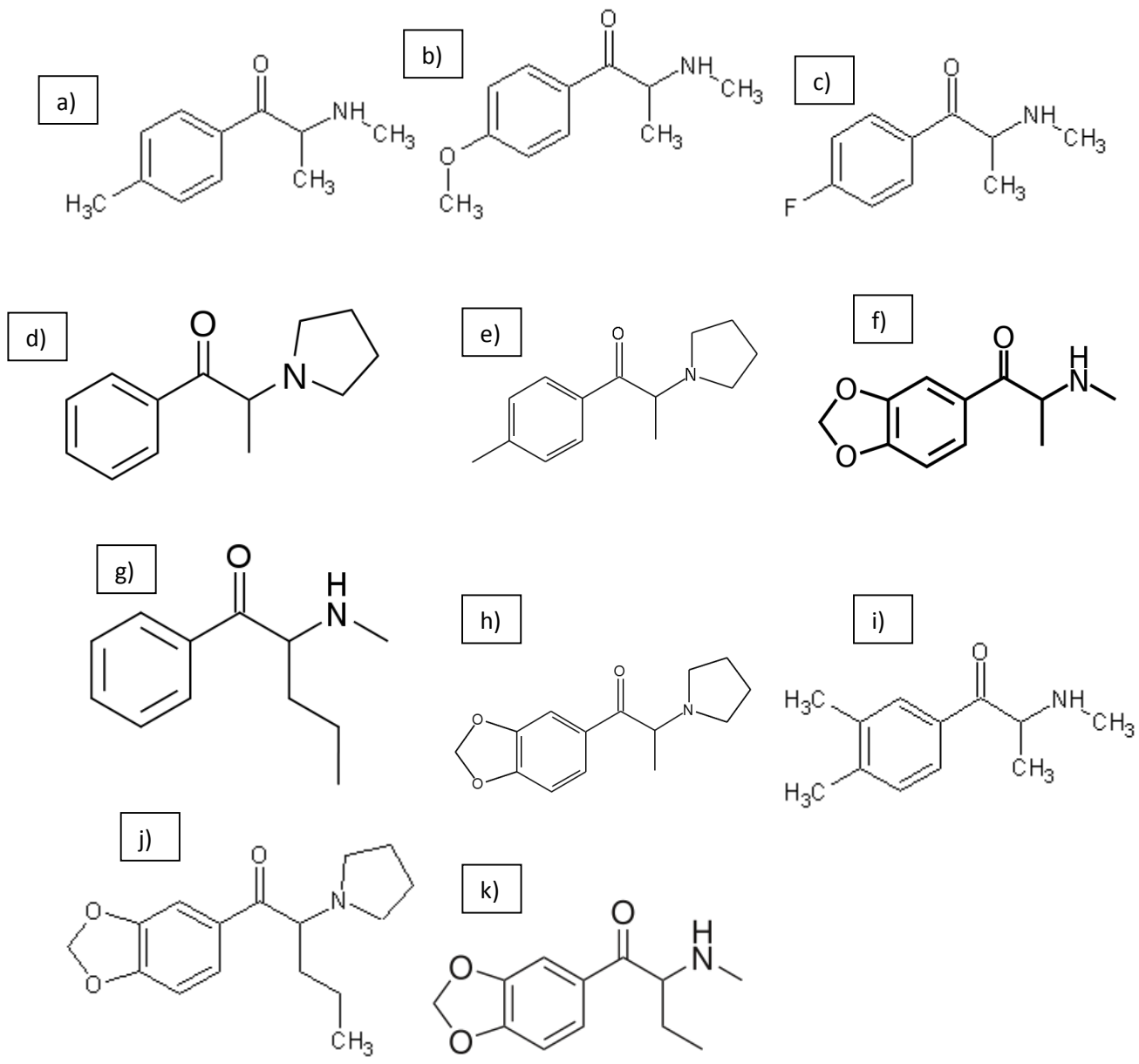

Figure 1. Structure of: a) 4-methylmethcathinone, b) 4-methoxymethcathinone, c) 4-fluoromethcathinone, d) α-PPP, e) 4-methylα-PPP, f) 3,4-methylenedioxymethcathinone, g) Pentedrone, h) 3,4-methylenedioxy-α-PPP, i) 3,4-dimethylmethcathinone, j) MDPV, k) Butylone

Statistics were done on the retention time from the GC-FID and the wavenumbers of characteristic bands in the IR spectra. The average, standard deviation and relative standard deviation were determined for each data set.

Fresh standards of the nineteen drugs were made and analyzed to ensure the spectrum produced matched the spectrum from the original standards. The new standards were then used to perform a linearity study. For each drug, a sequence of five runs was performed in which the amount of sample injected into the GC changed from 1 μL to 5 μL.

Results and Discussion:

Validation Study

The pseudoephedrine spectrum obtained from the study to determine the best IR settings is shown in Figure 2. The aperture automatically changed to 69 when the resolution was changed to 2.0. The best settings for the IR were discovered to be an aperture of 100, 16 scans with a resolution of 16 (a resolution of 8 was found to give fairly good spectra as well and could be used depending on the sample).

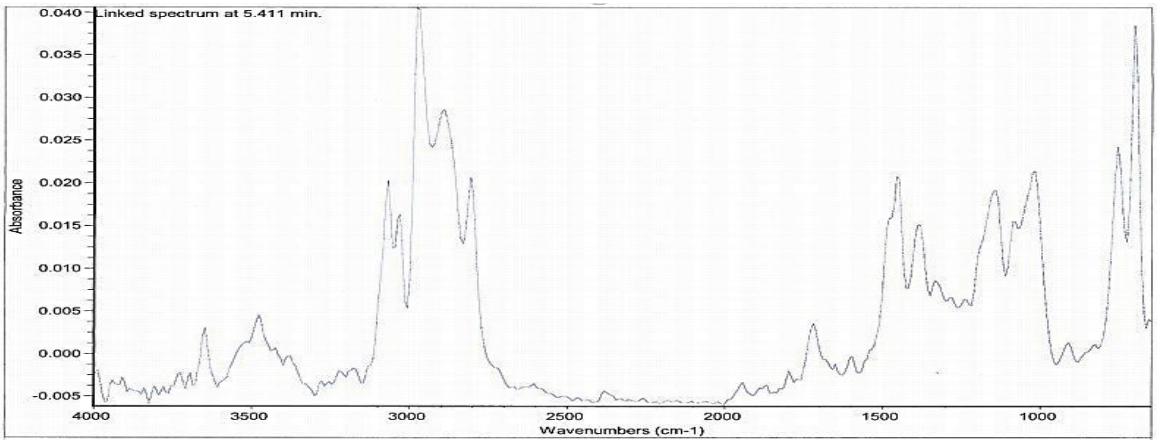

Figure 2. Pseudoephedrine spectrum obtained with 16 scans, 16.0 resolution, aperture 100 and single-sided interferograms.

The average retention time and standard deviation from the GC-FID for the 19 phenethylamines and antihistamines are shown in Table 1. Three compounds had RSDs above 2.0% for their retention times. The retention times for these compounds were erratic most likely due to overloading of the column.

Table 1. The average retention time, standard deviation and relative standard deviation for each drug

Drug	Retention Time (minutes)	Retention Time RSD (%)
Benzphetamine	8.4±0.025	0.30
Chlorpheniramine	9.2±0.018	0.20
d-amphetamine	3.9±0.0046	0.12
Diphenhydramine	8.4±0.023	0.27
DOB	8.2±0.10	1.22
Doxylamine	8.7±0.011	0.13
Ephedrine	5.5±0.036	0.65
Fenfluramine	4.7±0.13	2.55
Ketamine	8.5±0.025	0.28
Lisdexamphetamine	10.6±0.0155	0.15
MDA	6.2±0.024	0.39
MDEA	6.8±0.018	0.26
MDMA	6.5±0.014	0.22
Mephentermine	4.8±0.0065	0.14
Methamphetamine	5.9±0.31	5.25
p-methoxyamphetamine	5.5±0.0017	0.03
Phentermine	5.3±0.62	11.70
Phenylpropanolamine	5.2±0.016	0.31
Pseudoephedrine	5.5±0.020	0.36

Ephedrine and Pseudoephedrine

The GC-IR spectra obtained for ephedrine and pseudoephedrine are shown in Figures 3 and 4, respectively. Table 2 shows the bands found in each as well as the standard deviation and

relative standard deviation for each band. The linearity study graph for ephedrine and pseudoephedrine are shown in Figures 5 and 6, respectively.

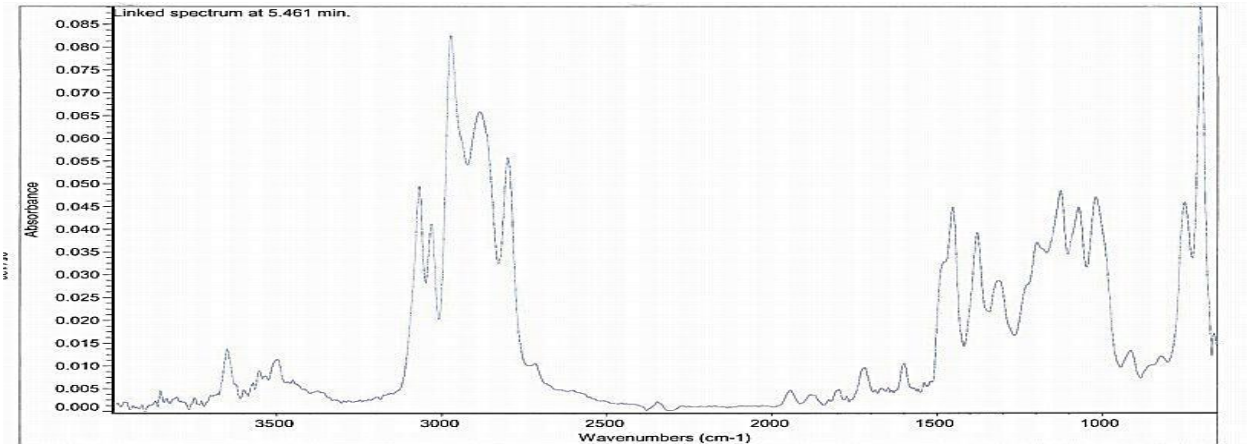

Figure 3. GC-IR spectrum for Ephedrine

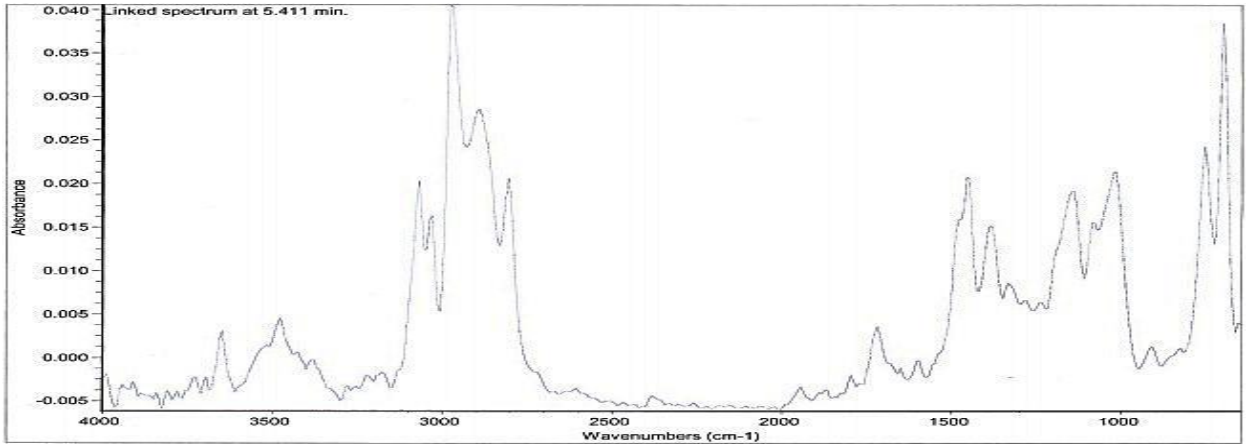

Figure 4. GC-IR spectrum for Pseudoephedrine

Table 2. The bands found in the GC-IR spectra for ephedrine and pseudoephedrine

Pseudoephedrine			Ephedrine		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
3650	3.833	0.1050	3071	0.4992	0.01626
3479	4.885	0.1404	3033	0.4243	0.01399
3071	1.274	0.04148	2973	0.9713	0.03267
3034	1.998	0.06584	2886	2.323	0.08051
2975	1.652	0.05554	2803	1.889	0.06741
2898	3.578	0.1235	1721	0.7500	0.04358
2807	1.341	0.04778	1452	0.9946	0.06851
1724	3.678	0.2133	1379	0.5228	0.03791
1600	0.9678	0.06049	1312	5.037	0.3840
1453	1.360	0.09363	1196	1.764	0.1475
1382	1.687	0.1221	1126	0.8539	0.07585
1143	4.259	0.3726	1070	2.666	0.2492
1022	1.547	0.1513	1021	0.2872	0.02815
755	1.84	0.243	748	2.43	0.325
700	0.953	0.136	700	0.171	0.0244

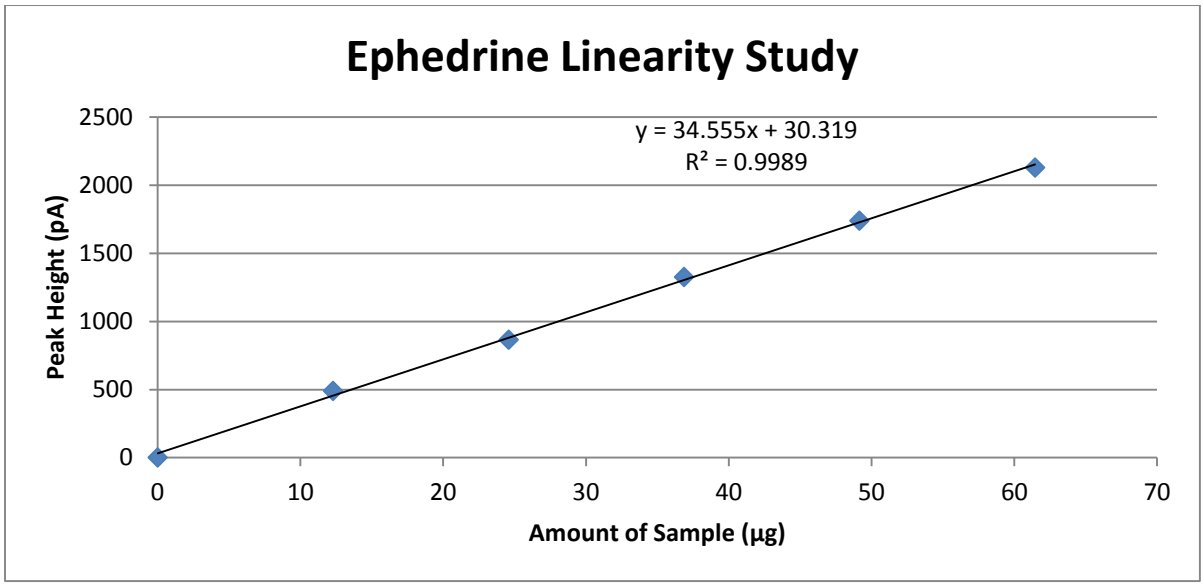

Figure 5. Linearity study for Ephedrine

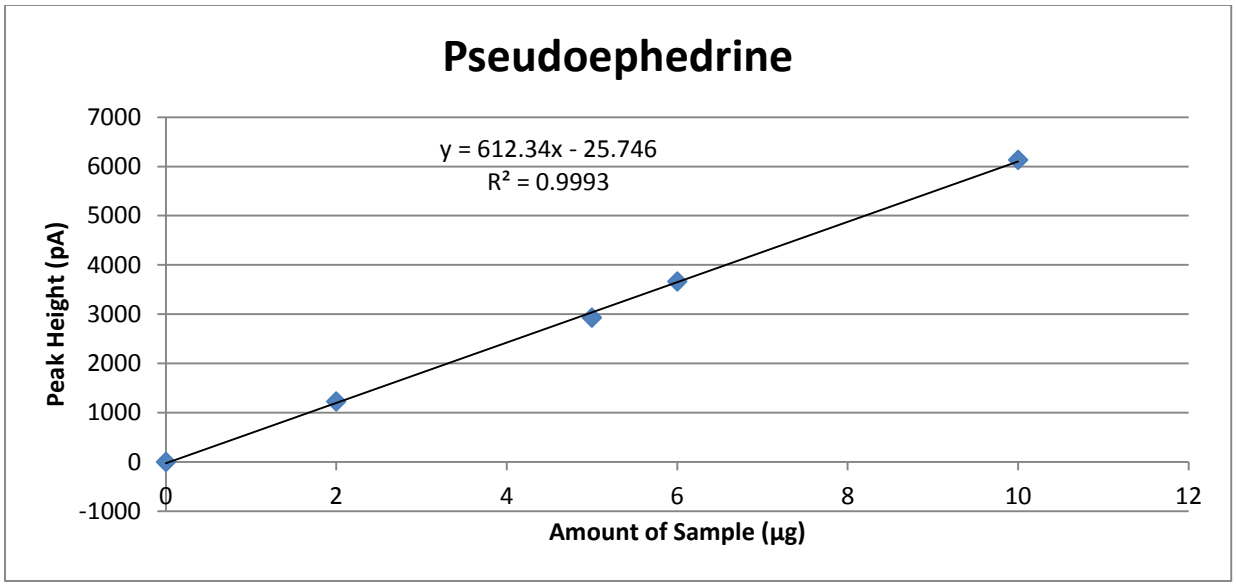

Figure 6. Linearity study for Pseudoephedrine

Amphetamines

Five amphetamines were analyzed: d-amphetamine, 2,5-dimethoxy-4-bromoamphetamine (DOB), lisdexamphetamine, methamphetamine and p-methoxyamphetamine. The GC-IR spectra for d-amphetamine, DOB, lisdexamphetamine, methamphetamine and p-methoxyamphetamine are shown in Figures 7-11, respectively. Tables 3 and 4 show the bands found in each spectrum with the standard deviation and relative standard deviation. The linearity study graphs are shown in Figures 12-16.

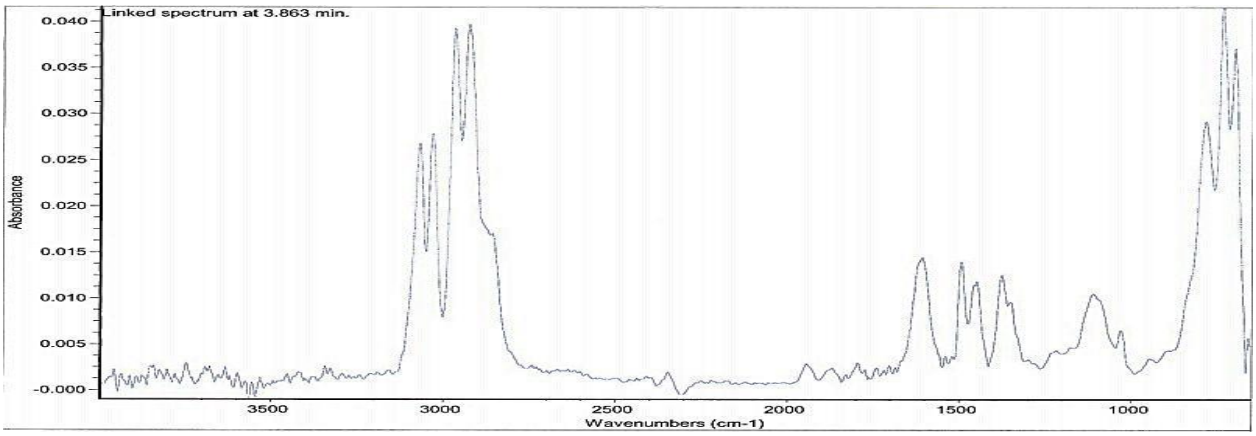

Figure 7. GC-IR spectrum for d-amphetamine

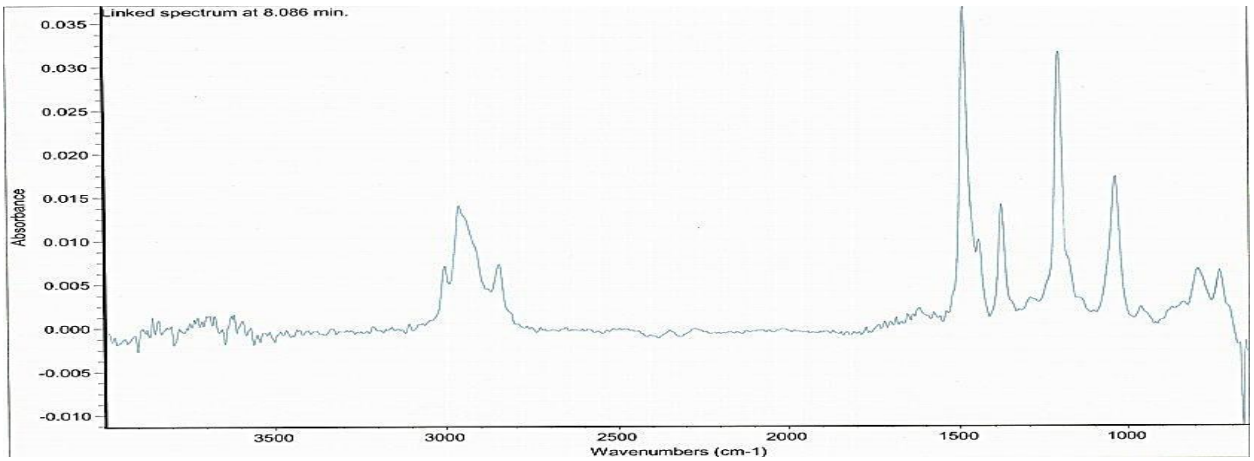

Figure 8. GC-IR spectrum for DOB

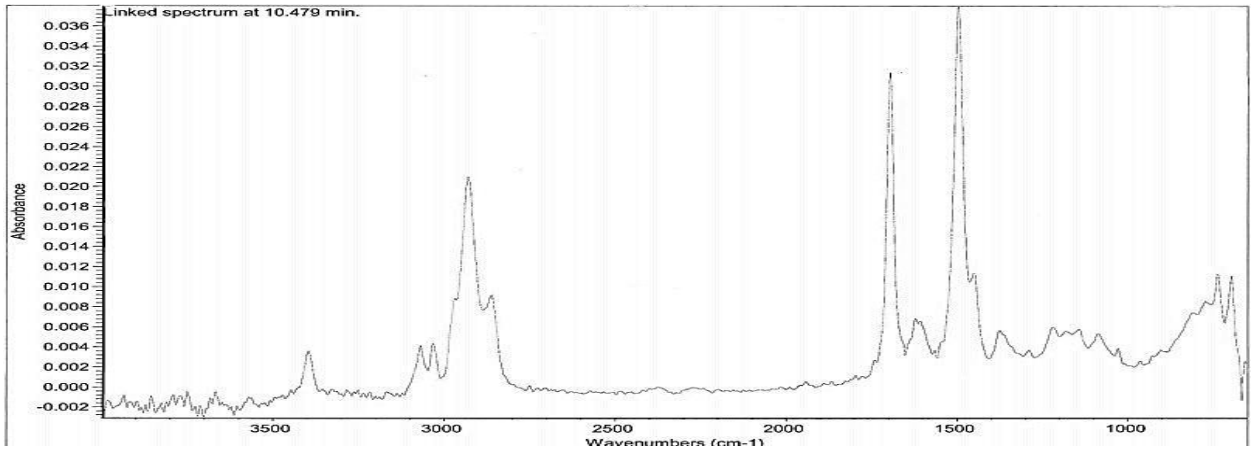

Figure 9. GC-IR spectrum for Lisdexamphetamine

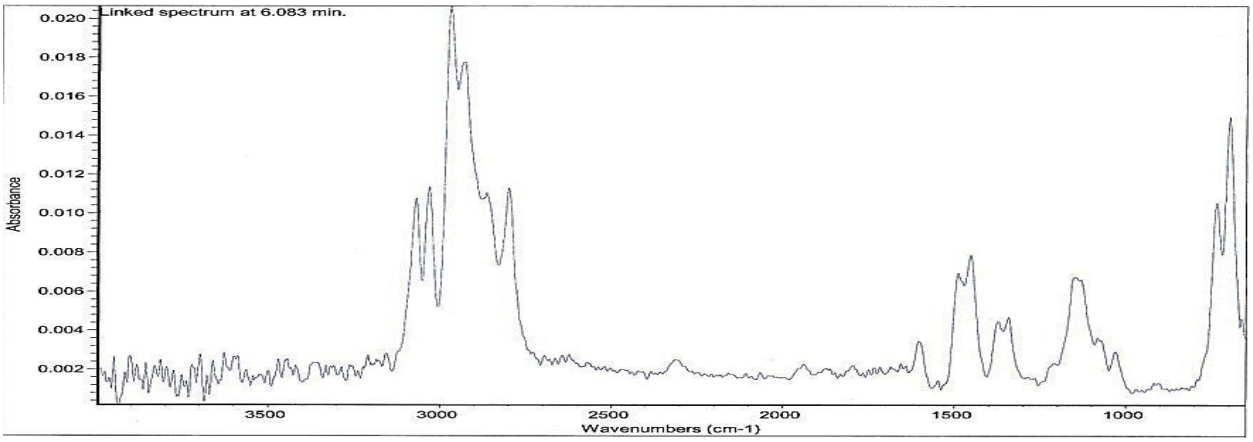

Figure 10. GC-IR spectrum for Methamphetamine

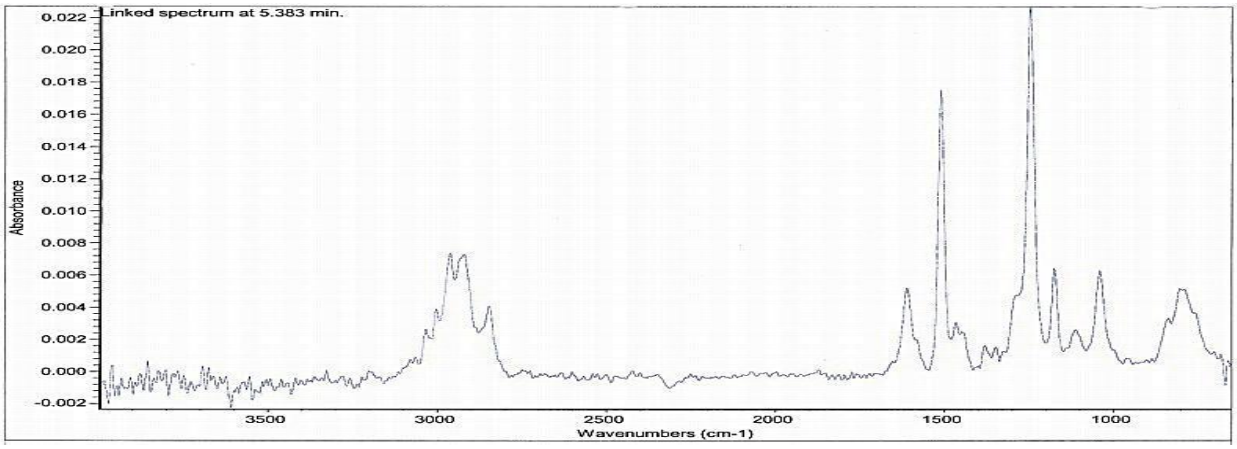

Figure11. GC-IR spectrum for p-Methoxyamphetamine

Table 3. Bands found in the GC-IR spectra of d-Amphetamine, DOB and Lisdexamphetamine

d-Amphetamine			DOB			Lisdexamphetamine		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
3071	1.917	0.06244	3005	1.041	0.03466	3399	2.103	0.06187
3034	2.722	0.08972	2963	1.788	0.06033	3070	0.8185	0.02666
2968	1.176	0.03962	2850	1.229	0.04312	3033	1.360	0.04485
2926	1.902	0.06501	1490	0.4260	0.02860	2931	0.6013	0.02051
2876	0.2121	0.007376	1447	0.7681	0.05309	1698	0.3118	0.01836
1616	5.043	0.3121	1380	0.2843	0.02060	1623	1.760	0.1084
1610	3.482	0.2162	1213	0.2498	0.02059	1498	0.2051	0.01369
1496	1.402	0.09376	1039	0.7414	0.07139	1379	1.160	0.08412
1456	3.740	0.2569	792	2.15	0.271			
1377	1.166	0.08471	737	1.90	0.258			
1113	3.172	0.2850						
1086	3.536	0.3255						
783	3.25	0.415						
735	0.822	0.112						
701	1.69	0.242						

Table 4. Bands found in the GC-IR spectra of Methamphetamine and p-Methoxyamphetamine

Methamphetamine			p-Methoxyamphetamine		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
3070	0.5223	0.01701	3033	1.338	0.04410
3033	0.7960	0.02625	3004	1.641	0.05463
2971	0.5593	0.01882	2965	0.9695	0.03270
2933	2.347	0.08001	2924	1.767	0.06044
2861	2.272	0.07943	2847	0.8381	0.02944
2800	0.6519	0.02328	1611	1.290	0.08003
1600	1.411	0.08818	1512	0.3094	0.02046
1492	1.973	0.1322	1466	2.151	0.1467
1459	4.359	0.2987	1247	0.07559	0.006063
1374	2.736	0.1991	1175	0.09759	0.008304
1347	1.417	0.1052	1041	0.4180	0.04016
1145	5.449	0.4759	799	3.47	0.435
1076	2.427	0.2256			
737	0.682	0.0926			
699	0.795	0.114			

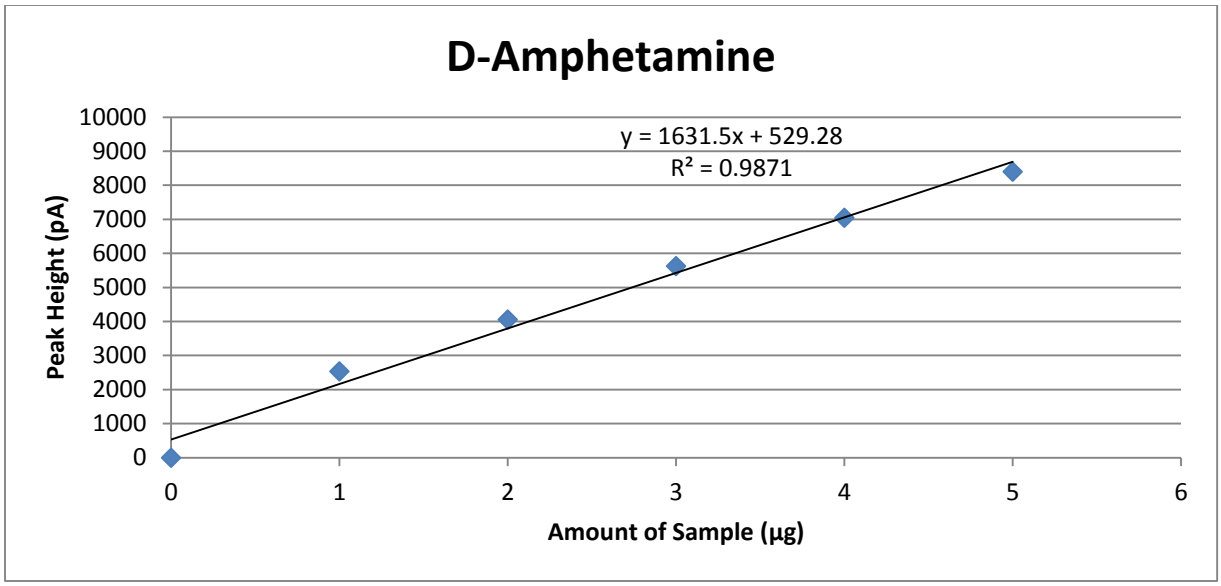

Figure 12. D-amphetamine Linearity Study

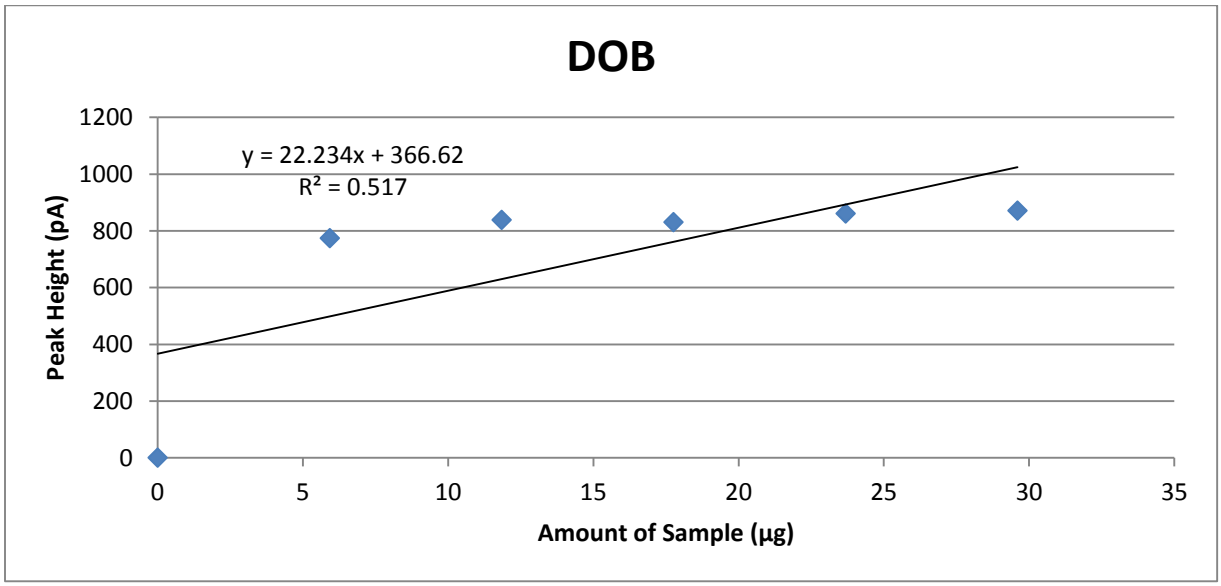

Figure 13. DOB Linearity Study

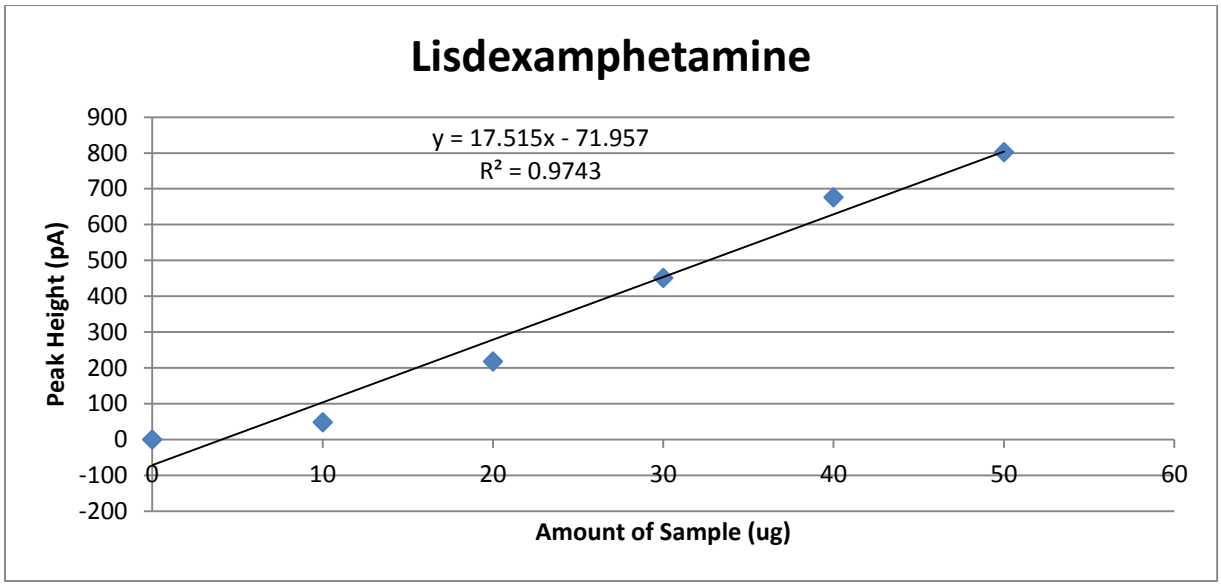

Figure 14. Lisdexamphetamine Linearity Study

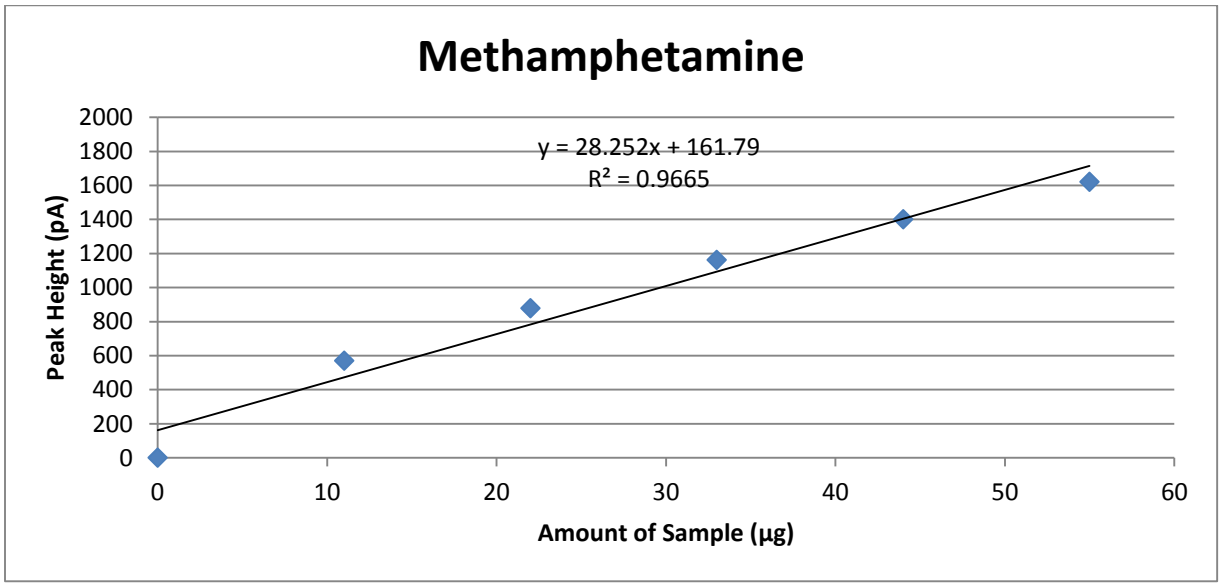

Figure 15. Methamphetamine Linearity Study

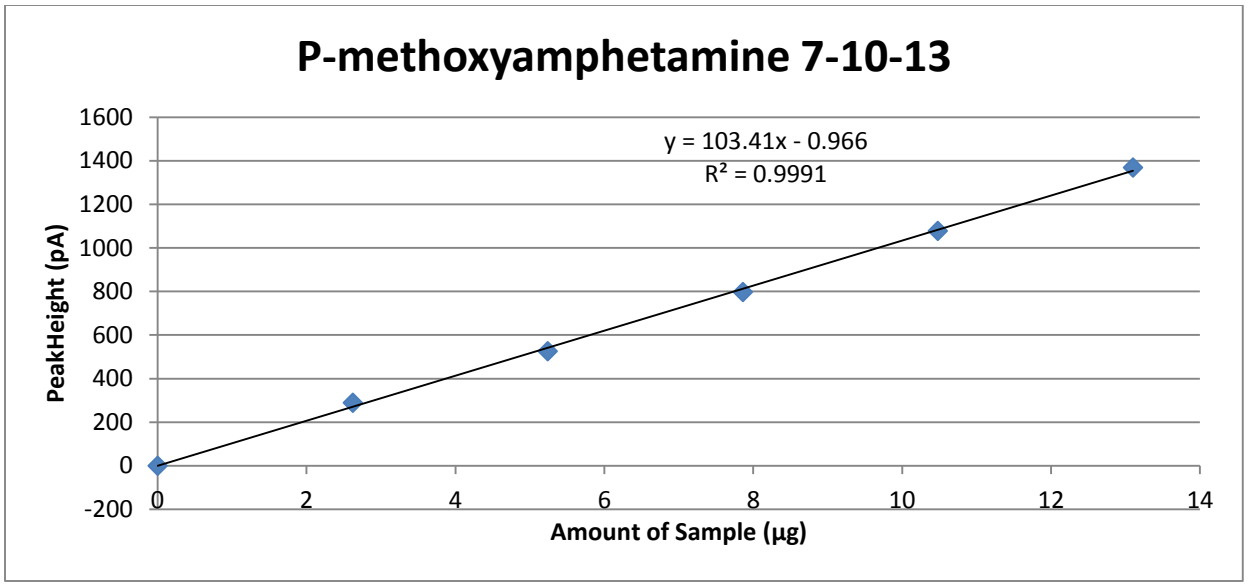

Figure 16. P-methoxyamphetamine Linearity Study

Amines

Seven amine compounds were analyzed: benzphetamine, chlorpheniramine, diphenhydramine, doxylamine, fenfluramine, ketamine and phenylpropanolamine. The GC-IR spectra for the amines are shown in Figures 17-23. Tables 5, 6 and 7 show the bands found in each spectrum with the standard deviation and relative standard deviation. The linearity study graphs are shown in Figures 24-30.

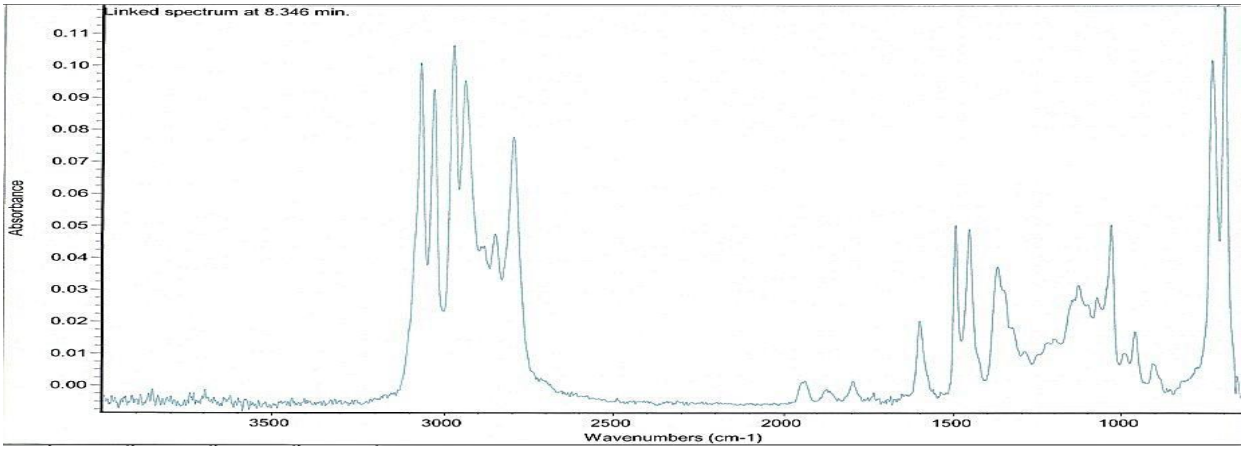

Figure 17. GC-IR spectrum for Benzphetamine

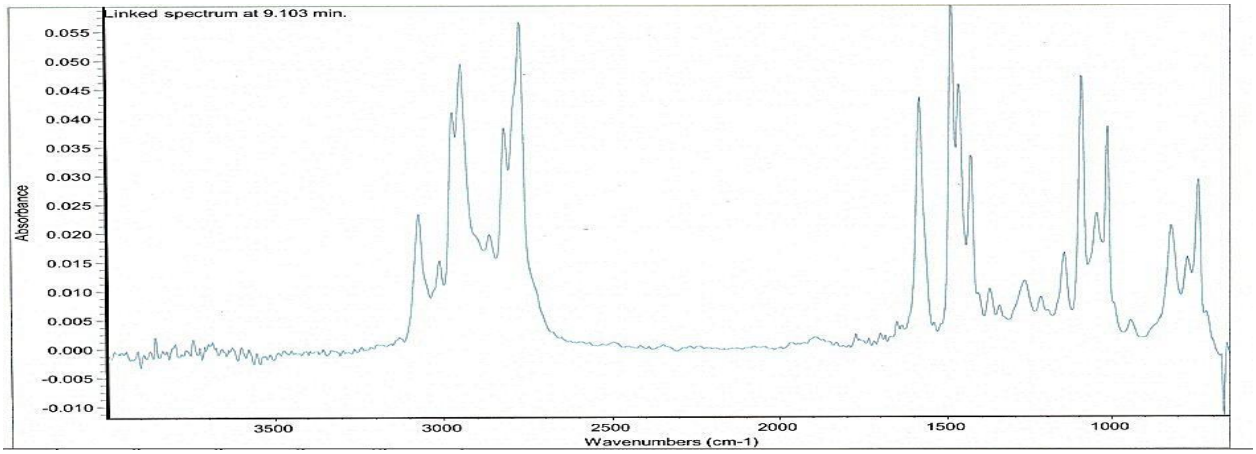

Figure 18. GC-IR spectrum for Chlorpheniramine

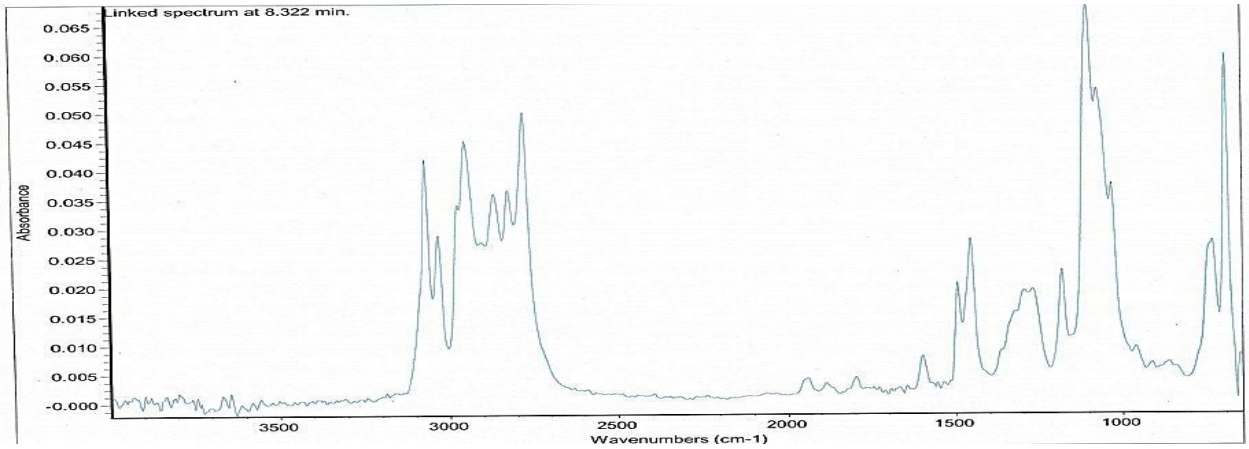

Figure 19. GC-IR spectrum for Diphenhydramine

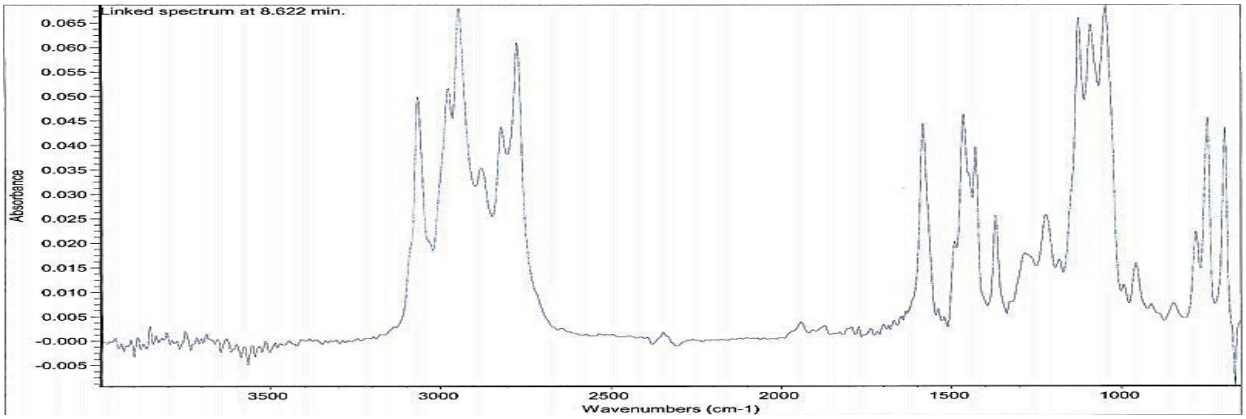

Figure 20. GC-IR spectrum for Doxylamine

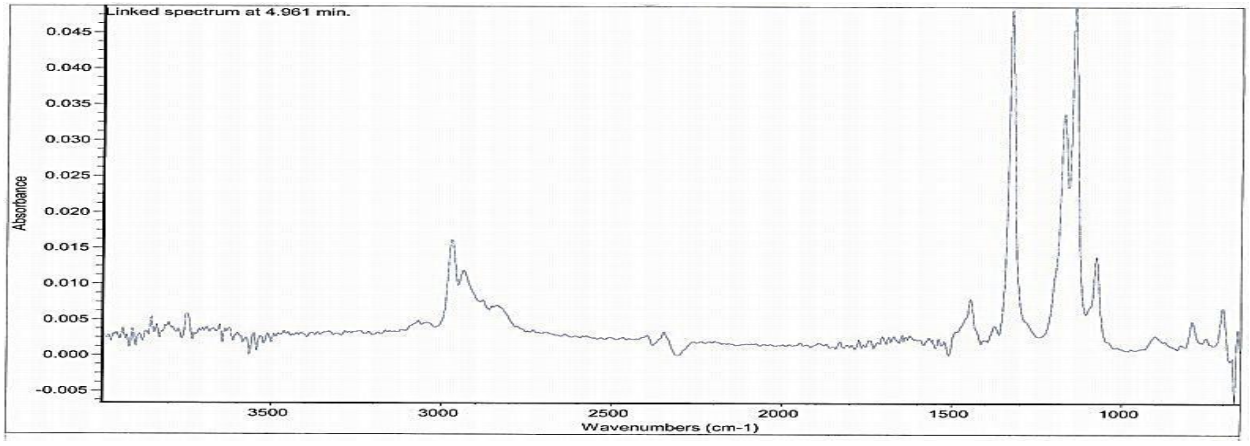

Figure 21. GC-IR spectrum for Fenfluramine

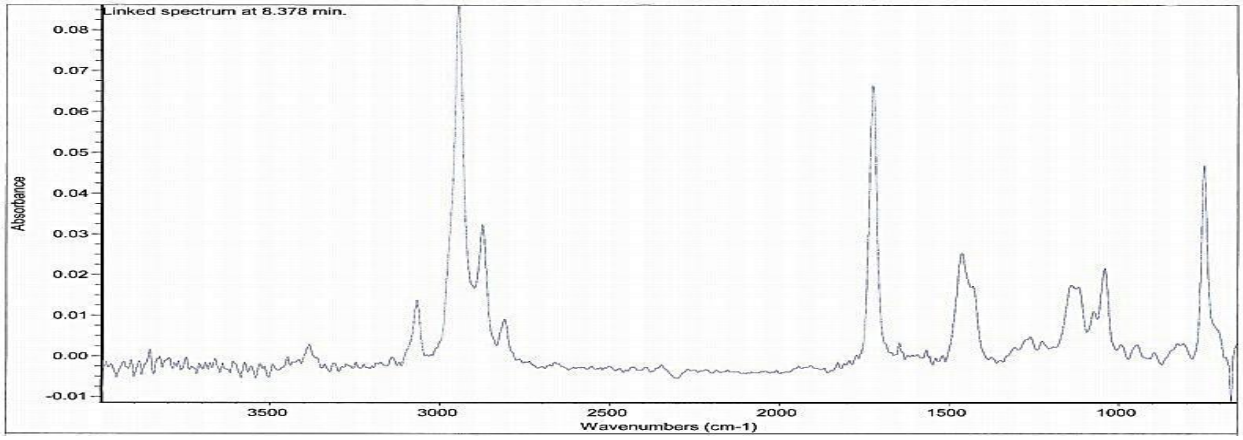

Figure 22. GC-IR spectrum for Ketamine

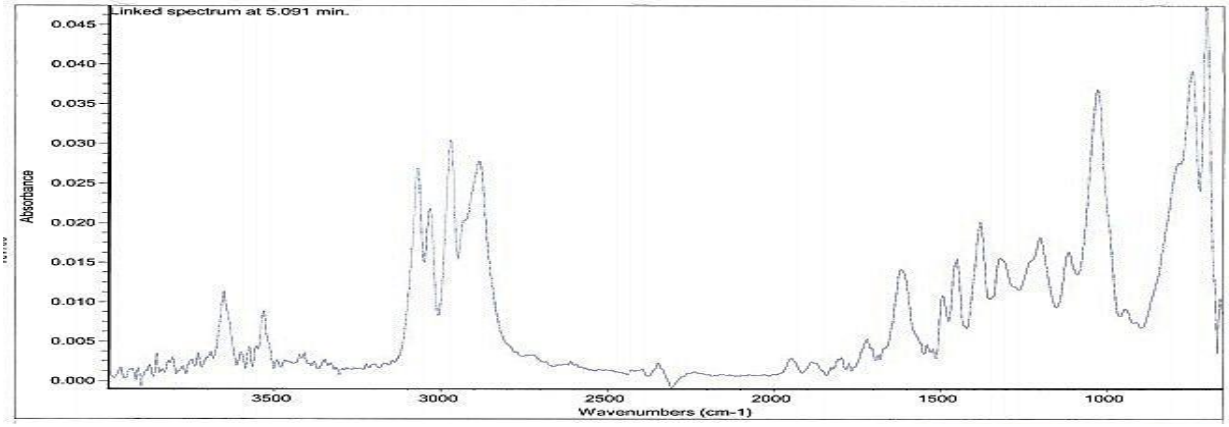

Figure 23. GC-IR spectrum for Phenylpropanolamine

Table 5. Bands found in GC-IR spectra for Benzphetamine, Chlorpheniramine and Diphenhydramine

Benzphetamine			Chlorpheniramine			Diphenhydramine		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
3032	0.3424	0.01129	3075	0.6928	0.02253	3070	0.2210	0.007199
2973	0.8441	0.02840	2975	0.3748	0.01260	3033	0.4328	0.01427
2938	0.5665	0.01928	2951	0.5721	0.01939	2950	0.6186	0.02097
2851	0.8844	0.03102	2822	0.6934	0.02457	2866	0.6294	0.02196
2797	0.5834	0.02086	2776	1.077	0.03881	2824	0.6339	0.02244
1601	1.036	0.06472	1586	1.181	0.07446	2778	0.4431	0.01595
1495	0.2717	0.01818	1491	0.7683	0.05155	1493	0.8837	0.05919
1454	1.119	0.07694	1468	0.4012	0.02733	1453	2.487	0.1711
1371	1.818	0.1326	1433	0.6357	0.04437	1273	1.308	0.1028
1124	4.756	0.4230	1147	0.2691	0.02347	1181	0.1016	0.008608
1029	0.5938	0.05771	1094	0.1266	0.01157	1099	0.1916	0.01743
958	0.806	0.0840	1047	0.5041	0.04813	742	2.96	0.399
904	1.23	0.136	1016	0.6990	0.06882	699	0.217	0.0311
734	0.422	0.0575	820	0.637	0.0777			
698	0.414	0.0593	775	0.391	0.0504			
			746	0.632	0.0846			

Table 6. Bands found in the GC-IR spectra for Doxylamine, Fenfluramine and Ketamine

Doxylamine			Fenfluramine			Ketamine		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
3068	0.7440	0.02425	2972	0.9589	0.03226	3387	1.936	0.05718
2979	1.408	0.04726	2881	6.193	0.2149	3070	1.241	0.04041
2947	0.9303	0.03157	2835	3.433	0.1211	2948	0.3301	0.01120
2823	1.386	0.04910	1446	1.231	0.08513	2877	0.7245	0.02519
2777	0.9234	0.03326	1328	0.3990	0.03004	2812	2.109	0.07500
1584	0.9350	0.05905	1173	0.7723	0.06582	1727	0.3651	0.02115
1466	0.9015	0.06150	1143	0.1056	0.009235	1464	1.271	0.08681
1431	0.5312	0.03713	1076	0.5695	0.05290	1142	1.534	0.1344
1371	1.382	0.1008	793	2.48	0.312	1125	3.640	0.3235
1222	1.574	0.1288	704	1.03	0.146	1042	1.173	0.1125
1127	0.2086	0.01852	659	1.05	0.159	749	0.402	0.0536
1090	1.334	0.1224						
1048	0.7249	0.06919						
781	1.03	0.132						
750	0.593	0.0791						
698	0.812	0.116						

Table 7. Bands found in the GC-IR spectrum for Phenylpropanolamine

Phenylpropanolamine		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
3653	2.264	0.06199
3535	3.117	0.08820
3072	1.416	0.04609
3035	1.401	0.04618
2973	1.155	0.03887
2887	3.161	0.1095
1618	2.793	0.1726
1493	1.981	0.1327
1451	1.238	0.08533
1381	1.189	0.08611
1320	4.114	0.3116
1202	2.352	0.1957
1114	1.947	0.1747
1028	1.154	0.1122
745	2.39	0.320
700	1.04	0.149

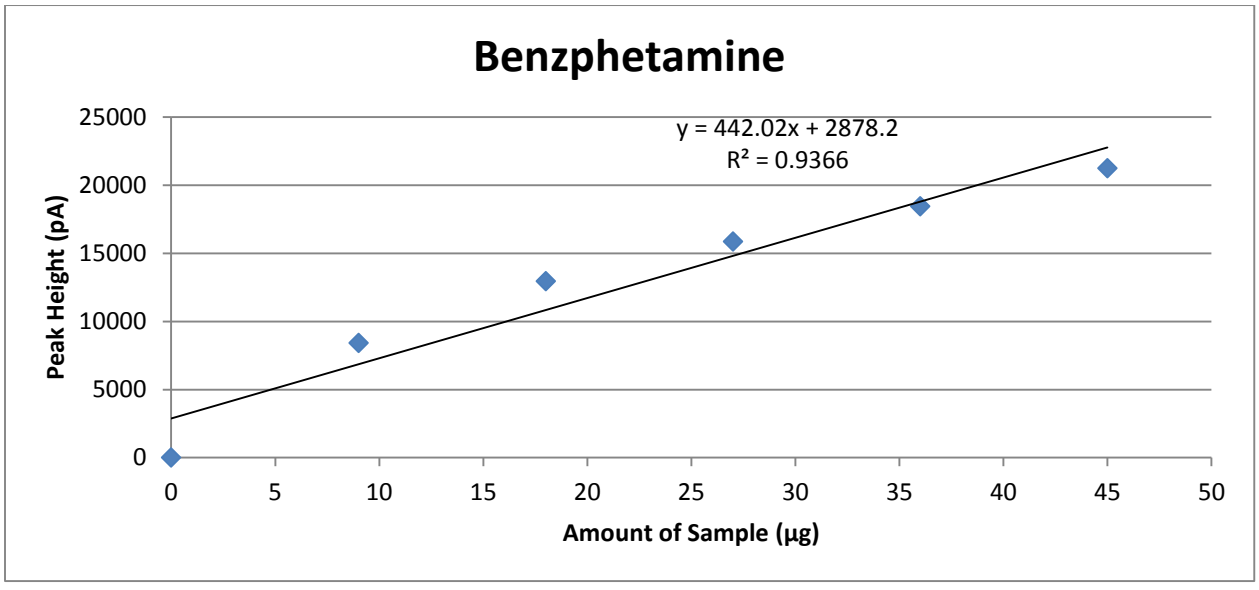

Figure 24. Benzphetamine Linearity Study

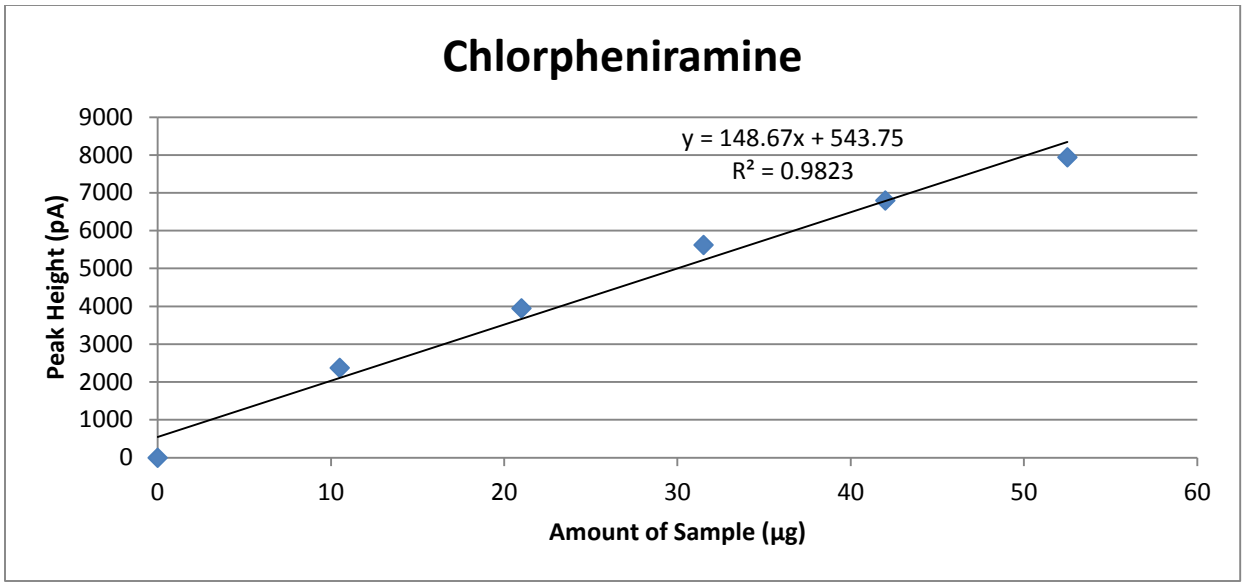

Figure 25. Chlorpheniramine Linearity Study

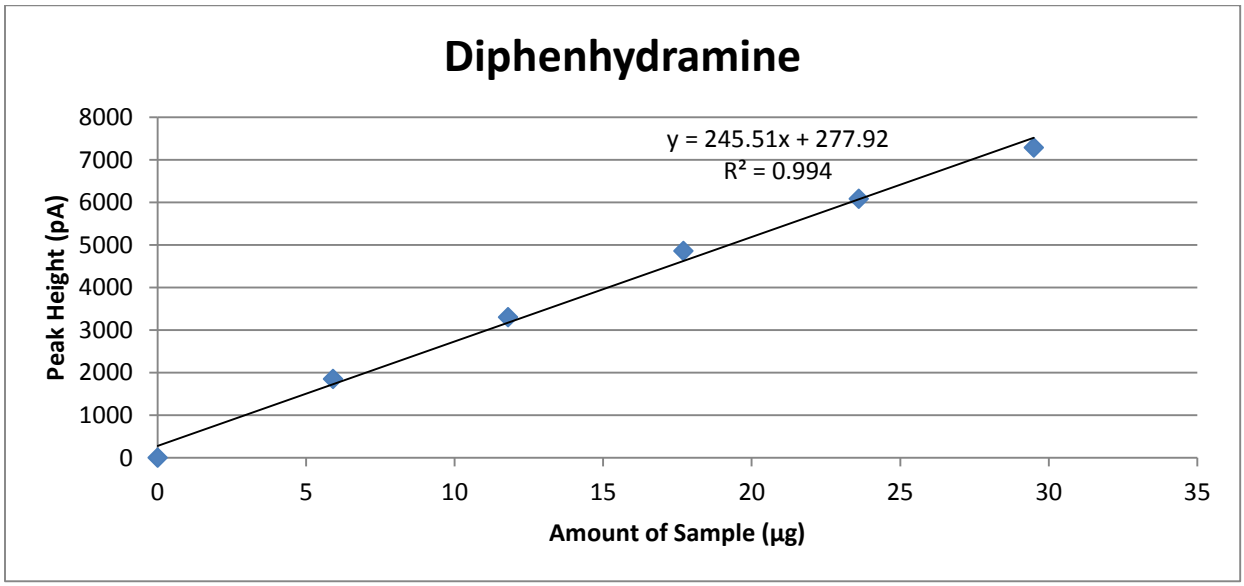

Figure 26. Diphenhydramine Linearity Study

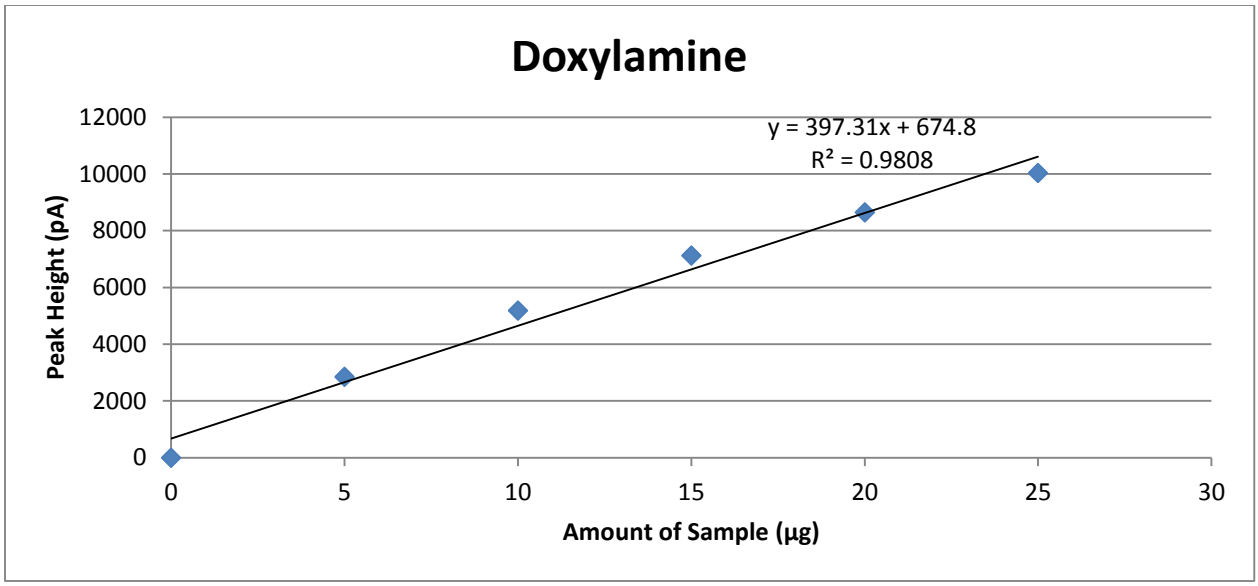

Figure 27. Doxylamine Linearity Study

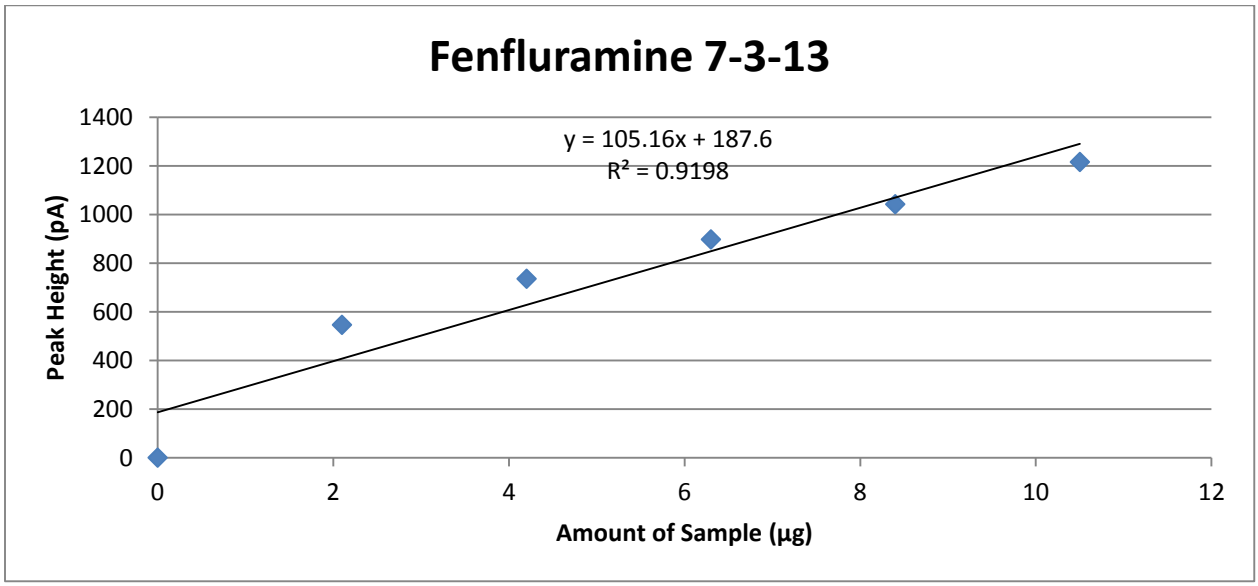

Figure 28. Fenfluramine Linearity Study

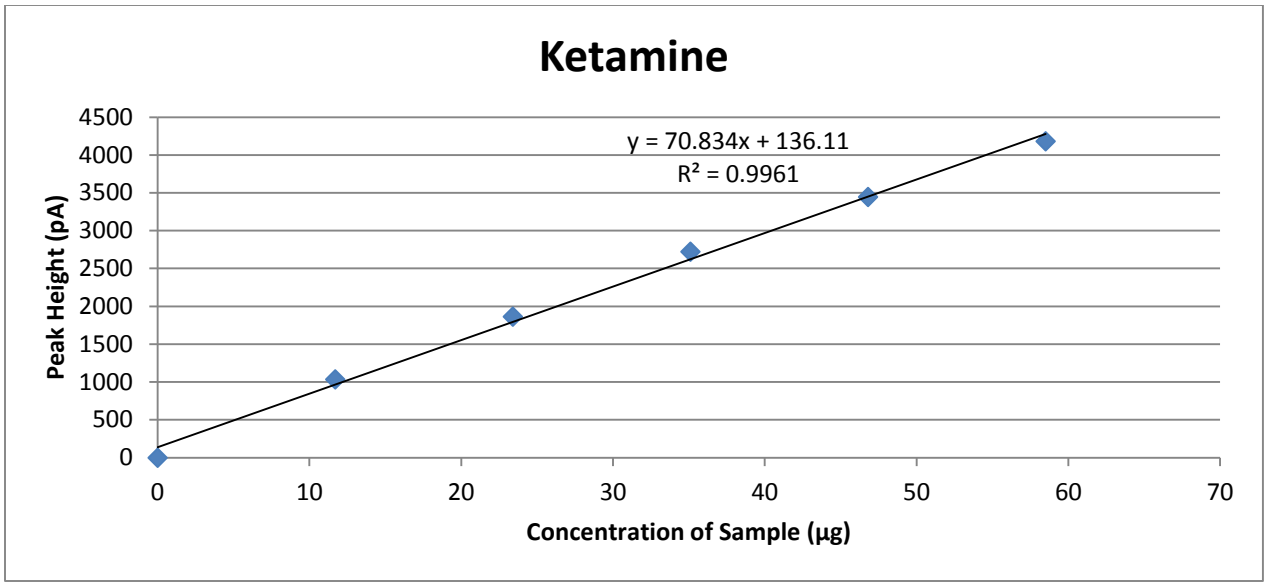

Figure 29. Ketamine Linearity Study

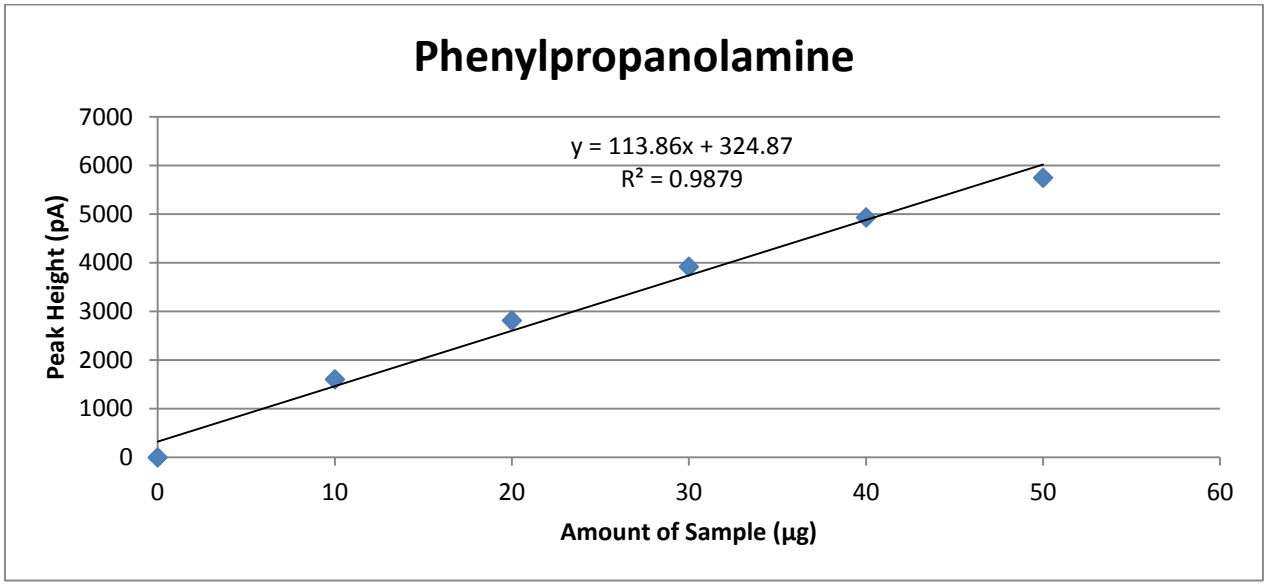

Figure 30. Phenylpropanolamine Linearity Study

Methylenedioxy containing drugs

Three drugs were analyzed that contain a methylenedioxy group: 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxyethylamphetamine (MDEA), and 3,4-methylenedioxymethamphetaime (MDMA). The GC-IR spectra obtained for MDA, MDEA and MDMA are shown in Figures 31-33, respectively. Table 8 shows the bands found in each

spectrum with the standard deviation and relative standard deviation. Figures 34-36 show the linearity study graphs.

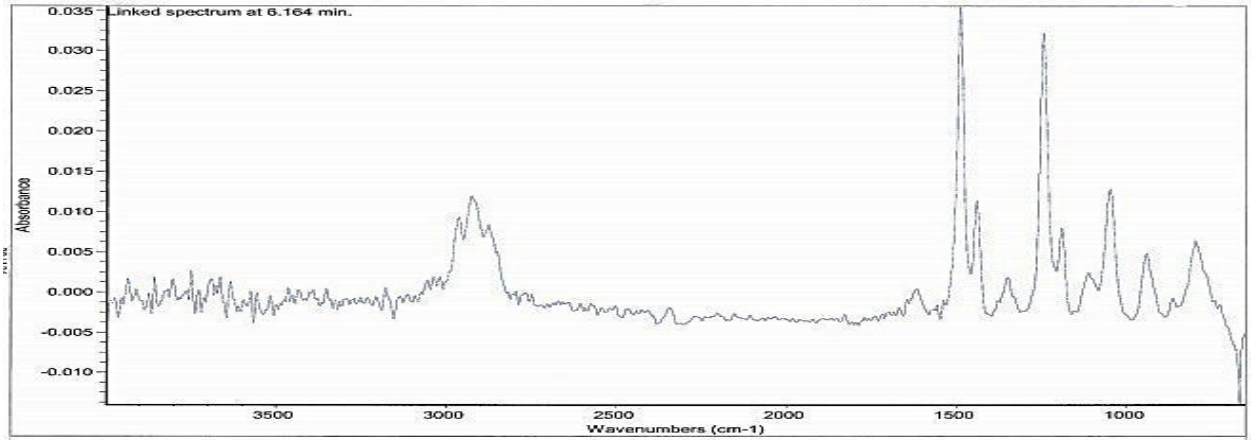

Figure 31. GC-IR spectrum for MDA

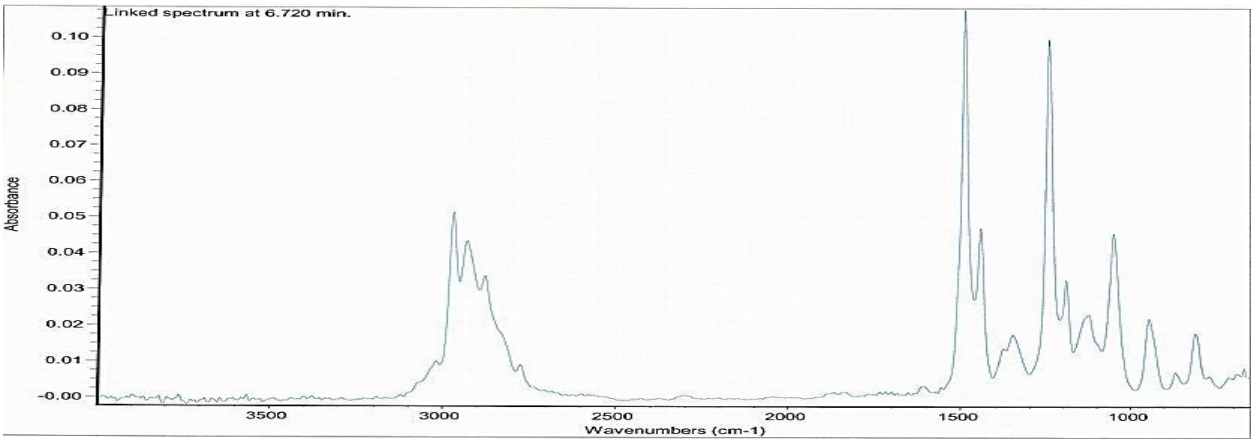

Figure 32. GC-IR spectrum for MDEA

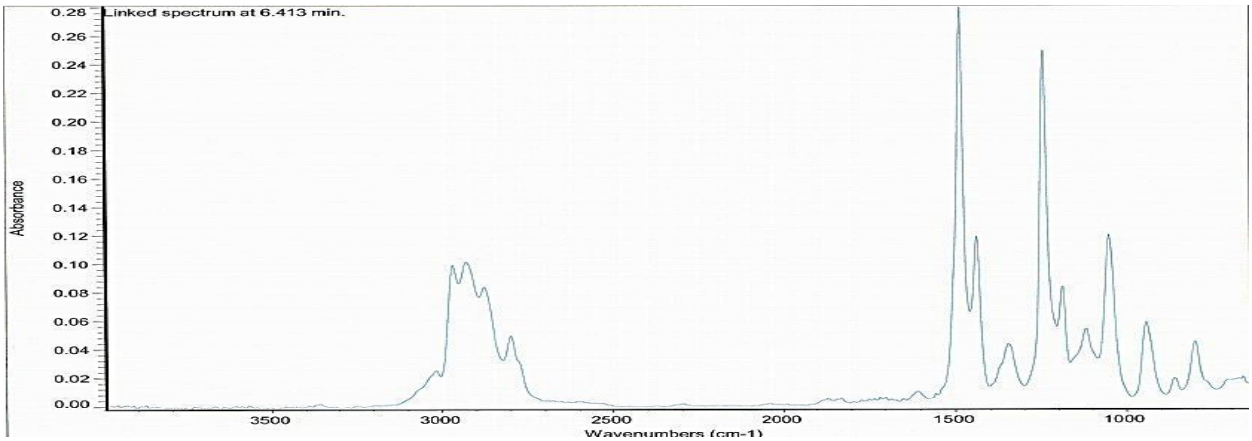

Figure 33. GC-IR spectrum for MDMA

Table 8. Bands found in the GC-IR spectra for MDA, MDEA and MDMA

MDA			MDEA			MDMA		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
2966	2.282	0.07692	2971	0.8338	0.02806	2971	1.462	0.04921
2923	2.053	0.07021	2931	1.364	0.04653	2931	2.825	0.09638
2879	2.655	0.09222	2879	2.725	0.09467	2800	0.7429	0.02653
1618	3.107	0.1920	2775	2.0380	0.07345	1489	0.4531	0.03042
1490	0.6990	0.04692	1489	0.7450	0.05002	1442	0.3275	0.02271
1441	0.4459	0.03094	1442	0.3395	0.02355	1246	0.1328	0.01066
1350	1.165	0.08628	1349	1.206	0.08937	1190	0.4480	0.03765
1246	0.1474	0.01183	1246	0.1092	0.008766	1050	0.3863	0.03681
1191	0.3322	0.02789	1190	1.768	0.1485	943	0.899	0.0954
1050	2.057	0.1959	1128	5.180	0.4593	804	1.26	0.157
943	1.67	0.177	1049	0.6795	0.06475			
797	2.80	0.351	943	2.67	0.283			
			805	1.29	0.160			

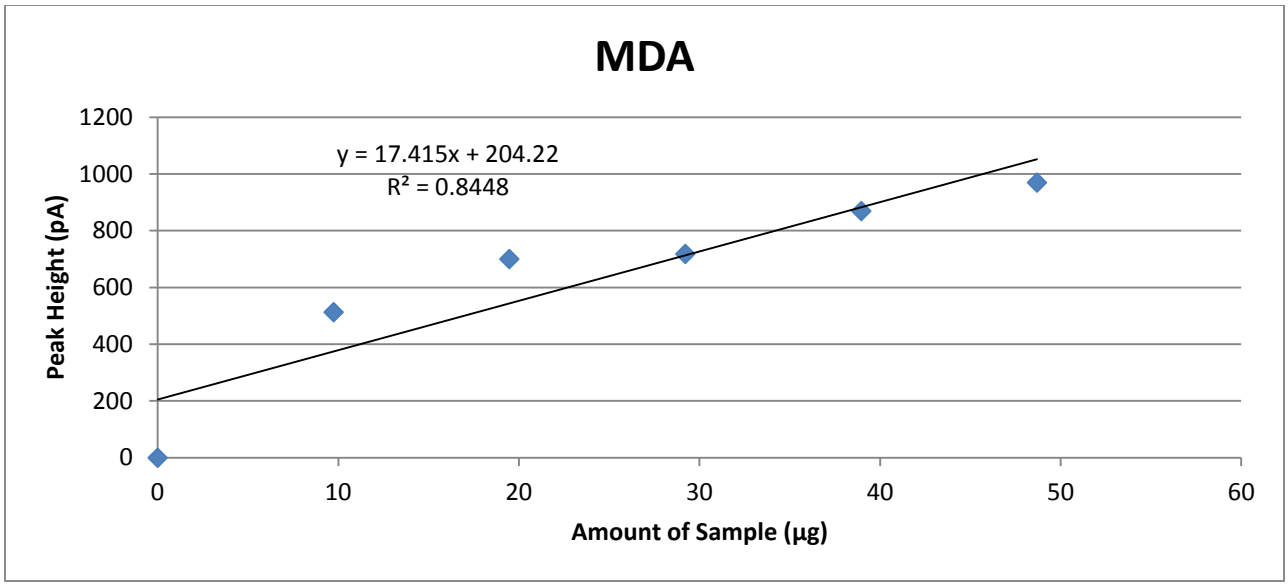

Figure 34. MDA Linearity Study

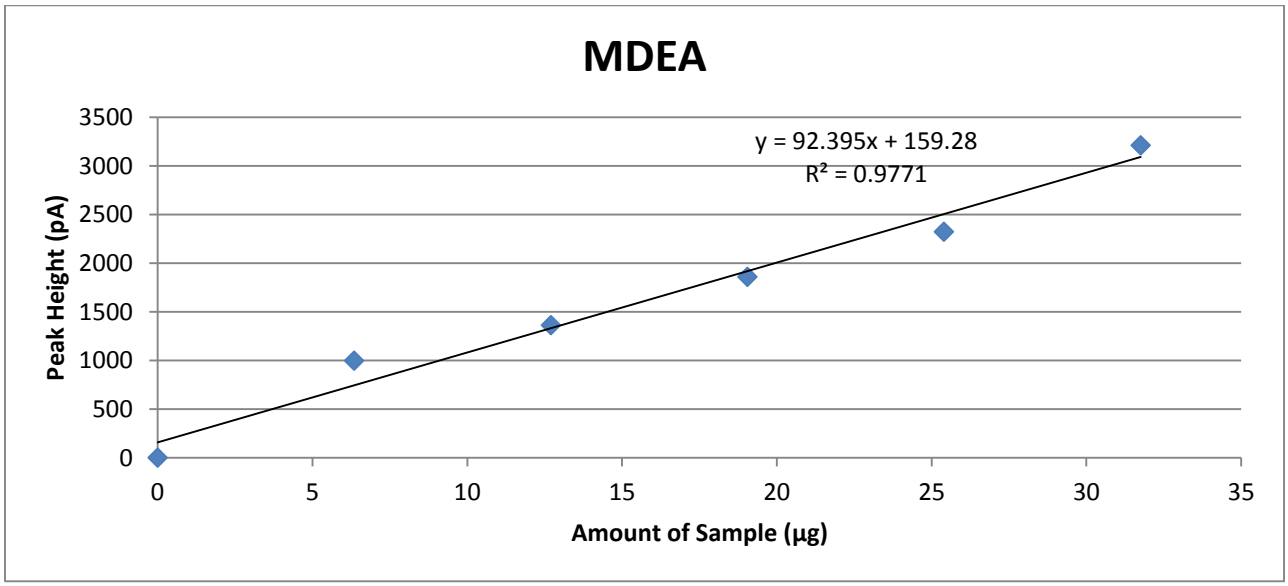

Figure 35. MDEA Linearity Study

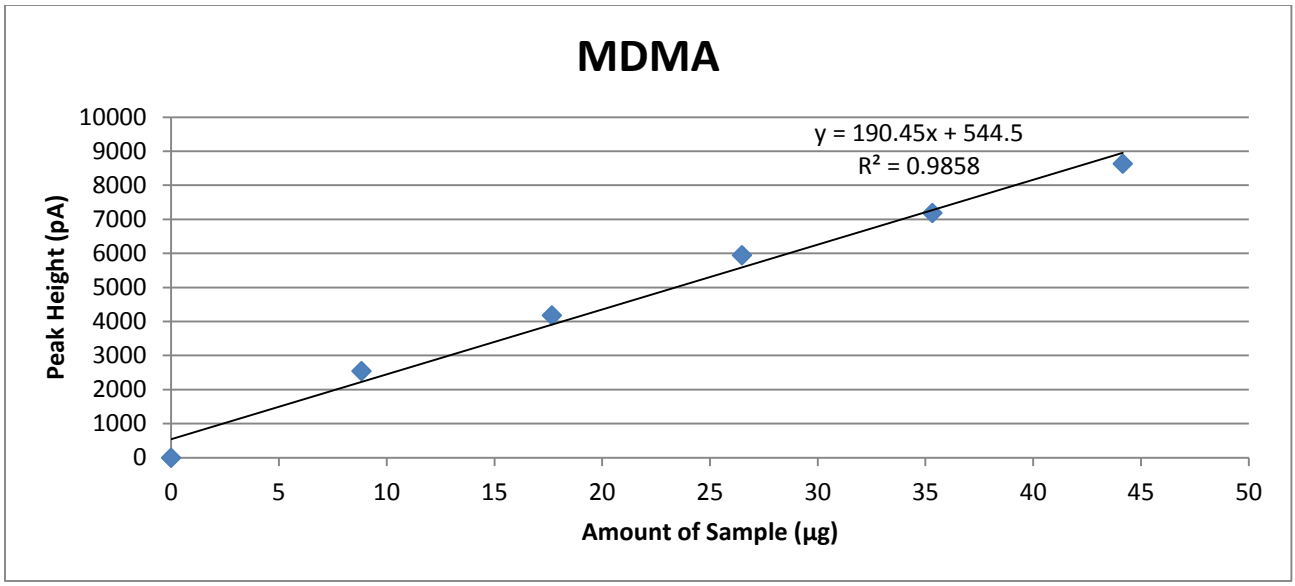

Figure 36. MDMA Linearity Study

Mephentermine and Phentermine

The GC-IR spectra obtained for mephentermine and phentermine are shown in Figures 37 and 38, respectively. Table 9 shows the bands found in each spectrum and the standard deviation and relative standard deviation. Figures 39 and 40 show the linearity study graphs.

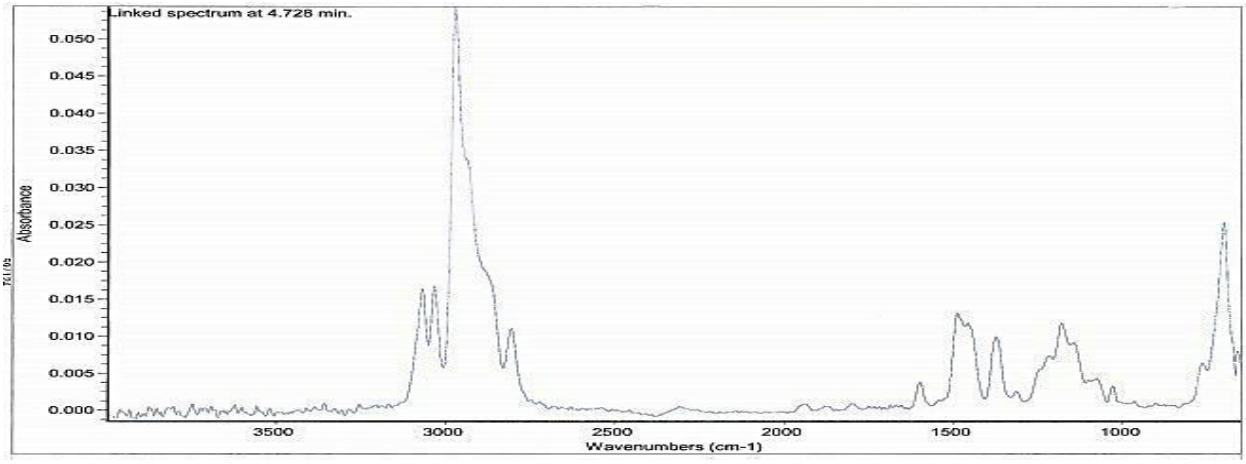

Figure 37. GC-IR spectrum for Mephentermine

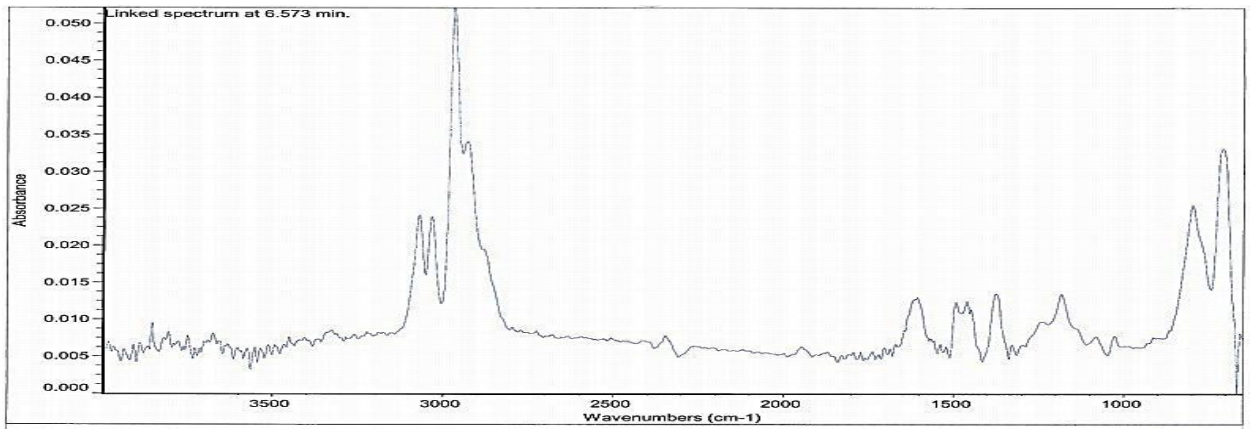

Figure 38. GC-IR Spectrum for Phentermine

Table 9. Bands found in the GC-IR spectra for Mephentermine and Phentermine

Mephentermine			Phentermine		
Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)	Mean (cm^{-1})	STDEV (cm^{-1})	RSD (%)
3070	2.368	0.07713	3073	3.526	0.1148
3033	1.339	0.04415	3033	1.159	0.03820
2971	1.717	0.05777	2968	1.226	0.04131
2808	0.7939	0.02828	2930	2.211	0.07548
1491	2.113	0.1418	1613	6.462	0.4005
1374	2.382	0.1733	1494	2.176	0.1457
1182	2.189	0.1852	1460	3.539	0.2424
767	4.31	0.562	1376	3.545	0.2577
702	0.674	0.0960	1182	3.515	0.2972
			800	1.87	0.234
			712	3.47	0.488

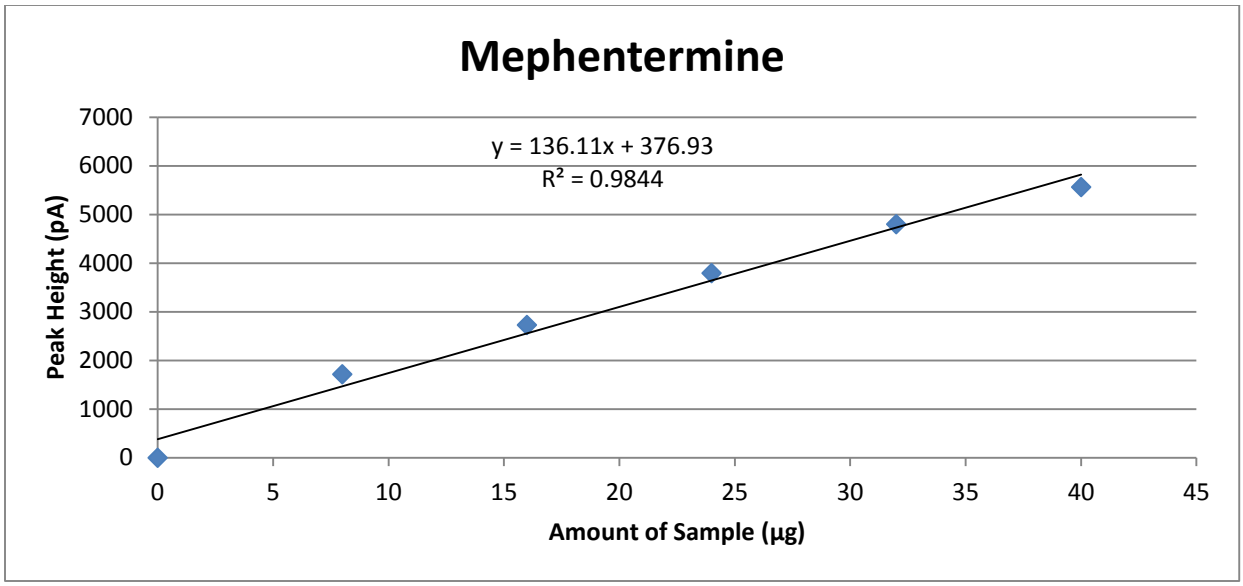

Figure 39. Mephentermine Linearity Study

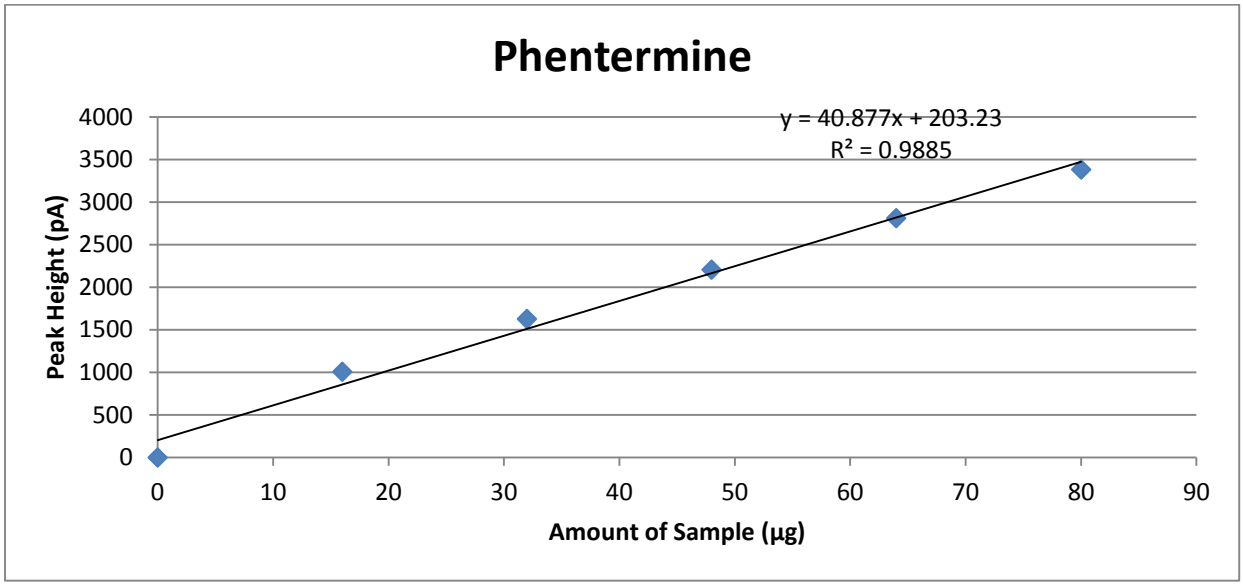

Figure 40. Phentermine Linearity Study

Methcathinone Study

Methcathinones containing a pyrrolidine ring

Seven methcathinone analogs containing a pyrrolidine ring were analyzed: n-methyl-α-pyrrolidinopropiophenone (PPP), 4-methoxy-α-PPP, α-PPP, 3,4-methylendioxy-α-PPP and MDPV. The mass spectra obtained for these drugs are shown in Figures 41-47 and the bands of interest are shown in Table 10. The GC-IR spectra are shown in Figures 48-54. Table 11 shows the bands found in each spectrum. The retention times for both the GC-MS and the GC-IR analyses are shown in Table 12.

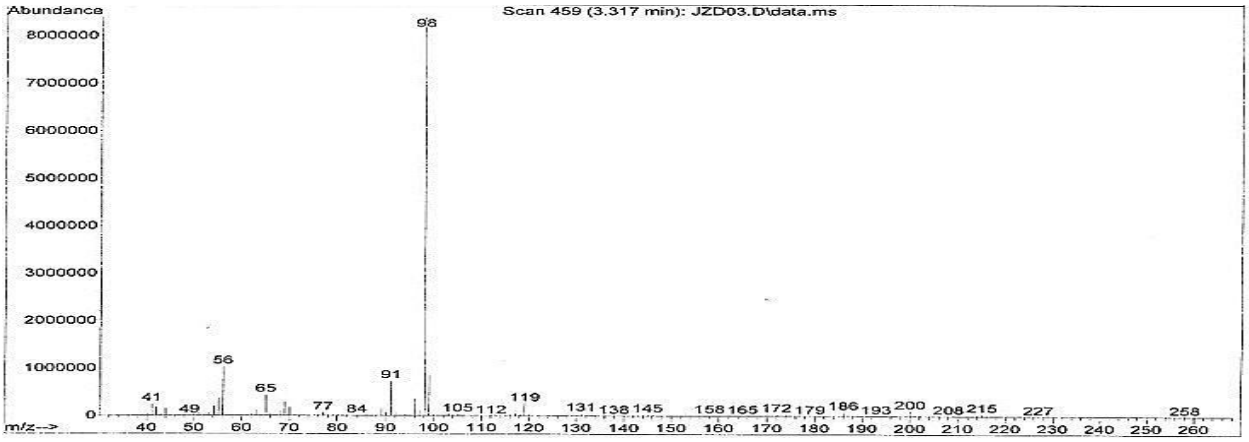

Figure 41. Mass spectrum for 2-methyl-a-PPP

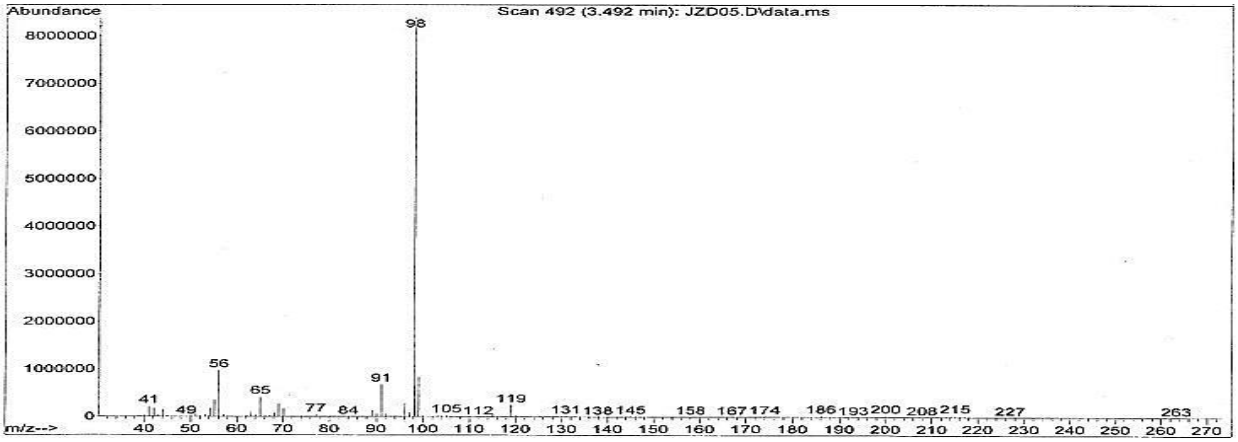

Figure 42. Mass spectrum for 3-methyl-a-PPP

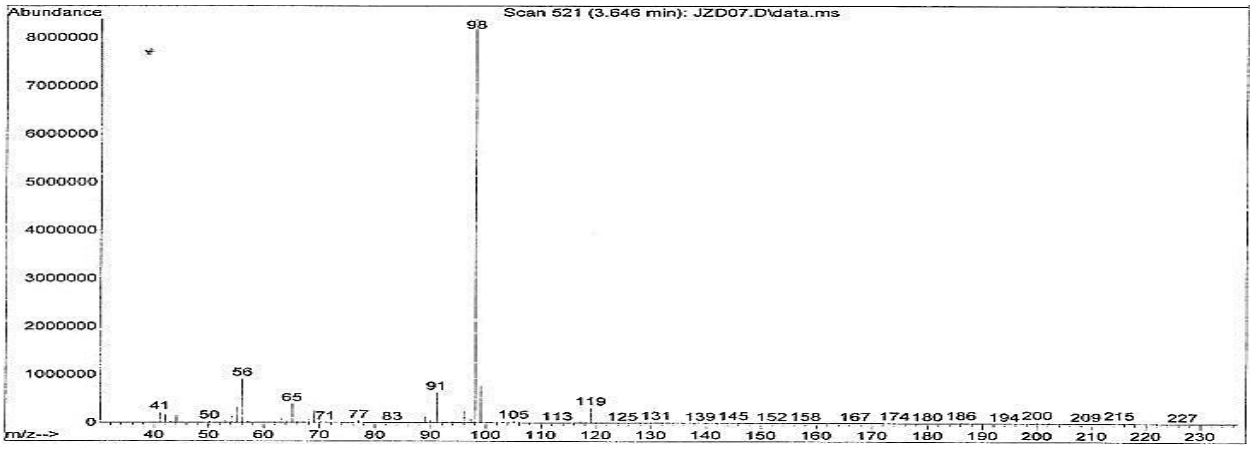

Figure 43. Mass spectrum for 4-methyl-a-PPP

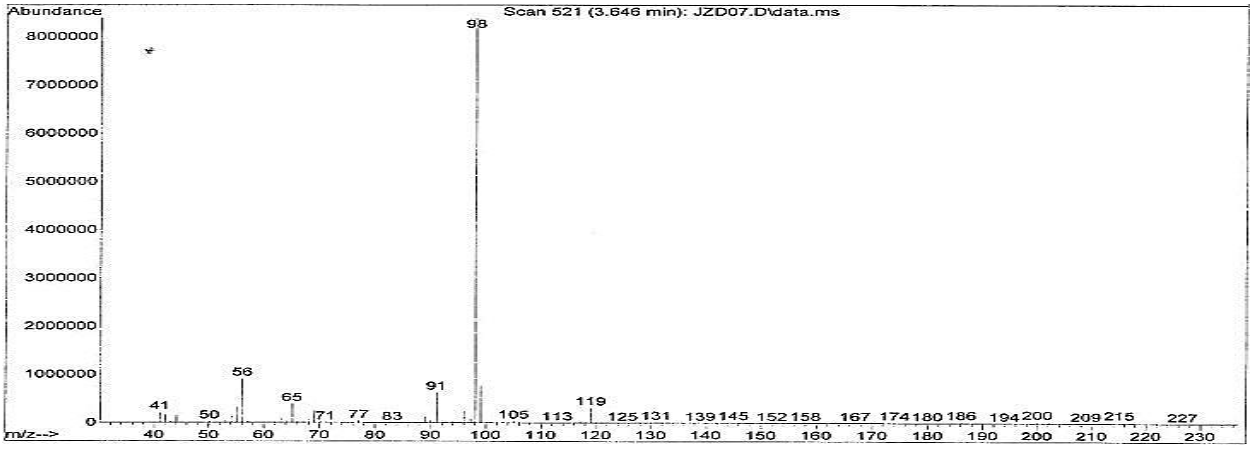

Figure 44. Mass spectrum for 4-methoxy-a-PPP

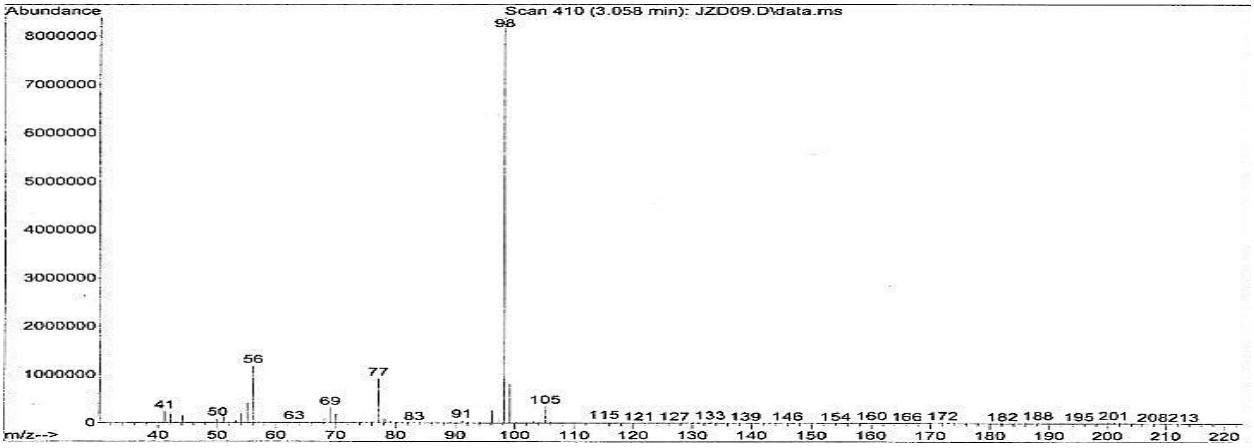

Figure 45. Mass spectrum for a-PPP

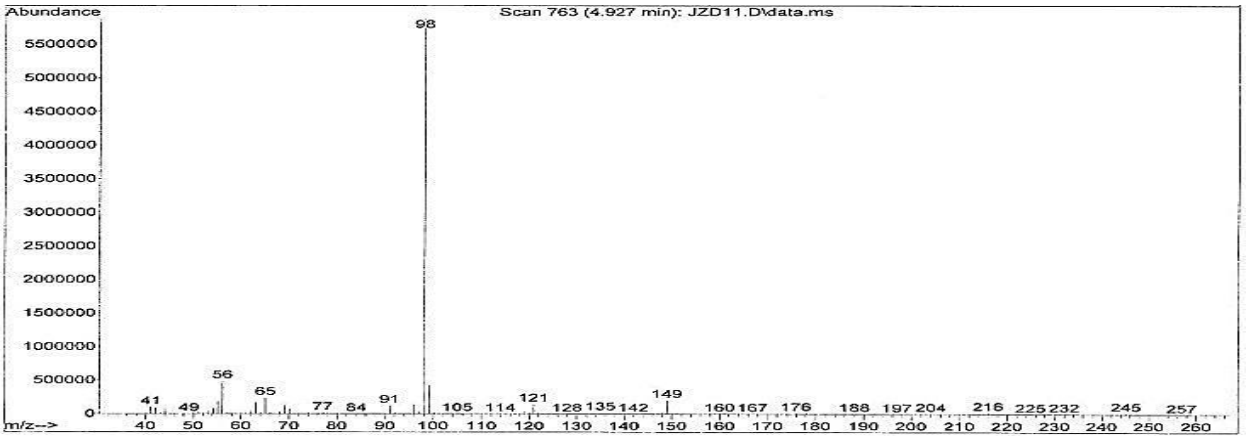

Figure 46. Mass spectrum for 3,4-methylenedioxy-a-PPP

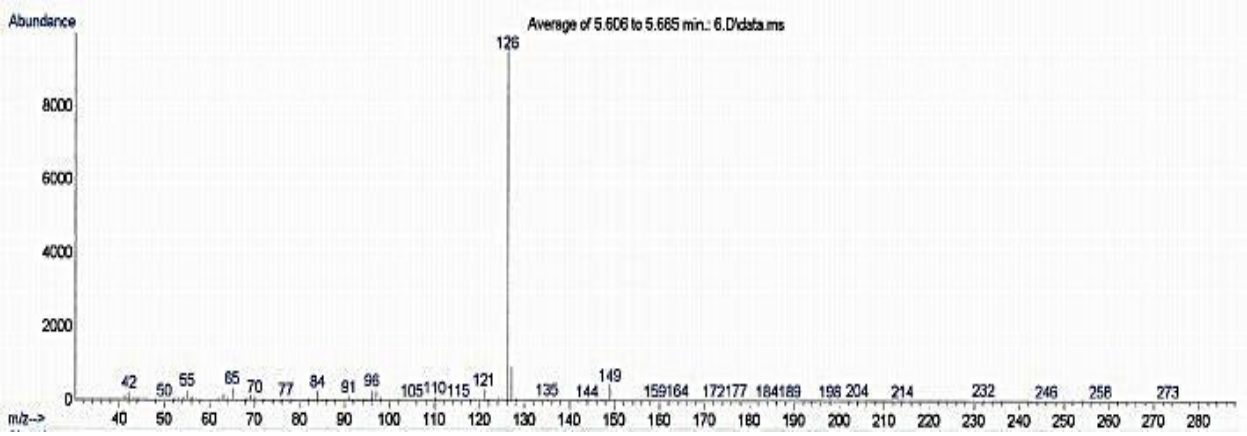

Figure 47. Mass spectrum for MDPV

Table 10. Peaks of interest found in the mass spectra for the analogs containing the pyrrolidine ring (the bolded numbers represent the base peak)

2-methyl – α-PPP	3-methyl- α-PPP	4-methyl- α-PPP	α -PPP	4-methoxy- α-PPP	3,4-methylenedioxy- α-PPP	MDPV
41	41	41	41	41	41	42
56	56	56	56	56	56	55
65	65	65	69	69	65	65
91	91	91	77	77	91	84
98*	**98***	**98***	**98***	91	**98***	121
119	119	119	105	**98***	121	**126***
186	186	186		135	149	149
200	200	200				
m/z						

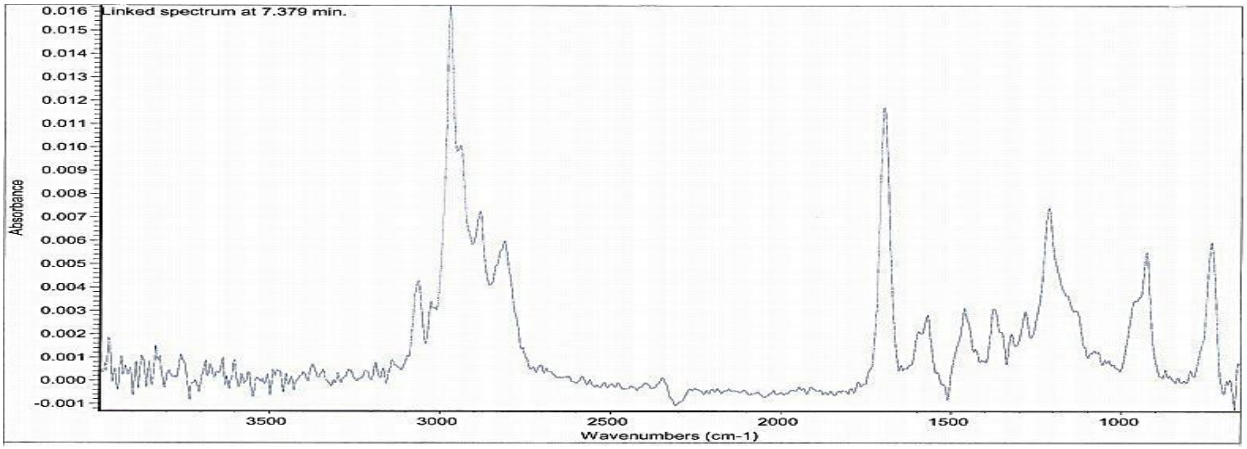

Figure 48. GC-IR spectra for 2-methyl-α-PPP

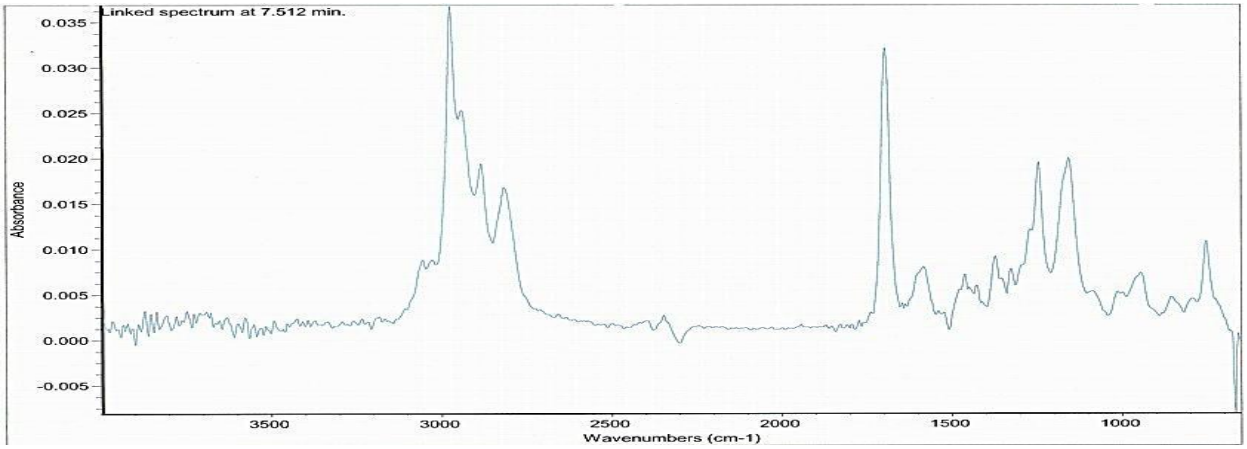

Figure 49. GC-IR spectrum for 3-methyl-α-PPP

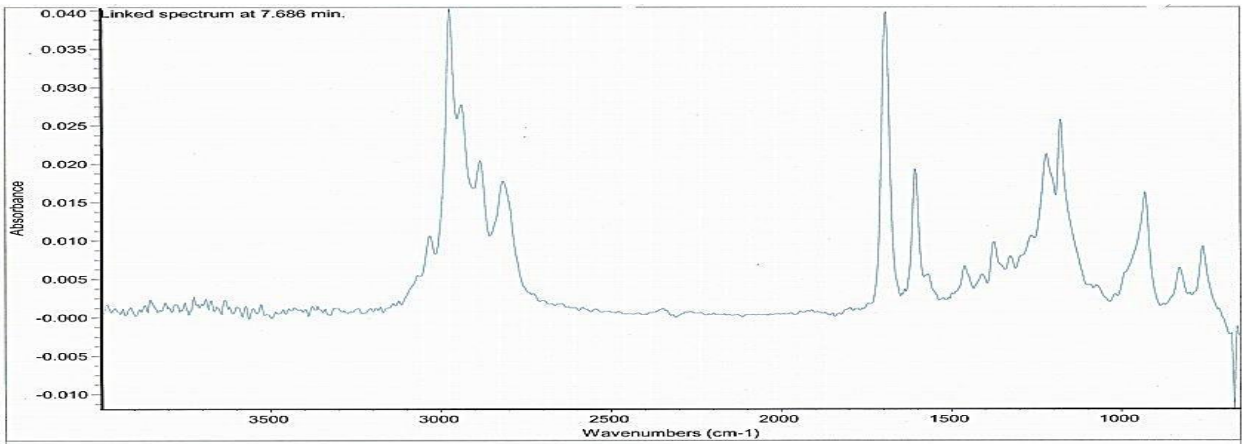

Figure 50. GC-IR spectrum for 4-methyl-α-PPP

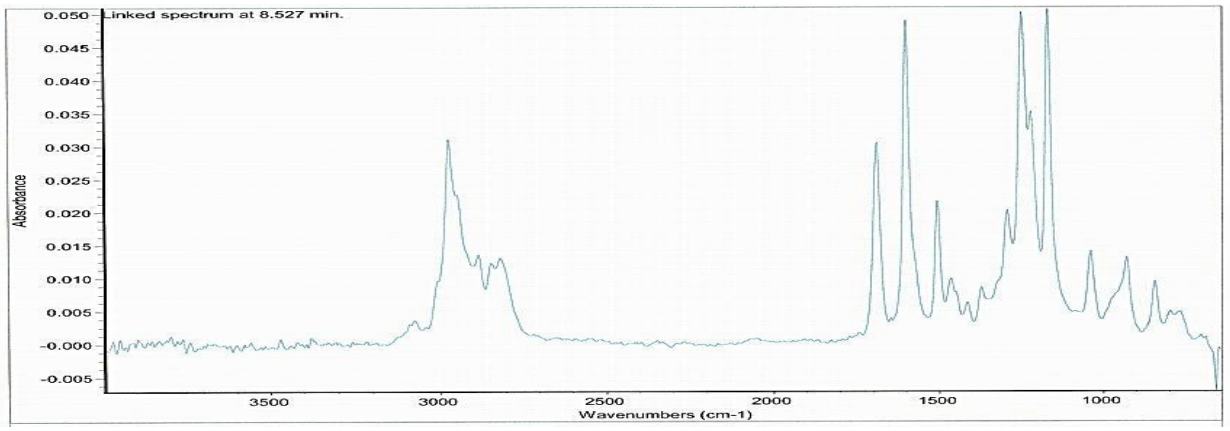

Figure 51. GC-IR spectrum for 4-methoxy-α-PPP

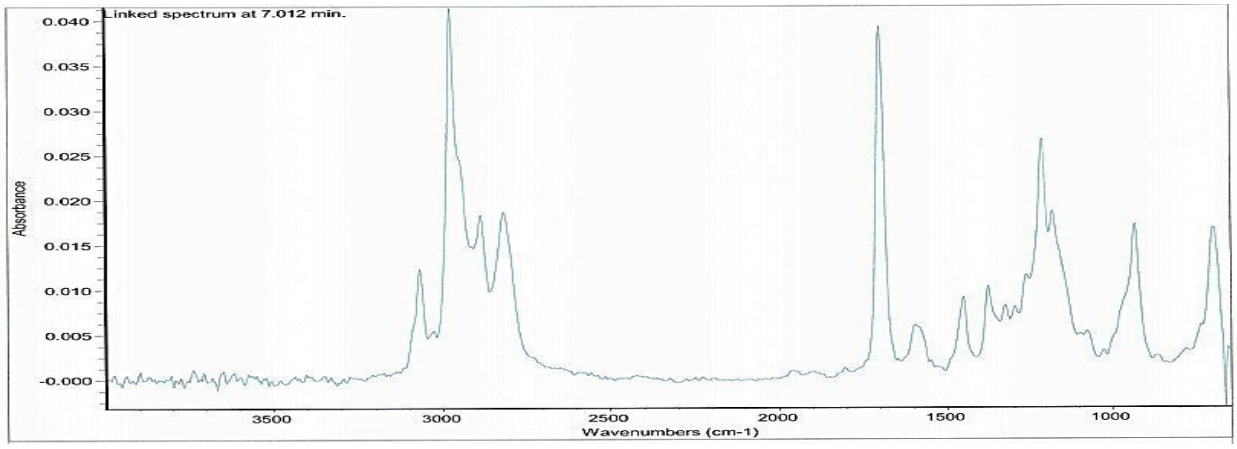

Figure 52. GC-IR spectrum for α-PPP

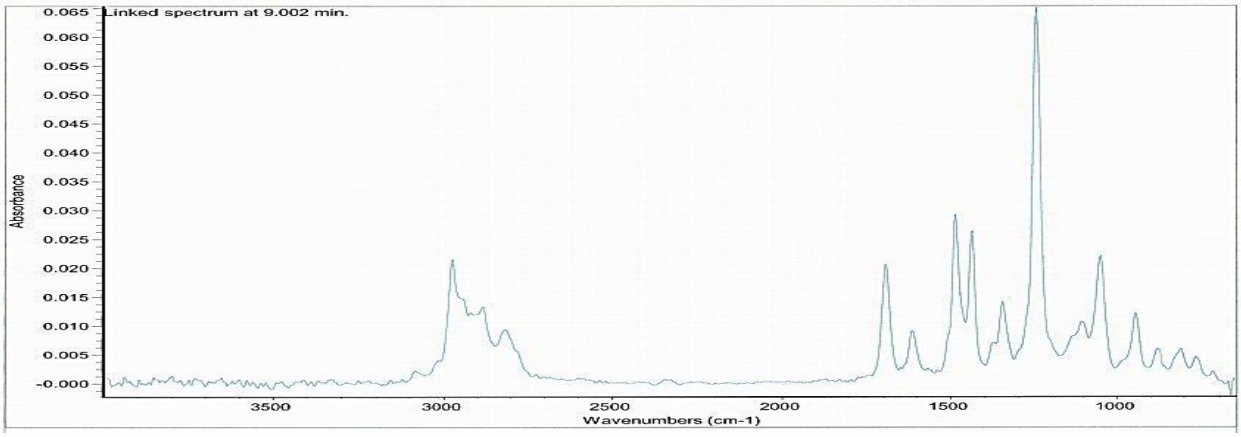

Figure 53. GC-IR spectrum for 3,4-methylenedioxy-α-PPP

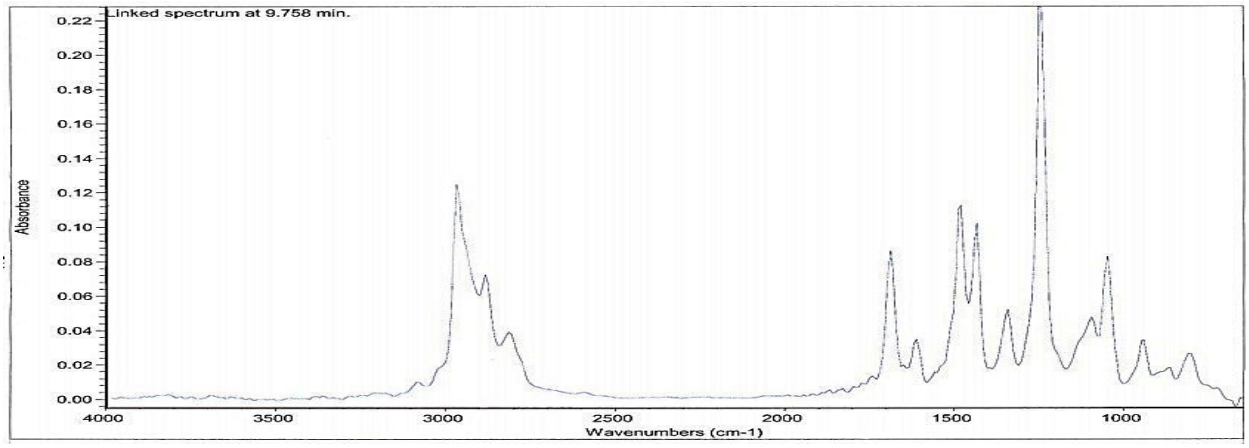

Figure 54. The GC-IR spectrum for MDPV

Table 11. The characteristic bands found in IR spectra for the analogs containing the pyrrolidine ring (W, M, and S represent weak, medium and strong, respectively)

2-methyl-α-PPP	3-methyl-α-PPP	4-methyl-α-PPP	α -PPP	4-methoxy-α-PPP	3,4-methylenedioxy-α-PPP	MDPV
3066 (W)	3056 (W)	3033 (W)	3070 (W)	3077 (W)	2973 (M)	2967 (M)
3024 (W)	3027 (W)	2973 (S)	2974 (S)	2972 (S)	2885 (W)	2884 (W)
2973 (S)	2973 (S)	2929 (M)	2885 (M)	2885 (M)	2817 (W)	2817 (W)
2884 (M)	2941	2885 (M)	2815 (M)	2845 (M)	1690 (M)	1689 (M)
2816 (M)	2884 (M)	2818 (M)	1697 (S)	2818 (M)	1614 (W)	1613 (W)
1699 (S)	2817 (M)	1694 (S)	1595 (W)	1690 (S)	1485 (M)	1484 (M)
1574 (W)	1696 (S)	1607 (M)	1449 (W)	1600 (S)	1436 (M)	1436 (M)
1215 (M)	1246 (M)	1220 (M)	1374 (W)	1505 (M)	1346 (W)	1344 (W)
927 (M)	1156 (M)	1179 (M)	1326 (W)	1464 (W)	1245 (S)	1245 (S)
736 (M)	945 (W)	929 (M)	1297 (W)	1373 (W)	1103 (W)	1095 (W)
	753 (M)	829 (W)	1261 (W)	1296 (M)	1049 (M)	1049 (M)
		760 (W)	1214 (M)	1252 (S)	944 (W)	944 (W)
			1178 (M)	1169 (S)	878 (W)	806 (W)
			929 (M)	1038 (M)	808 (W)	
			704 (M)	929 (M)	769 (W)	
				842 (W)		
				798 (W)		
				775 (W)		
cm^{-1}						

Table 12. Retention times for the analogs containing the pyrrolidine ring for both GC-MS and GC-IR analyses

	2-methyl-α-PPP	3-methyl-α-PPP	4-methyl-α-PPP	α-PPP	4-methoxy-α-PPP	3,4-methylenedioxy-α-PPP	MDPV
GC-MS	3.3	3.5	3.6	3.1	4.5	4.9	5.6
GC-IR	7.4	7.6	7.8	7.1	8.6	9.1	9.8
Minutes							

The GC-IR spectra are more unique than the mass spectra for each of the analogs except for 3,4-methylenedioxy-α-PPP and MDPV. MDPV has a more unique mass spectrum compared to the other six analogs due to the longer aliphatic side chain.

N,n-methylenedioxymethcathinone

The site of modification for the n,n-methylenedioxymethcathinones is the aromatic ring where a methylenedioxy group is attached at two points of the aromatic ring. The mass spectra of 2,3-methylenedioxymethcathinone and 3,4-methylenedioxymethcathinone are shown in Figures 55 and 56, respectively. The peaks of interest from the mass spectra are shown in Table 13. The GC-IR spectra for 2,3-methylenedioxymethcathinone and 3,4-methylenedioxymethcathinone are shown in Figures 57 and 58, respectively. The bands found in the GC-IR spectra are shown in Table 14. The retention times from the GC-MS and GC-IR analyses are shown in Table 15.

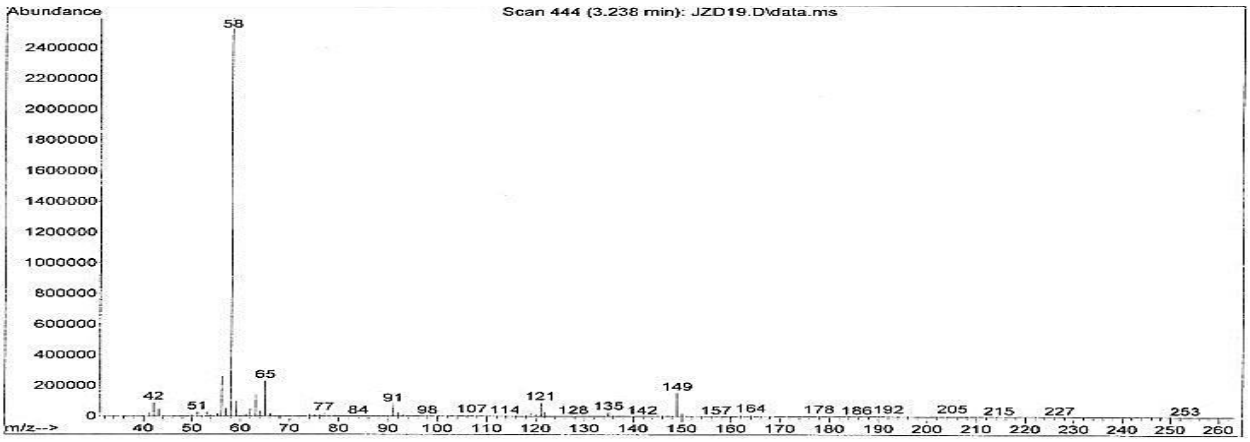

Figure 55. Mass spectrum for 2,3-methylenedioxymethcathinone

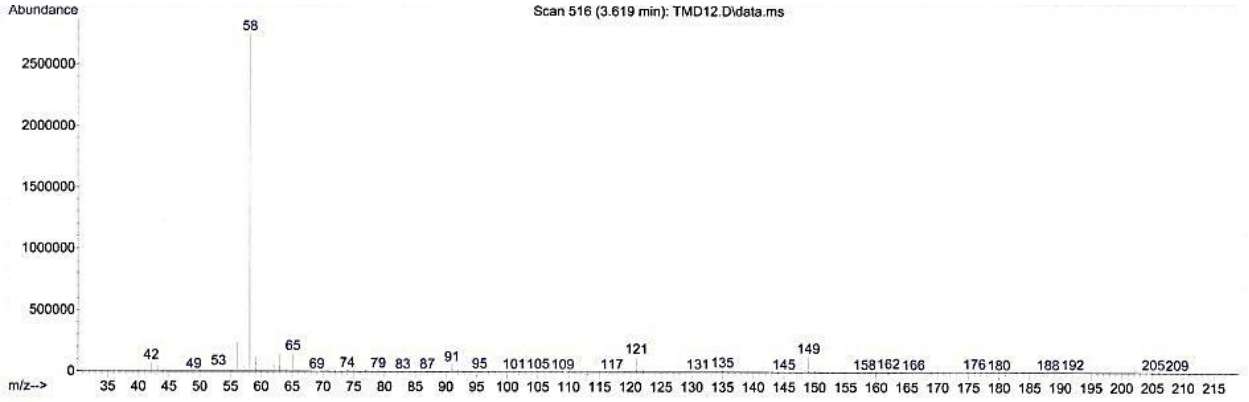

Figure 56. Mass spectrum for 3,4-methylenedioxymethcathinone

Table 13. Peaks of interest found in the mass spectra for 2,3-methylenedioxymethcathinone and 3,4-methylenedioxymethcathinone (the bolded numbers represent the base peak)

2,3-methylenedioxymethcathinone	3,4-methylenedioxymethcathinone
42	42
58*	**58***
65	65
91	91
121	121
149	149
m/z	

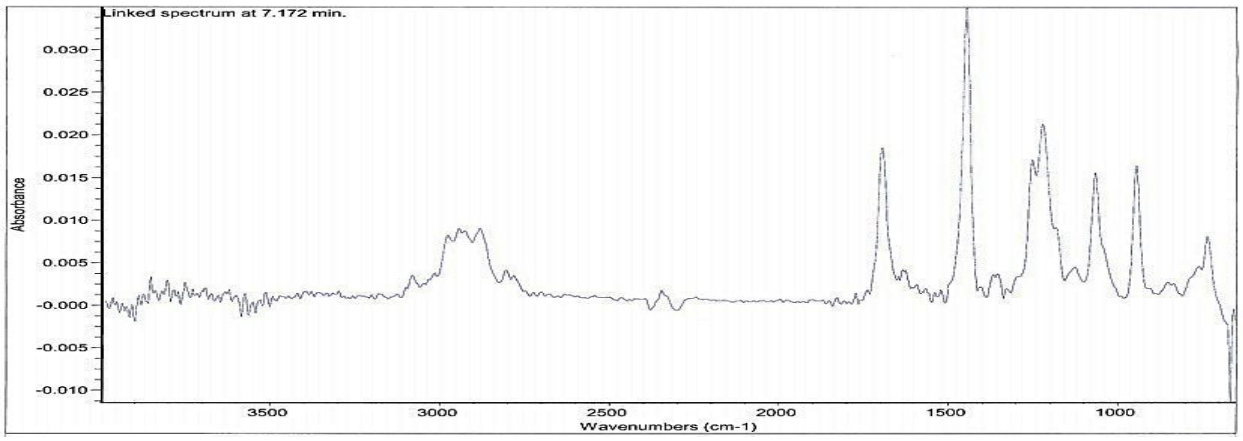

Figure 57. GC-IR spectrum for 2,3-methylenedioxymethcathinone

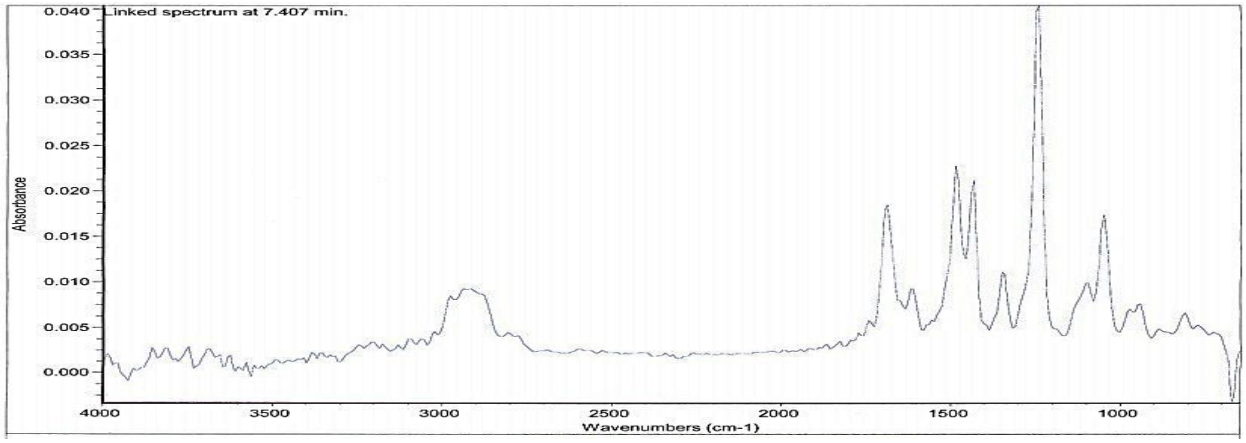

Figure 58. GC-IR spectrum for 3,4-methylenedioxymethcathinone

Table 14. Characteristic bands for 3,4-methylenedioxy-α-PPP and MDPV (W, M and S represent weak, medium and strong, respectively)

2,3-methylenedioxymethcathinone	3,4-methylenedioxymethcathinone
3082 (W)	3024 (W)
2978 (W)	2977 (W)
2945 (W)	2937 (W)
2883(W)	2807 (W)
2806 (W)	1691 (M)
1697 (M)	1615 (W)
1635 (W)	1486 (M)
1448 (S)	1437 (M)
1355 (W)	1346 (W)
1253 (M)	1245 (S)
1223 (S)	1098 (W)
1067 (M)	1050 (M)
946 (M)	944 (W)
852 (W)	810 (W)
735 (W)	771 (W)
cm^{-1}	

Table 15. Retention times for the methylenedioxymethcathinone analogs for the GC-MS and GC-IR analyses

	2,3-methylenedioxymethcathinone	3,4-methylenedioxymethcathinone
GC-MS	3.2	3.6
GC-IR	7.3	7.5
Minutes		

Miscellaneous Methcathinone Analogs

The miscellaneous methcathinone analogs that were analyzed include 3,4-dimethylmethcathinone, butylone and pentedrone. The mass spectra obtained for these analogs are shown in Figures 59-61. The peaks of interest found in the mass spectra are shown in Table

16. The GC-IR spectra are shown in Figures 62-64. The bands found in the GC-IR spectra are shown in Table 17. The retention times for the GC-MS and GC-IR analyses are shown in Table 18.

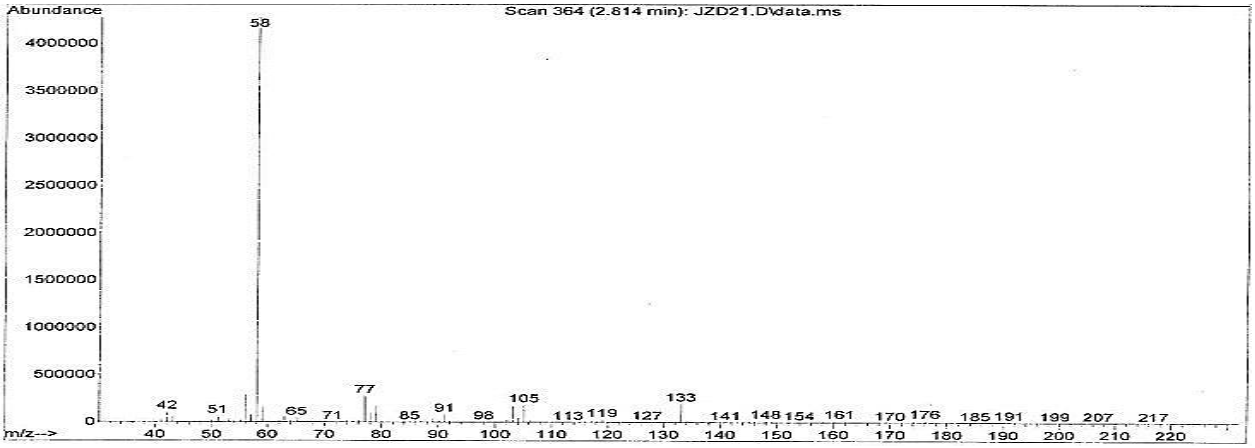

Figure 59. Mass spectrum for 3,4-dimethylmethcathinone

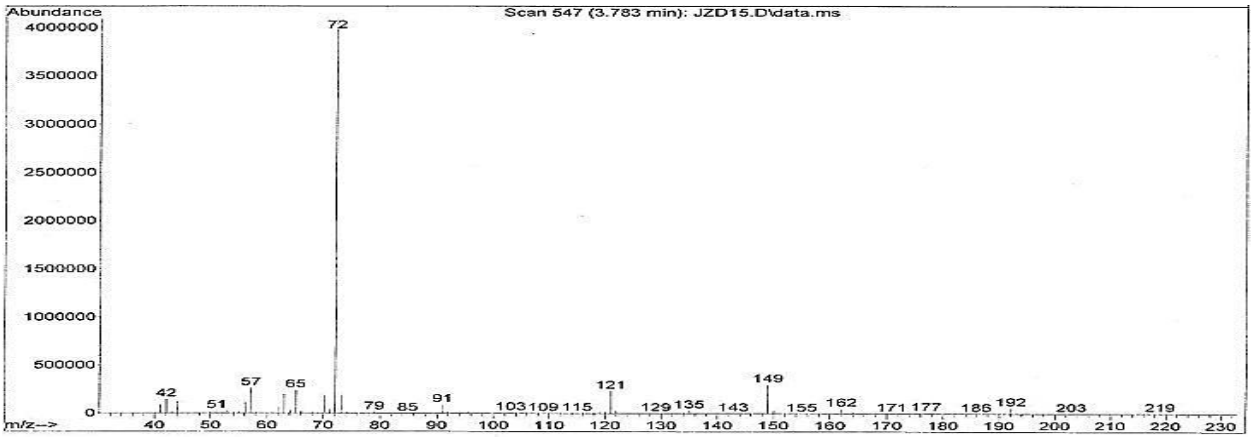

Figure 60. Mass spectrum for Butylone

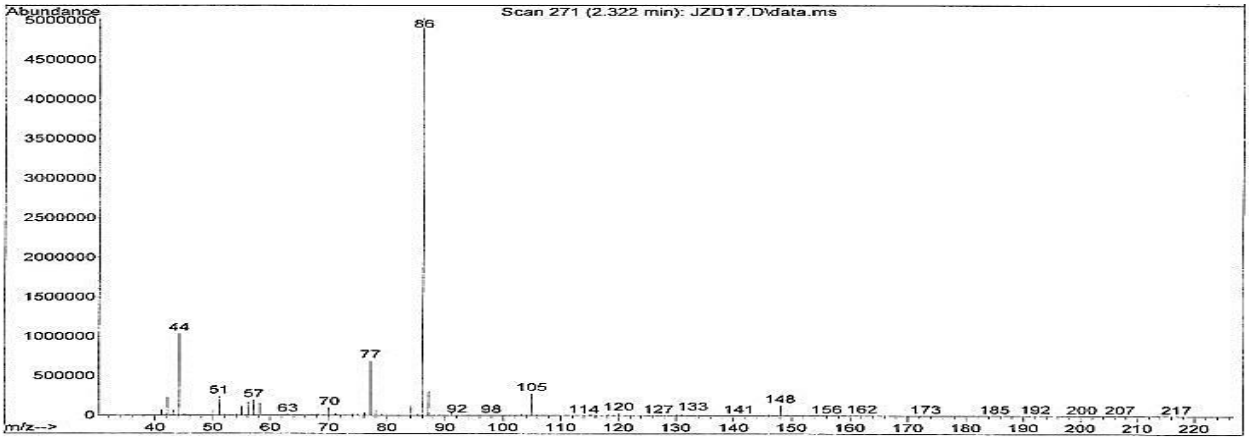

Figure 61. Mass spectrum for Pentedrone

Table 16. The peaks of interest found in the mass spectra for 3,4-dimethylmethcathinone, butylone, and pentedrone (bolded numbers represent the base peak).

3,4-dimethylmethcathinone	Butylone	Pentedrone
42	42	44
58*	57	51
77	65	57
105	**72***	70
133	91	77
	121	**86***
	149	105
	192	148
m/z		

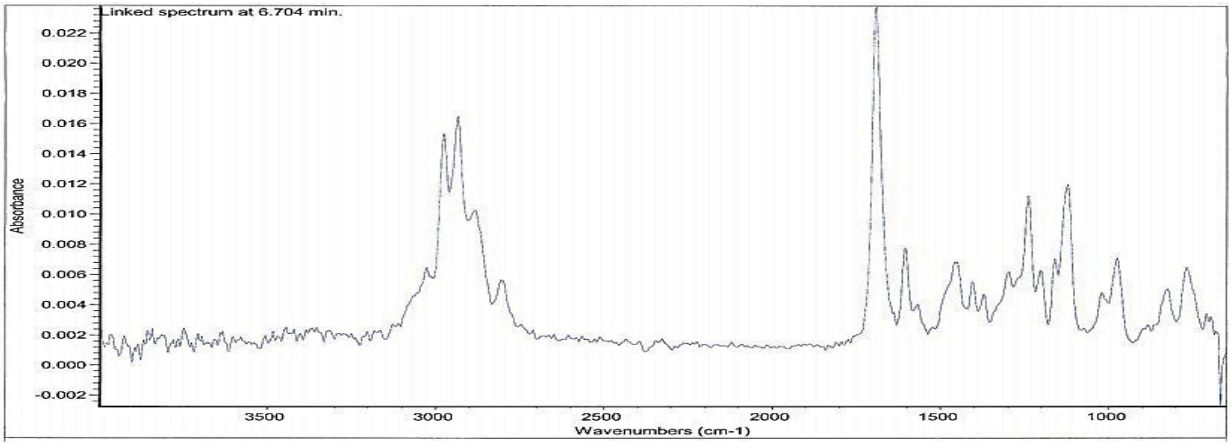

Figure 62. GC-IR spectrum for 3,4-dimethylmethcathinone

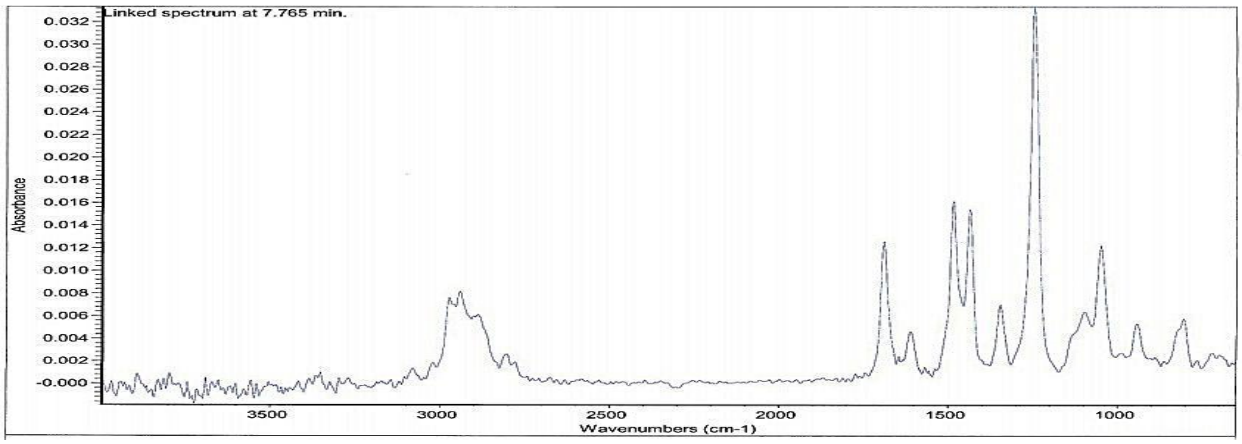

Figure 63. GC-IR spectrum for Butylone

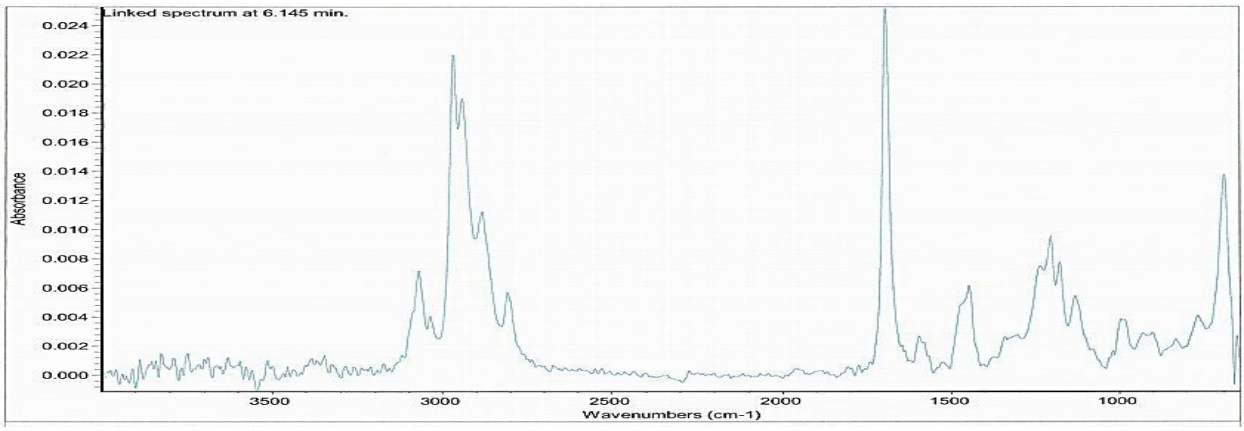

Figure 64. GC-IR spectrum for Pentedrone

Table 17. Characteristic bands for 3,4-dimethylmethcathinone (W, M and S represent weak, medium and strong, respectively)

3,4-dimethylmethcathinone	Pentedrone	Butylone
3025 (W)	3070 (W)	2971 (W)
2978 (S)	3036 (W)	2942 (W)
2936 (S)	2968 (S)	2887 (W)
2884 (M)	2941 (S)	2806 (W)
2805 (W)	2883 (M)	1690 (M)
1694 (S)	2806 (W)	1613 (W)
1606 (M)	1696 (S)	1486 (M)
1568 (W)	1596 (W)	1437 (M)
1460 (W)	1448 (W)	1347 (W)
1299 (W)	1242 (W)	1246 (S)
1240 (M)	1208 (M)	1097 (W)
1160 (M)	1179 (W)	1049 (M)
1124 (M)	1131 (W)	943 (W)
976 (M)	988 (W)	805 (W)
829 (W)	770 (W)	cm^{-1}
767 (W)	697 (M)	
cm^{-1}	cm^{-1}	

Table 18. Retention times for the miscellaneous methcathinones for the GC-MS and GC-IR analyses

	3,4-dimethylmethcathinone	Butylone	Pentedrone
GC-MS	2.8	3.8	2.3
GC-IR	6.8	7.9	6.2
Minutes			

n-methoxymethcathinone

The site of modification for n-methoxymethcathinone is at the aromatic ring where a methoxy group is attached. The mass spectra for 2-methoxymethcathinone, 3-methoxymethcathinone and 4-methoxymethcathinone are shown in Figures 65-67, respectively.

The peaks of interest found in the mass spectra are shown in Table 19. The GC-IR spectra for 2-methoxy, 3-methoxy and 4-methoxy are shown in Figures 68-70, respectively. The bands found in the GC-IR spectra are shown in Table 20. The retention times for the methoxymethcathinones for GC-MS and GC-IR analyses are shown in Table 21.

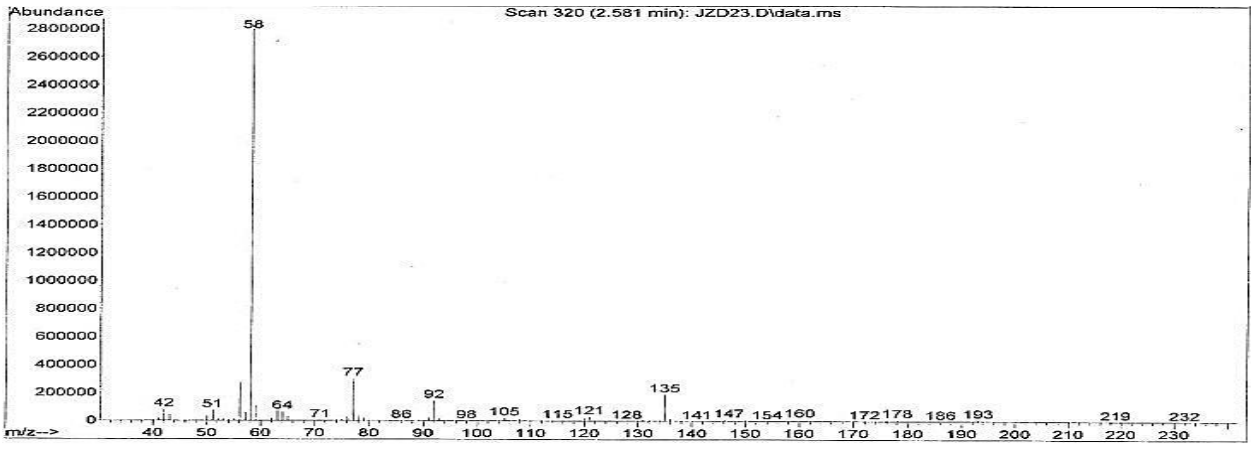

Figure 65. Mass spectrum for 2-methoxymethcathinone

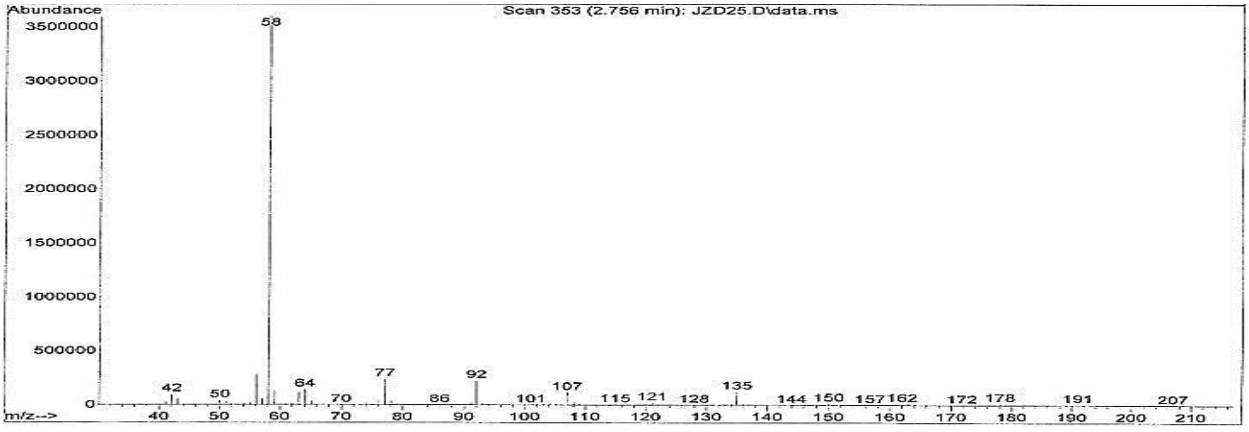

Figure 66. Mass spectrum for 3-methoxymethcathinone

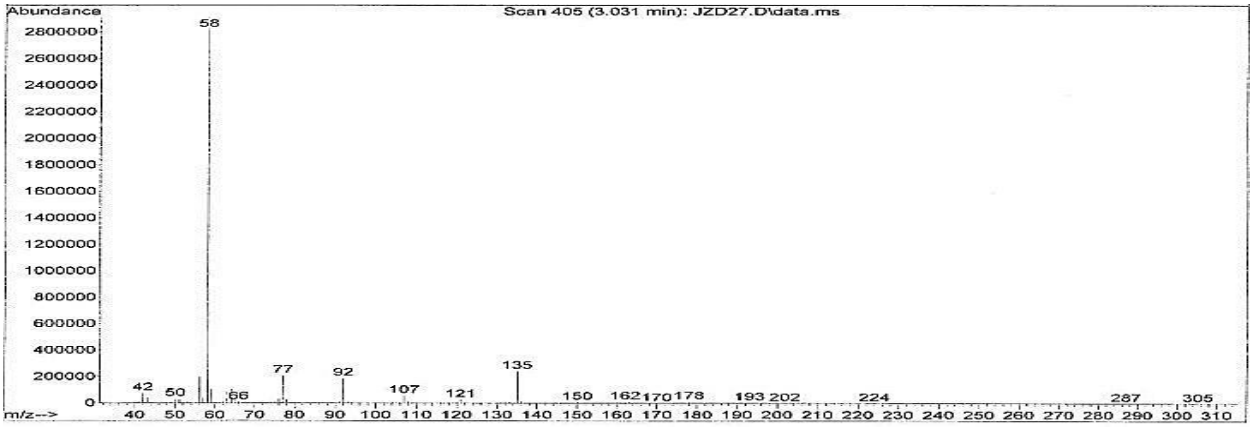

Figure 67. Mass spectrum for 4-methoxymethcathinone

Table 19. Peaks of interest found in the mass spectra for the methoxymethcathinones (bolded numbers represent the base peak)

2-methoxymethcathinone	3-methoxymethcathinone	4-methoxymethcathinone
42	42	42
51	51	50
58	**58**	**58**
77	64	77
92	77	92
121	92	107
135	107	135
	135	
m/z		

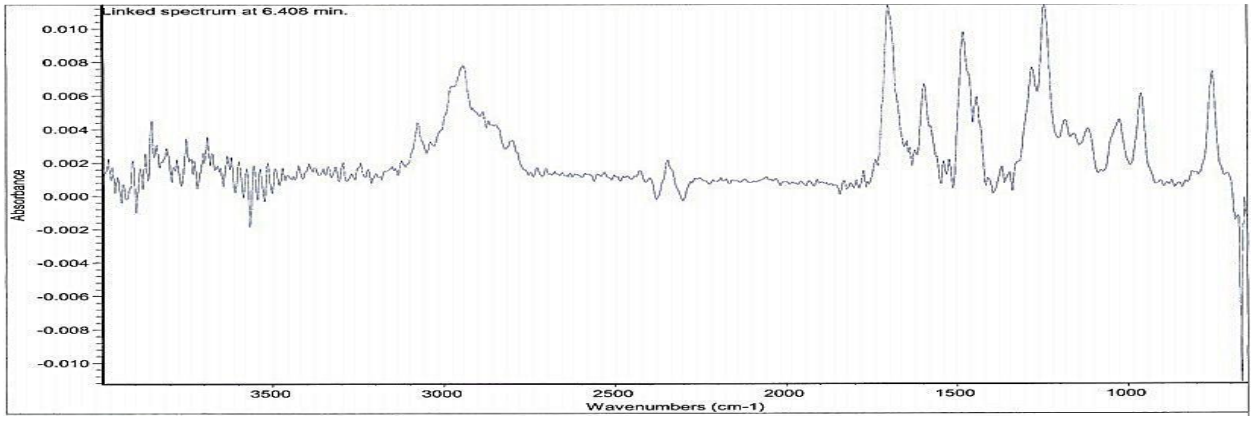

Figure 68. GC-IR spectrum for 2-methoxymethcathinone

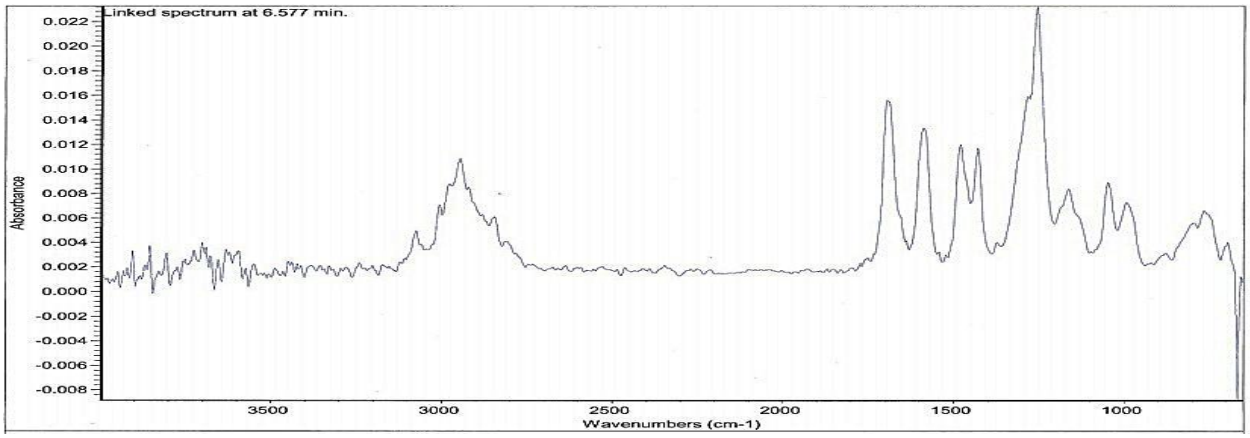

Figure 69. GC-IR spectrum for 3-methoxymethcathinone

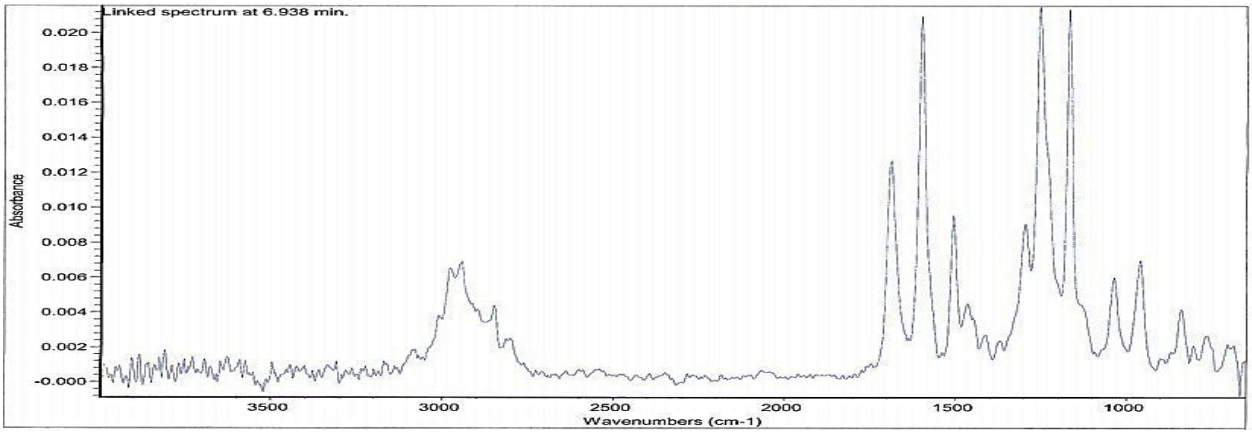

Figure 70. GC-IR spectrum for 4-methoxymethcathinone

Table 20. Characteristic bands for n-methoxymethcathinone (W, M and S represent weak, medium and strong, respectively)

2-methoxymethcathinone	3-methoxymethcathinone	4-methoxymethcathinone
3074 (W)	3077 (W)	3081 (W)
2945 (M)	2977 (M)	2975 (M)
2803 (W)	2948 (M)	2946 (M)
1699 (S)	2808 (W)	2851 (W)
1595 (M)	1698 (M)	2811 (W)
1480 (S)	1588 (M)	1691 (S)
1443 (M)	1480 (M)	1600 (S)
1279 (M)	1429 (M)	1507 (M)
1242 (S)	1258 (S)	1464 (W)
1185 (M)	1166 (W)	1416 (W)
1119 (M)	1048 (M)	1296 (M)
1026 (M)	992 (W)	1253 (S)
961 (M)	764 (W)	1169 (S)
753 (M)		1037 (M)
		960 (M)
		840 (W)
		766 (W)
		701 (W)
cm^{-1}		

Table 21. Retention times for the methoxymethcathinones for the GC-MS and GC-IR analyses

	2-methoxymethcathinone	3-methoxymethcathinone	4-methoxymethcathinone
GC-MS	2.6	2.8	3.0
GC-IR	6.5	6.7	7.0
Minutes			

n-methylmethcathinone

The modification made to create the methylmethcathinones is a methyl group attached to the aromatic ring. The mass spectra of 2-, 3- and 4-methylmethcathinone are shown in Figures

71-73, respectively. The peaks of interest found in the spectra are shown in Table 22. The GC-IR spectra for 2-, 3- and 4-methylmethcathinone are shown in Figures 74-76, respectively. Table 23 shows the bands found in the GC-IR spectra. The retention times for the methylmethcathinones for the GC-MS and GC-IR analyses are shown in Table 24.

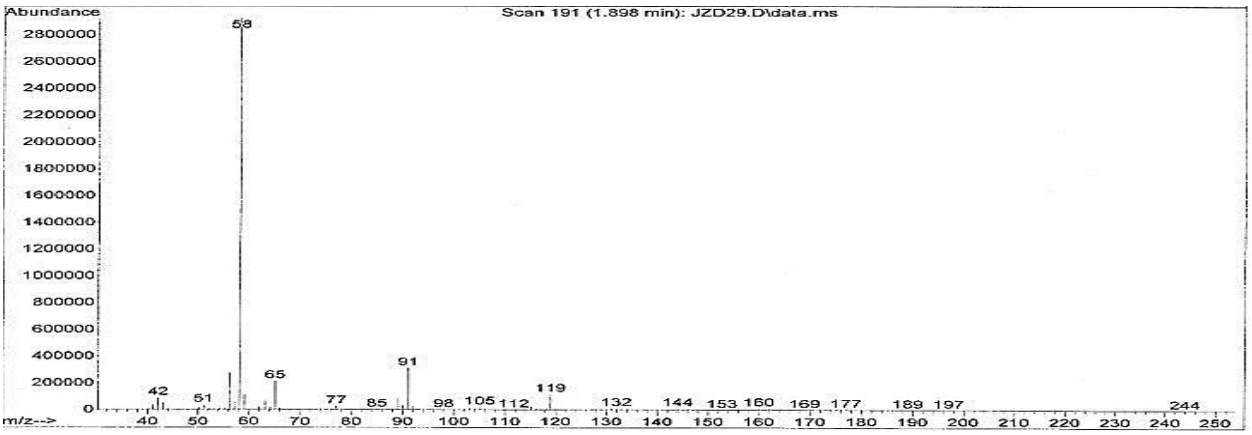

Figure 71. Mass spectrum for 2-methylmethcathinone

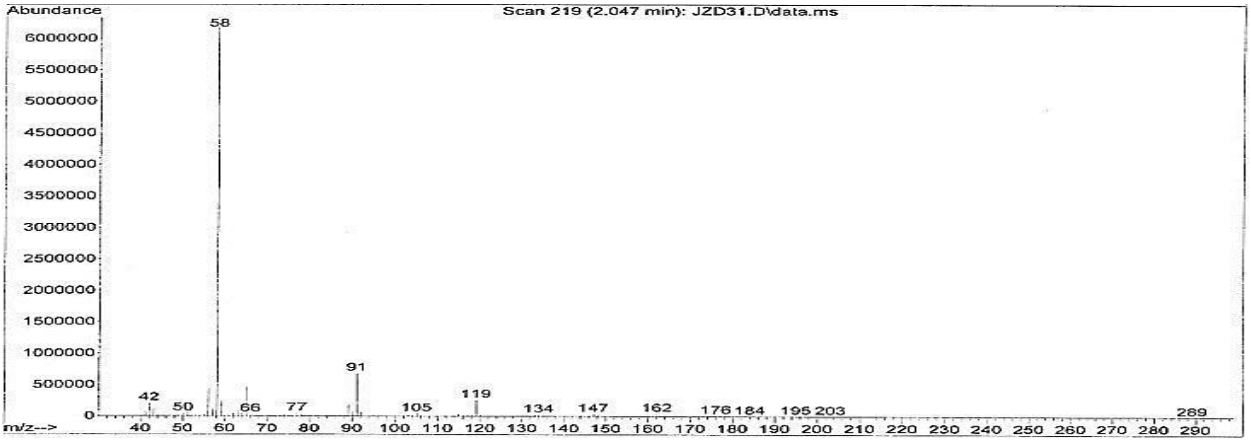

Figure 72. Mass spectrum for 3-methylmethcathinone

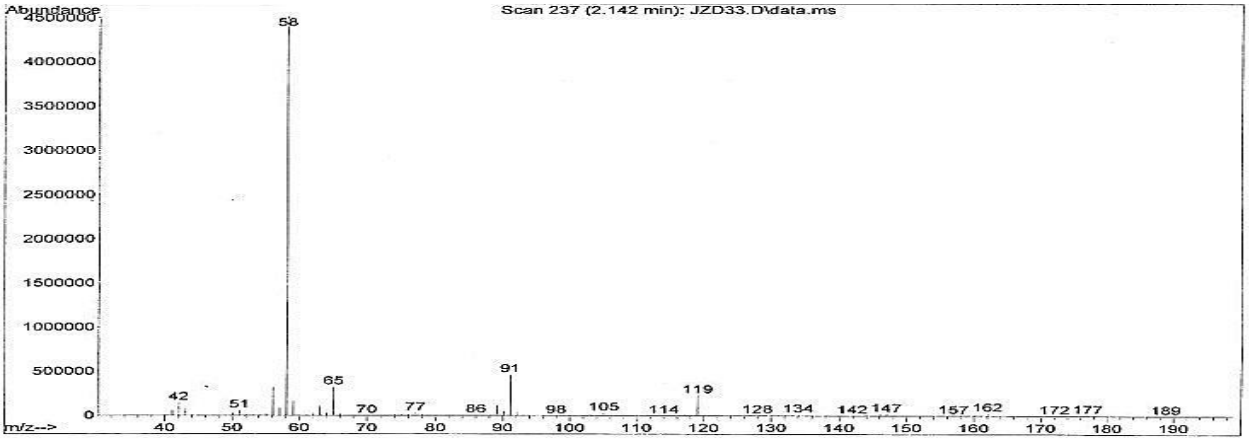

Figure 73. Mass spectrum for 4-methylmethcathinone

Table 22. Peaks found in the mass spectra for the methylmethcathinones (bolded numbers represent the base peak)

2-methylmethcathinone	3-methylmethcathinone	4-methylmethcathinone
42	42	42
51	50	51
58*	**58***	**58***
65	65	65
91	91	91
119	119	119
m/z		

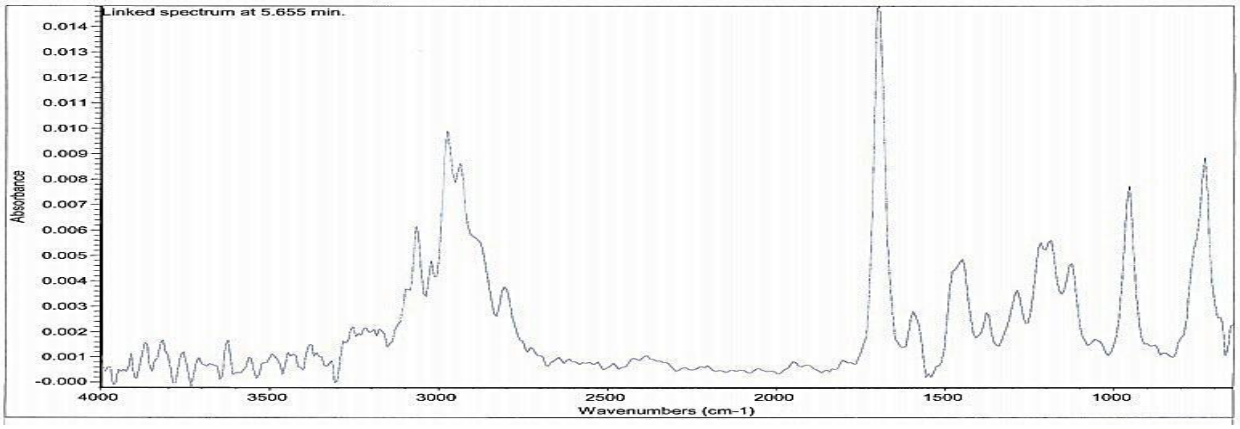

Figure 74. GC-IR spectrum for 2-methylmethcathinone

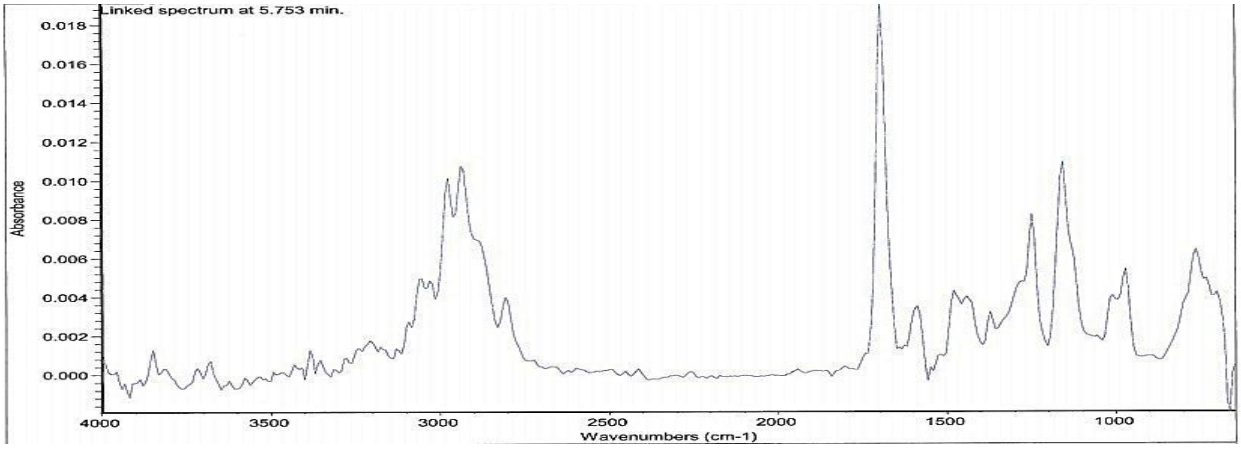

Figure 75. GC-IR spectrum for 3-methylmethcathinone

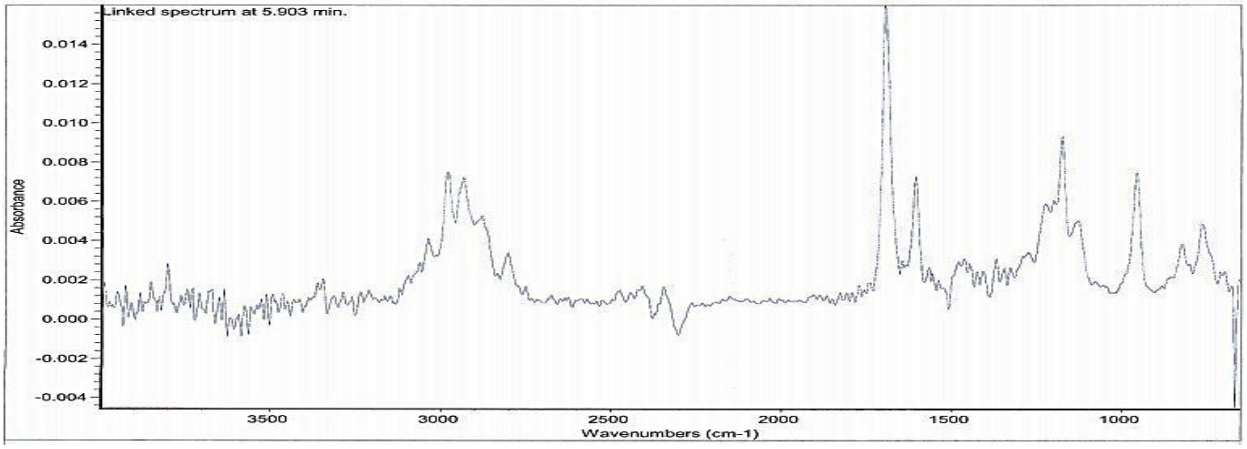

Figure 76. GC-IR spectrum for 4-methylmethcathinone

Table 23. Characteristic bands for n-methylmethcathinone (W, M, S represent weak, medium and strong, respectively)

2-methylmethcathinone	3-methylmethcathinone	4-methylmethcathinone
3067 (M)	3058 (W)	3032 (W)
3024 (M)	2978 (M)	2979 (M)
2977 (S)	2934 (M)	2935 (M)
2940 (S)	2807 (W)	2887 (M)
2806 (W)	1697 (S)	2803 (W)
1700 (S)	1590 (W)	1694 (S)
1597 (W)	1480 (W)	1607 (M)
1459 (M)	1441 (W)	1475 (W)
1378 (W)	1373 (W)	1371 (W)
1290 (W)	1249 (M)	1178 (M)
1218 (M)	1159 (M)	1129 (M)
1191 (M)	1010 (W)	958 (M)
1128 (M)	972 (W)	824 (W)
957 (M)	763 (M)	764 (M)
733 (M)		702 (W)
cm^{-1}		

Table 24. Retention times for the methylmethcathinones for the GC-MS and GC-IR analyses

	2-methylmethcathinone	3-methylmethcathinone	4-methylmethcathinone
GC-MS	1.9	2.0	2.1
GC-IR	5.7	5.8	6.0
Minutes			

n-fluoromethcathinone

The fluoromethcathinones are created by substituting a fluorine group onto the aromatic ring of the methcathinone structure. The mass spectra for 2-, 3- and 4-fluoromethcathinone are shown in 77-79, respectively. The peaks of interest found in the mass spectra are shown in Table

24. The GC-IR spectra for 3-fluoromethcathinone and 4-fluoromethcathinone are shown in Figures 80 and 81, respectively. Unfortunately, no GC-IR spectrum could be obtained for 2-fluoromethcathinone. It is suspected that degradation occurred in the GC column. The bands found in the GC-IR spectra are shown in Table 25. The retention times for the fluoromethcathinones GC-MS and GC-IR analyses are shown in Table 26.

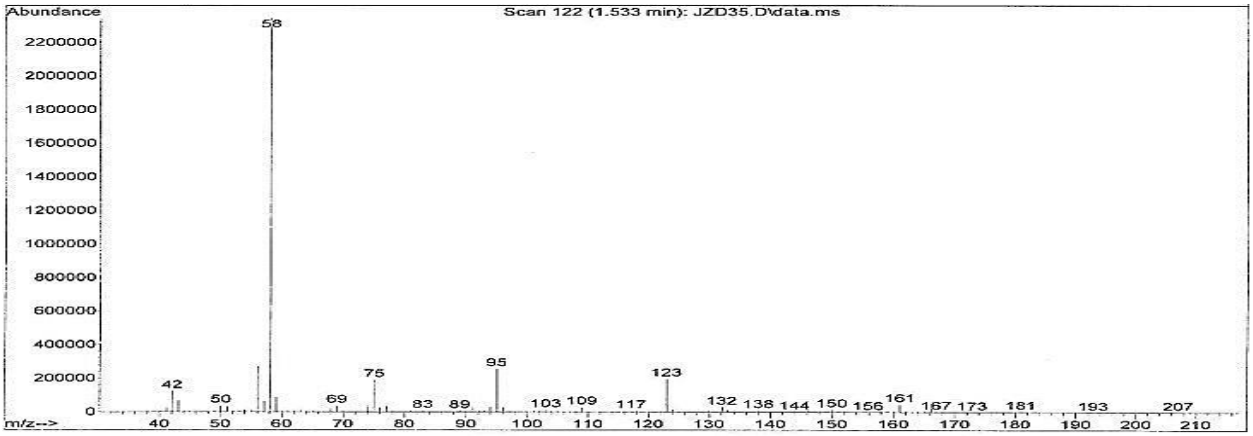

Figure 77. Mass spectrum for 2-fluoromethcathinone

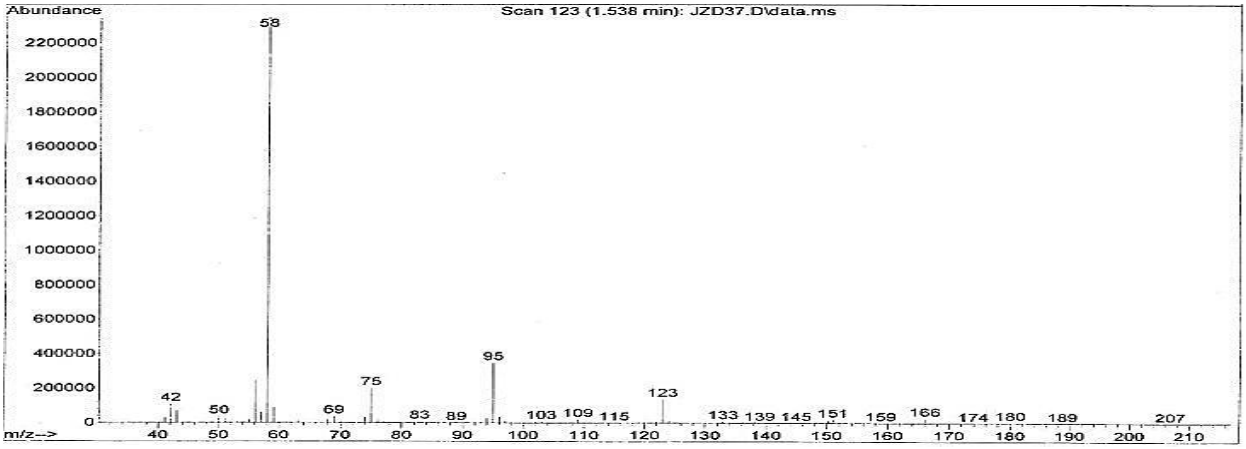

Figure 78. Mass spectrum for 3-fluoromethcathinone

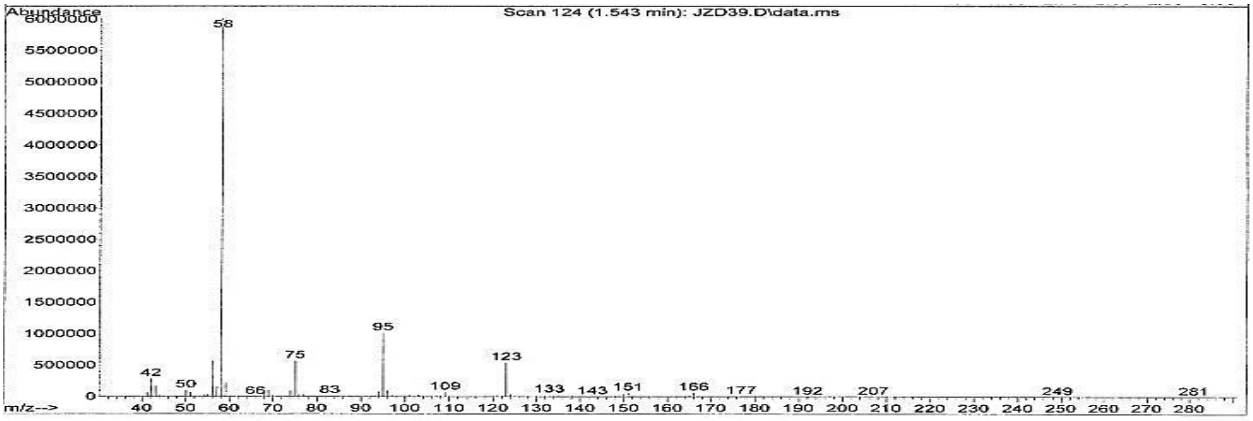

Figure 79. Mass spectrum for 4-fluoromethcathinone

Table 24. Peaks of interest found in the mass spectra of the fluoromethcathinones (bolded numbers represent the base peak)

2-fluoromethcathinone	3-fluoromethcathinone	4-fluoromethcathinone
42	42	42
50	50	50
58	**58**	**58**
75	75	75
95	95	95
123	123	123
161	166	166
m/z		

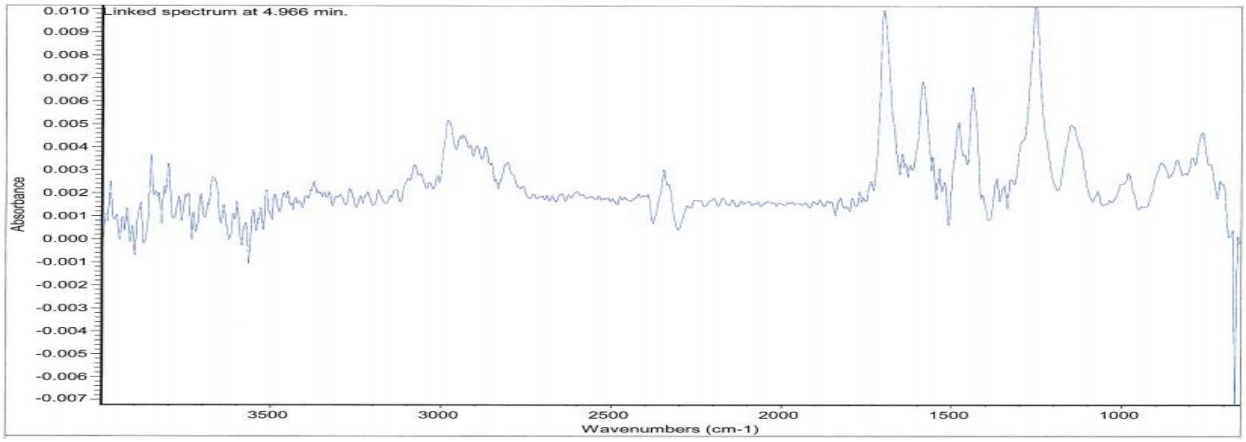

Figure 80. GC-IR spectrum for 3-fluoromethcathinone

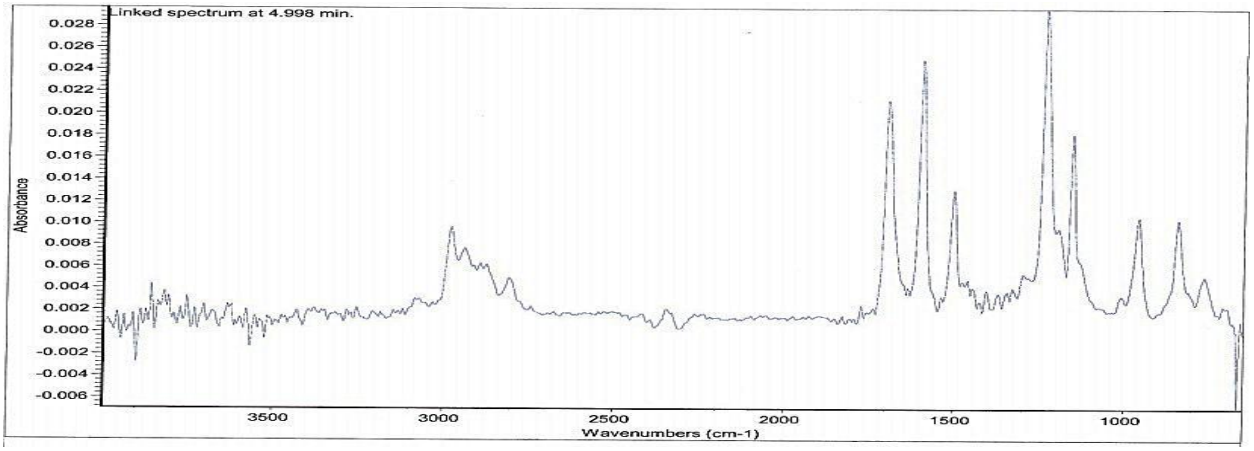

Figure 81. GC-IR spectrum for 4-fluoromethcathinone

Table 25. Characteristic bands for n-fluoromethcathinone (W, M, and S represent weak, medium and strong, respectively)

3-fluromethcathinone	4-fluoromethcathinone
3070 (W)	3071 (W)
2979 (M)	2980 (M)
2942 (W)	2940 (W)
2807 (W)	2809 (W)
1702 (S)	1697 (S)
1586 (M)	1598 (S)
1481 (W)	1504 (M)
1439 (M)	1235 (S)
1255 (S)	1156 (M)
1147 (W)	961 (M)
981 (W)	844 (M)
841 (W)	765 (W)
766 (W)	698 (W)
cm^{-1}	

Table 26. Retention times for the fluoromethcathinones for GC-MS and GC-IR analyses

	2-fluoromethcathinone	3-fluoromethcathinone	4-fluoromethcathinone
GC-MS	1.5	1.5	1.5
GC-IR	-	5.0	5.1
Minutes			

All of the methcathinones featured bands between 2967-2980 cm^{-1}, 2803-2818 cm^{-1} and 1689-1702 cm^{-1}, which correspond to the methyl group, the amino group and the aryl ketone group, respectively. The methcathinone analogs that contain a methylenedioxy group on the aromatic ring contained bands between 1344-1355 cm^{-1}, 1245-1253 cm^{-1}, 1049-1067 cm^{-1}, and 944-946 cm^{-1}. The analogs containing the pyrrolidine ring at the amino group contained bands between 927-945 cm^{1}. The differences between the 2-, 3- and 4-positional isomers are less defined than the bands shown above. The 2-positional isomers contained bands between 733-753 cm^{-1} and 957-961 cm^{-1}. The 3-positional isomers contained bands in the ranges 753-766 cm^{-1} and 972-992 cm^{-1}. The 4-positional isomers contained bands in the ranges 760-775 cm^{-1}, 958-961 cm^{-1}, and 1600-1607 cm^{-1}. The fluoromethcathinones contained bands between 1147 and 1156 cm^{-1} to indicate the presence of the fluorine group on the aromatic ring. The analogs containing the methoxy group on the aromatic ring featured bands in the range 1242-1258 cm^{-1}.

Conclusions:

All nineteen phenethylamines and antihistamine drugs were analyzed via GC-IR successfully. The wavenumbers for the bands from the spectra obtained for each drug did not differ greatly, showing that the method was a success. The FID retention times did not deviate greatly; with the exception of methamphetamine and phentermine (decreasing the concentration of the sample would most likely eliminate this problem). The majority of the drugs gave a relatively linear response with increasing amount of sample injected into the system. The GC-IR at the West Virginia State Police Drug Lab has been shown to work reproducibly and accurately.

Twenty of the twenty-one methcathinone analogs were analyzed via GC-IR successfully. The spectra obtained for 3,4-methylenedioxy-α-PPP and MDPV were nearly identical and were the only two analogs analyzed that were better identified by their mass spectra. In all of the infrared spectra obtained for the methcathinone analogs, there were two ranges that showed absorbance: 3100 – 2800 cm^{-1} and 1700 – 690 cm^{-1}. When analyzing positional isomers, the 3100-2800 cm^{-1} range was nearly identical and more valuable information was obtained from the 1700 – 690 cm^{-1}. GC-IR or GC-MS-IR should be the instruments used when analyzing methcathinones.

References

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