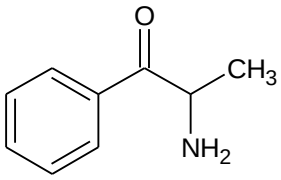
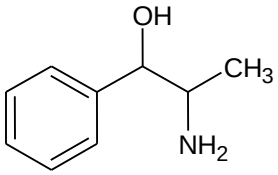
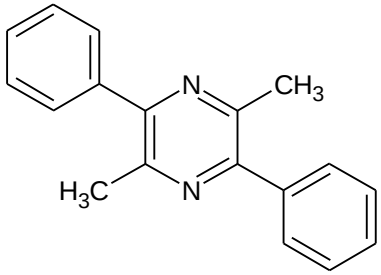


Cathinone



Cathine



3,6-dimethyl-2,5-diphenylpyrazine
(dimer of Cathinone)

1. SYNONYMS

CFR:	Cathinone Cathine
CAS #:	Cathinone Hydrochloride: 71031-15-7 Cathine Hydrochloride: 2153-98-2 Cathine Base: 492-39-7
Other Names:	*Catha edulis* Kat Mutsawhari Mutsawari Mdimamadzi Musitate Mirungi Miraa Ol meraa

Tumayot
Liruti
Ikwa
Arabian Tea

2. CHEMICAL AND PHYSICAL DATA

Khat is used as a stimulant or as a medicine in parts of Africa and the Arabian Peninsula. The plant is thought to have been in cultivation before the coffee plant; historical references date the use of the plant to the fourteenth century. Peter Forsskal, a physician and botanist, collected khat specimens in an expedition organized by the King of Denmark in the eighteenth century. Forsskal assigned the name *Catha edulis* to the plant.

The effects produced by the drug include excitation, hypersensitivity, anorexia, insomnia, euphoria, increased respiration, and hyperthermia. These effects closely parallel the effects of d-amphetamine.

Khat is a bush or tree that grows naturally in the humid mountainous regions (elevations of 5000 to 6500 feet) of East and South Africa. The trees can grow naturally to over 60 ft; however, cultivated khat trees are pruned and their height to kept to approximately 16 feet. Khat also grows to a height of 3 feet as a small bush in arid regions. Like opium, the alkaloid content of khat will vary with the soil, climatic conditions, and cultivation. Khat belongs to the genus *Catha edulis*. It is recognized that the genus consists of only one species; however, the plant exhibits extreme polymorphism. The plant comprises several cultural varieties, which do not have the same properties. The leaves may be thin and narrow or very broad. The leaves may be arranged on a branch in opposite pairs, but are sometimes displaced resulting in an alternating orientation. New leaves are a reddish-brown color, becoming greenish-yellow when fully grown. The leaves are bifarious (arranged in two rows), elliptical, lanceolate with sharp edges and coriaceous (leather like). Some have reported the leaves to be almost tasteless, while others report the leaves are aromatic, sweet, and astringent. Dimensions of the leaves vary from 0.5 cm to 7 cm in length.

The khat plant will produce small, white, or light green flowers. The flowers will be arranged in auxiliary cymes (a flower cluster, in which the main axis and branch end in a flower will open before the flowers below or to the side of it). The flowers have five equal sepals and five oblong petals.

Khat can be used in a variety of ways. Fresh plant material is generally chewed for the stimulant effect of the cathinone. Large leaves or dried leaves are powdered in a mortar. The powdered material is then mixed with sugar and sometimes spices and water making a paste, which is chewed. Dried leaves can also be brewed into a tea, or alternatively, the leaves can be crushed and rolled into cigarettes.

Khat is quality rated by connoisseurs in a manner similar to tea and coffee. The criteria utilized depend upon the part of the plant that will be used – leaves, buds, or twigs. This is coupled with the degree of maturity, the size of the leaf and the area of plant origin. Larger and older leaves will be tough and not easily chewed. Additionally, these leaves will contain a lower amount of cathinone as compared to younger leaves from the same plant. In addition, the red leaf type known as “dimma” is known to have more cathinone than the white leaf type known as “dallota”.

Three to six alkaloids have been identified in khat. The principle active alkaloid in khat is S-(-)-$\propto$-aminopropriophenone, or (-)-cathinone. In some khat samples this compound accounts for up to 70% of the phenylalkylamine fraction. The content of the (-)-cathinone is directly associated with the market price of khat. Cathinone exists in khat as the racemic mixture; the total cathinone content can vary with reported values

ranging from 0.9% up to 3.3% in a Kenyan khat sample. Other phenylalkylamines present in khat include (+)-norpseudoephedrine (cathine), norephedrine and 1-phenyl-1,2-propanedione.

The (-)-cathinone in the leaf material will begin to degrade to cathine and (-)-norephedrine once the leaf has been harvested. Traditionally, the conversion process is slowed by tightly wrapping the leaves in moist false banana leaves to retain moisture. The freshly harvested leaves can be air dried or frozen to preserve the (-)-cathinone. Air-dried leaf material had detectable levels of (-)-cathinone after ten days and frozen leaf material had detectable levels of (-)-cathinone after one year. Cathinone base will also dimerize in the presence of oxygen to form 3,6-dimethyl-2,5-diphenylpyrazine.

large and small Khat leaves

red Khat leaf

Left: top side of Khat leaf
Right: bottom side of Khat leaf

2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Cathinone base	$C_9H_{11}NO$	149.2 amu	77-78
Cathine Hydrochloride	$C_9H_{13}NO$ HCl	187.7 amu	180-181
3,6-dimethyl-2,5-diphenylpyrazine	$C_{18}H_{16}N_2$	260.3 amu	

2.2. SOLUBILITY

Cathinone and cathine are soluble in ethyl ether, hexane, chloroform and alcohol.

3. SCREENING TECHNIQUES

3.1. MICROSCOPIC EXAM

A microscopic examination of the leafy material should be conducted to note the general leaf characteristics.

3.2. COLOR TESTS

Color tests performed directly on plant material will not yield results. Extracted and purified material may give the following results.

REAGENT	COLOR PRODUCED
Cathine	
Marquis	No color development
Sodium Nitroprusside	Rose
Cathinone	
Marquis	No color development
Sodium Nitroprusside	Rose

3.3. THIN LAYER CHROMATOGRAPHY

Visualization

UV light Ninhydrin reagent

COMPOUND	RELATIVE R_f and COLOR	
	UV light	Ninhydrin spray
Cathine	0.26, brown	0.26, purple
Cathinone	0.48, brown	0.48, orange
Ephedrine	0.17, brown	0.17, purple
Phenylpropanolamine	0.26, red	0.26, orange

Pseudoephedrine	0.23, brown	0.23, no color

Developing Solvent: ethyl acetate – methanol – ammonia (85 : 10 : 5)

3.4. GAS CHROMATOGRAPHY

Method General Screen1

Instrument: Gas chromatograph operated in split mode with FID

Column: 5% diphenyl/95% dimethylsiloxane 15 m x 0.25 mm x 0.25 µm film thickness

Carrier gas: Helium at 1.6 mL/min

Temperatures: Injector: 275°C
Detector: 280°C
Oven program:
1) 100°C initial temperature for 2.0 min
2) Ramp to 300°C at 15 degrees/min

Injection Parameters: Split Ration = 35:1, 1 µL injected

Samples extracted with 1N NaOH into chloroform and filtered.

COMPOUND	RRT
amphetamine	0.694
methamphetamine	0.865
cathinone	1.000
cathine	1.003
1S,2R-(d)-phenylpropanolamine	1.340
1S,2R-(d)-ephedrine	1.456
1S,2S-(d)-pseudoephedrine	1.470

4. SEPARATION TECHNIQUES

The khat alkaloids are separated from the plant material by acid / base extractions into solvents. The khat alkaloids can then be separated by GC, HPLC or TLC and identified with GC-IRD or GC-MSD.

Extraction scheme A
Five grams of leafy material is macerated in a plant mill or torn into very small pieces. Ten milligrams of oxalic acid and 50 mL of water are added to the leafy material and either mechanically blended for three, one-minute increments or sonicated for 15 minutes. The mixture is filtered through a Buchner funnel to separate the liquid from the solid plant material. The liquid material is made basic (pH 9) with saturated sodium bicarbonate and extracted into two 10 mL aliquots of chloroform. The chloroform aliquots are combined and evaporated to near dryness under a stream of air. This extract can then be analyzed by GC, HPLC, TLC, GC-IRD or GC-MS.

Extraction scheme B
Five grams of leafy material is macerated in a plant mill or torn into very small pieces. Fifteen to 20 mL of methanol is added and sonicated for 15 minutes. The mixture is filtered through a Buchner funnel to separate the liquid from the solid plant material. The alcohol solution is evaporated to near dryness under a stream of air. The small volume is reconstituted in 0.02 N sulfuric acid, extracted into chloroform, and separated. The aqueous acidic layer is made basic with saturated sodium bicarbonate and extracted into dichloromethane. This extract can then be analyzed by GC, HPLC, TLC, GC-IRD or GC-MS.

5. Quantitative Procedures

N/A

6. Qualitative Data

6.1. Ultraviolet Spectroscopy

COMPOUND	SOLVENT	MAXIMUM ABSORBANCE (NM)
cathine	0.1 N H_2SO_4	249
cathinone	0.1 N H_2SO_4	256, 250, 262

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

7. REFERENCES

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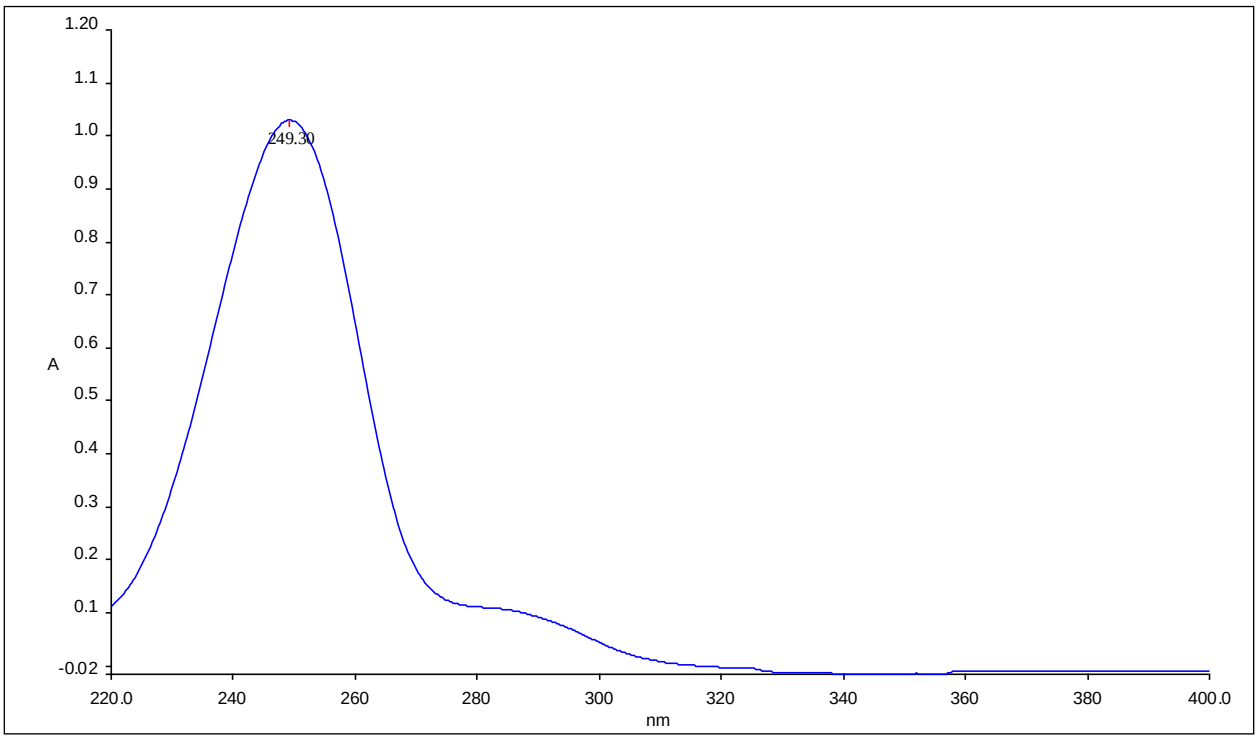
United Nations Narcotics Laboratory, “Studies on the Chemical Composition of Khat. IX. The phenylalkylamines of Catha edulis Forsk. The absolute configuration of cathinone”, *MNIR*/7/1978.

8. ADDITIONAL RESOURCES

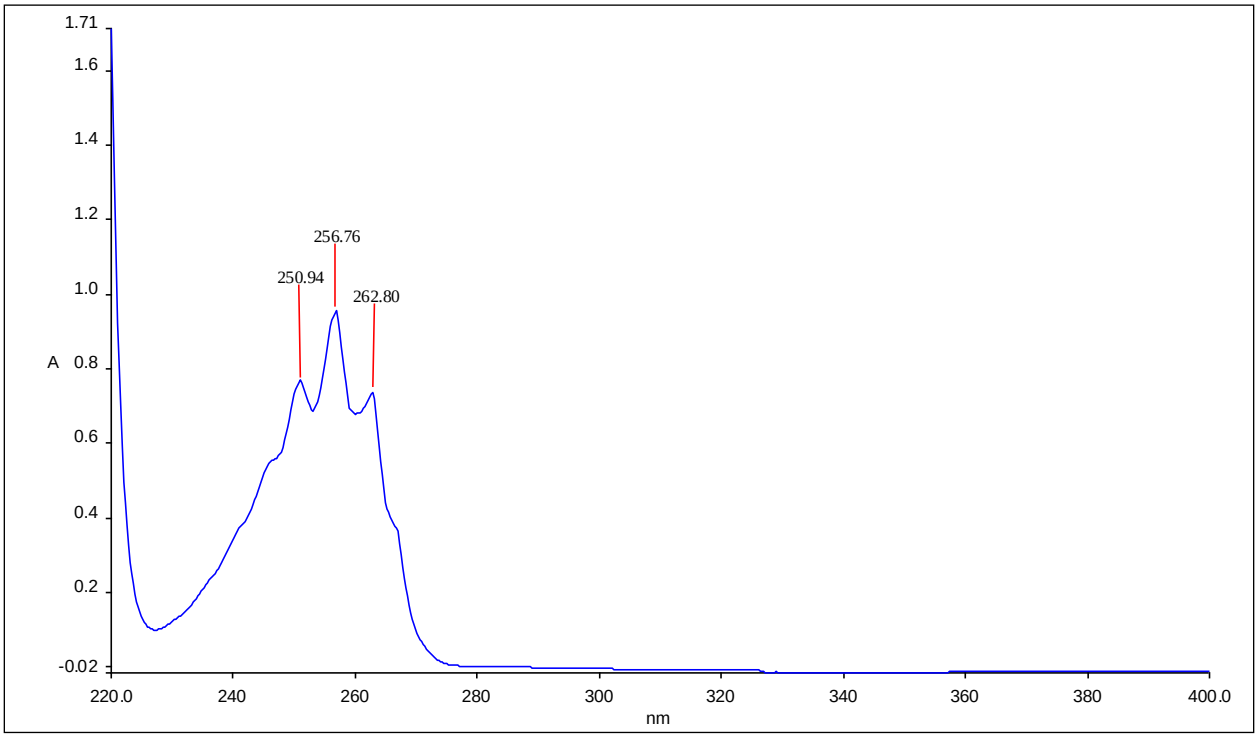
Forendex (cathinone, cathine)

Wikipedia

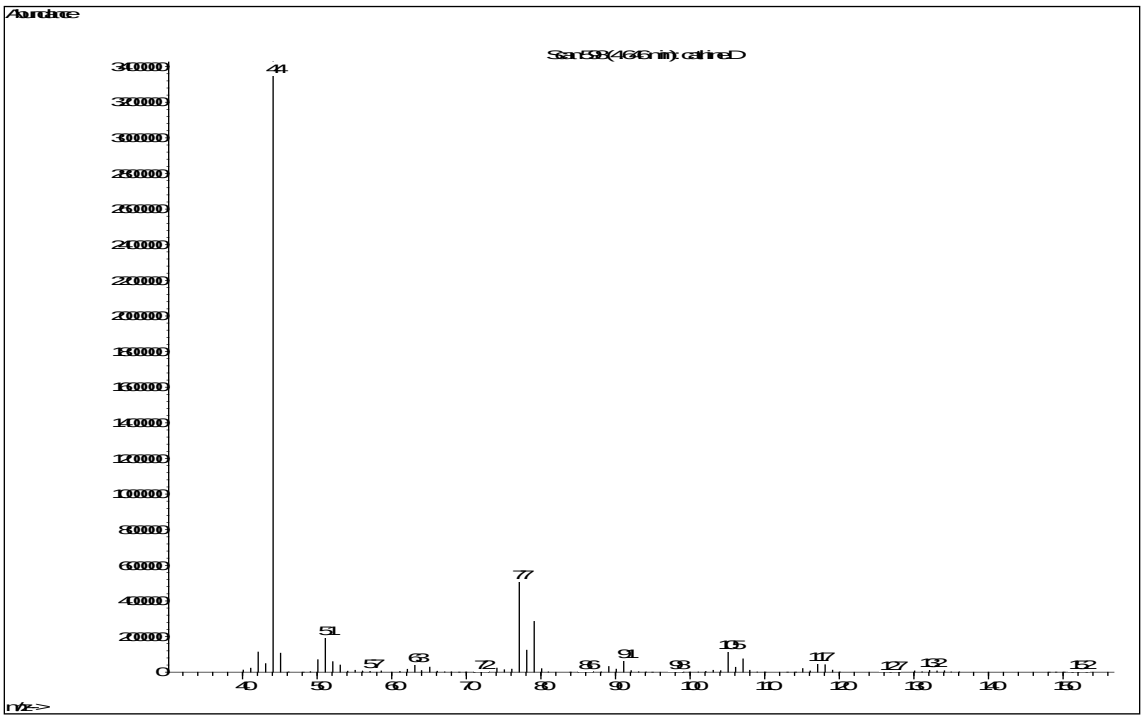
UV: Cathinone standard in 0.1 N H_2SO_4



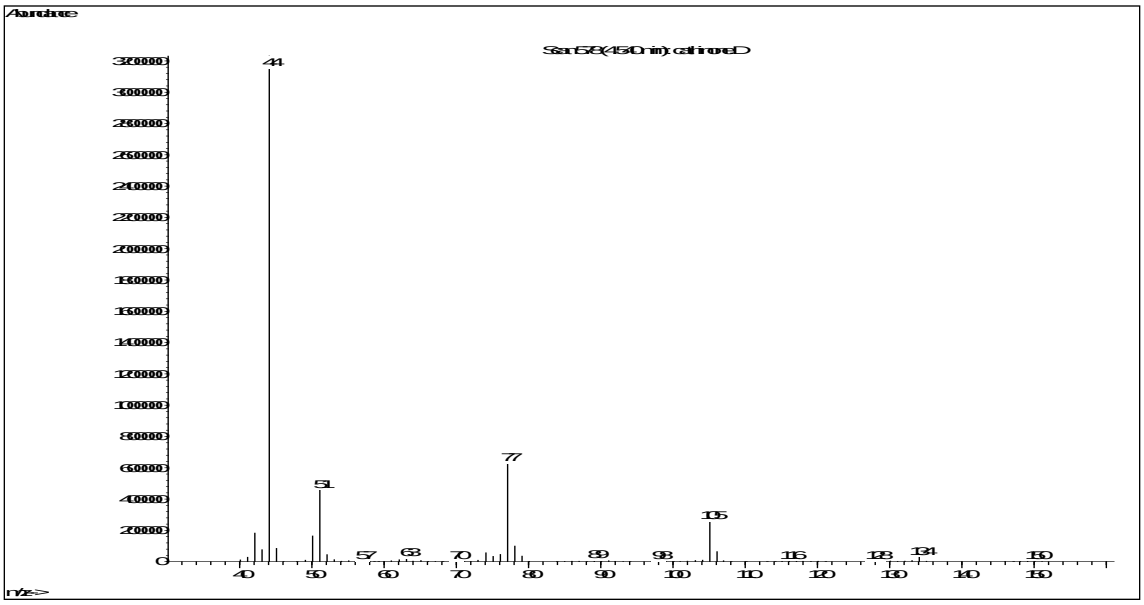
UV: Cathine standard in 0.1 N H_2SO_4



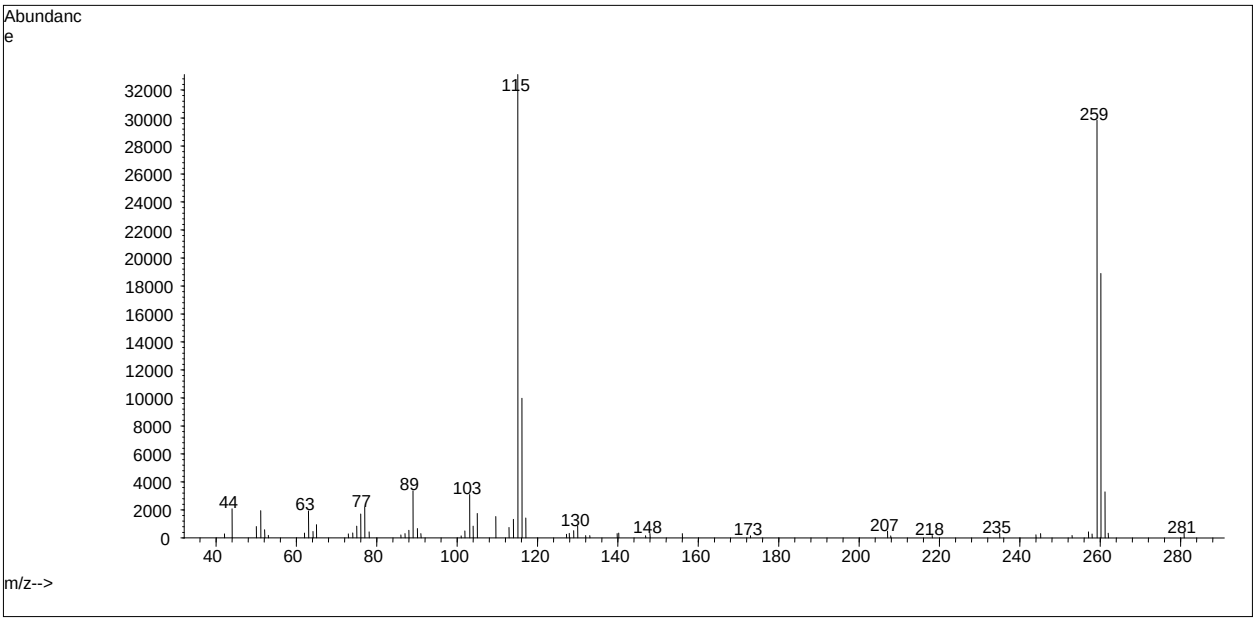
MS: Cathine



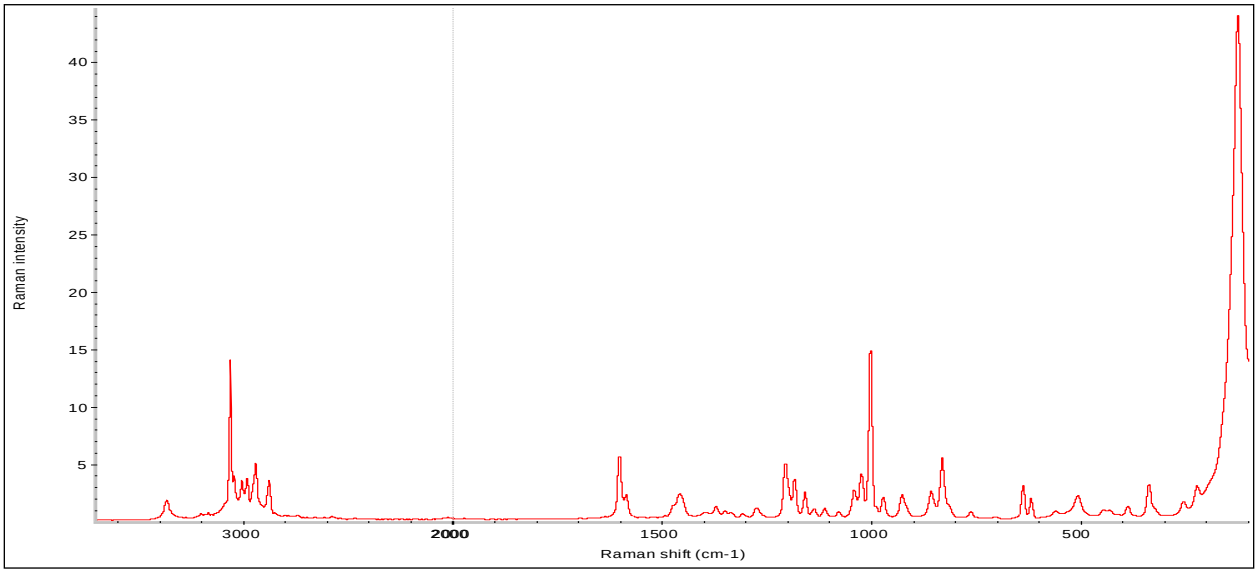
MS: Cathinone



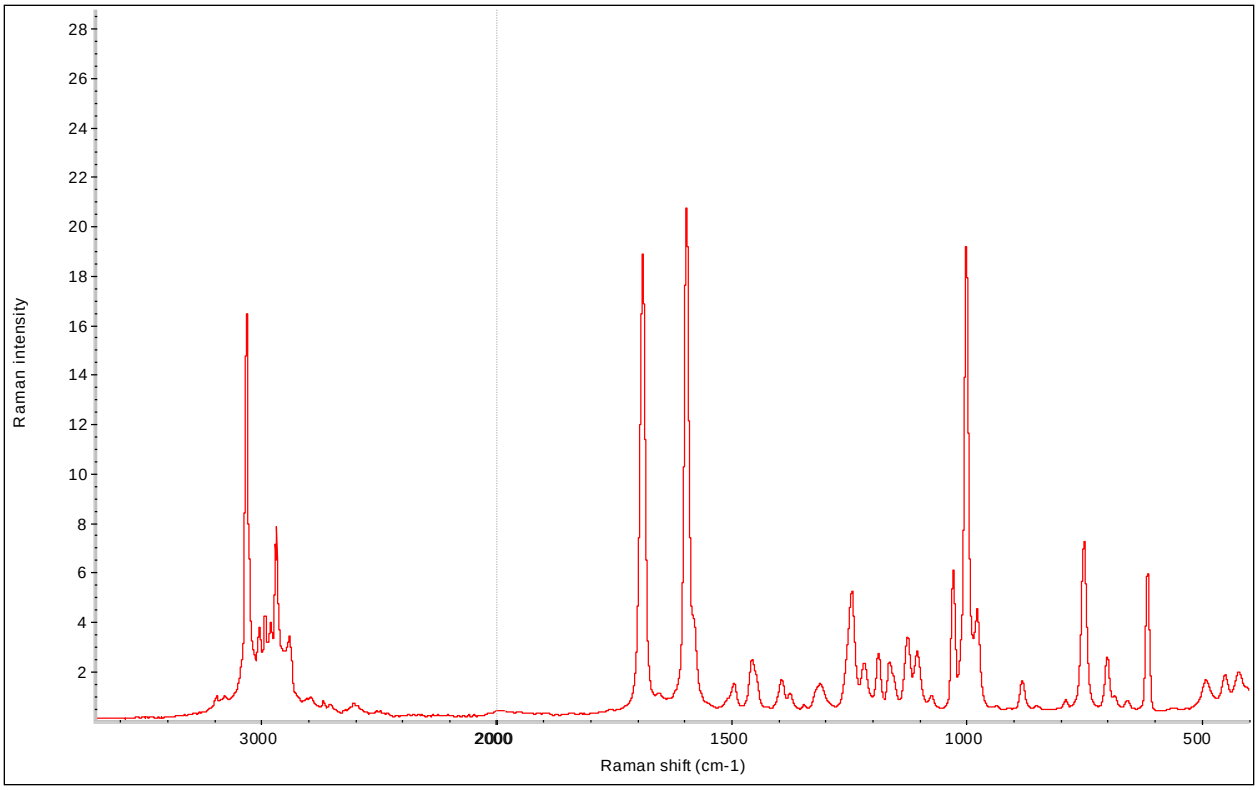
MS: 3,6-dimethyl-2,5-diphenylpyrazine
Cathinone dimer



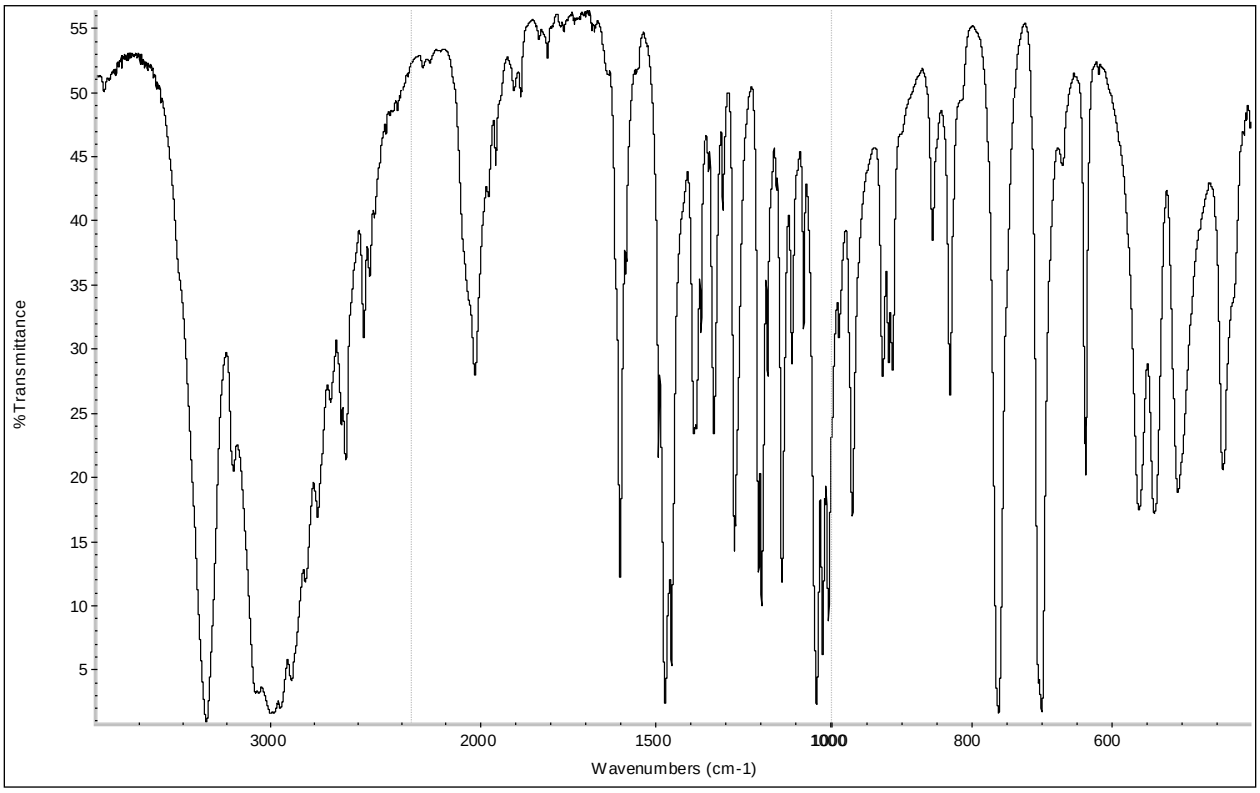
RAMAN:: Cathine HCl standard
16 scans, 8 cm-1 resolution



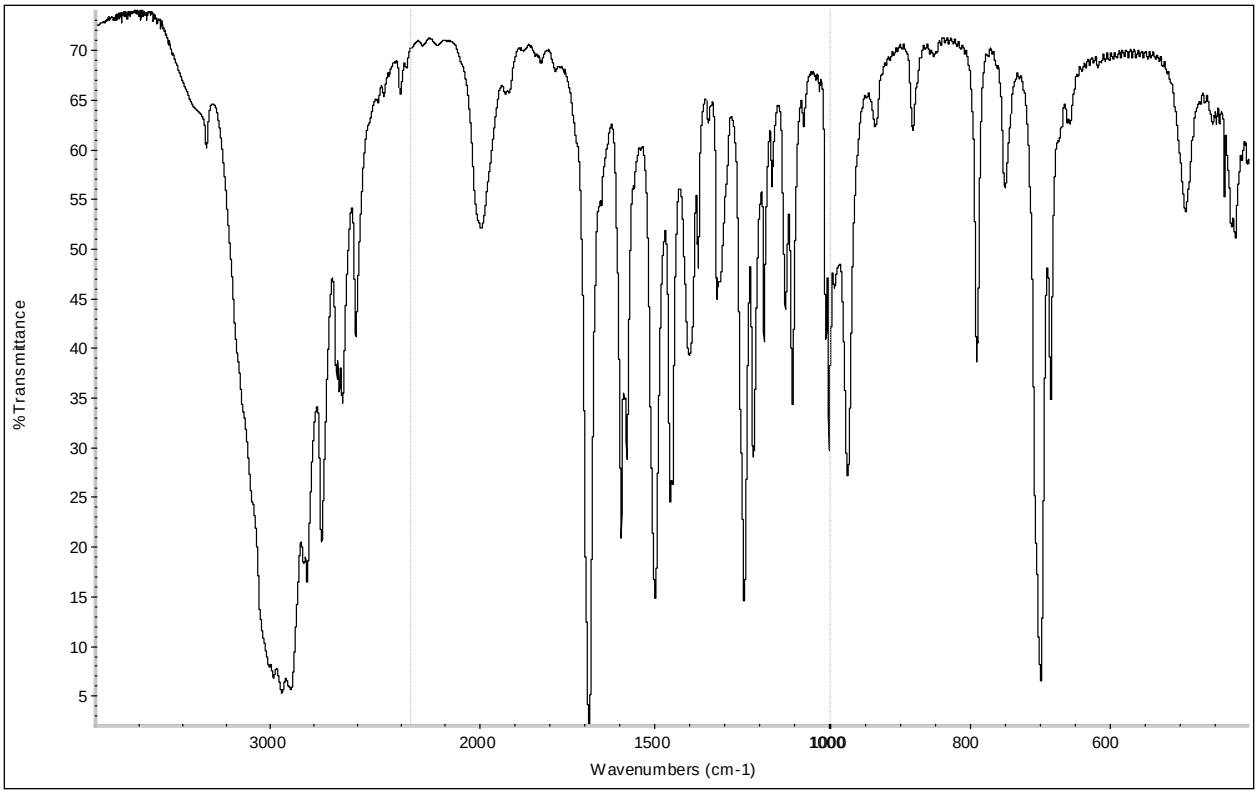
RAMAN: Cathinone HCl
6 scans, 8 cm^{-1} resolution



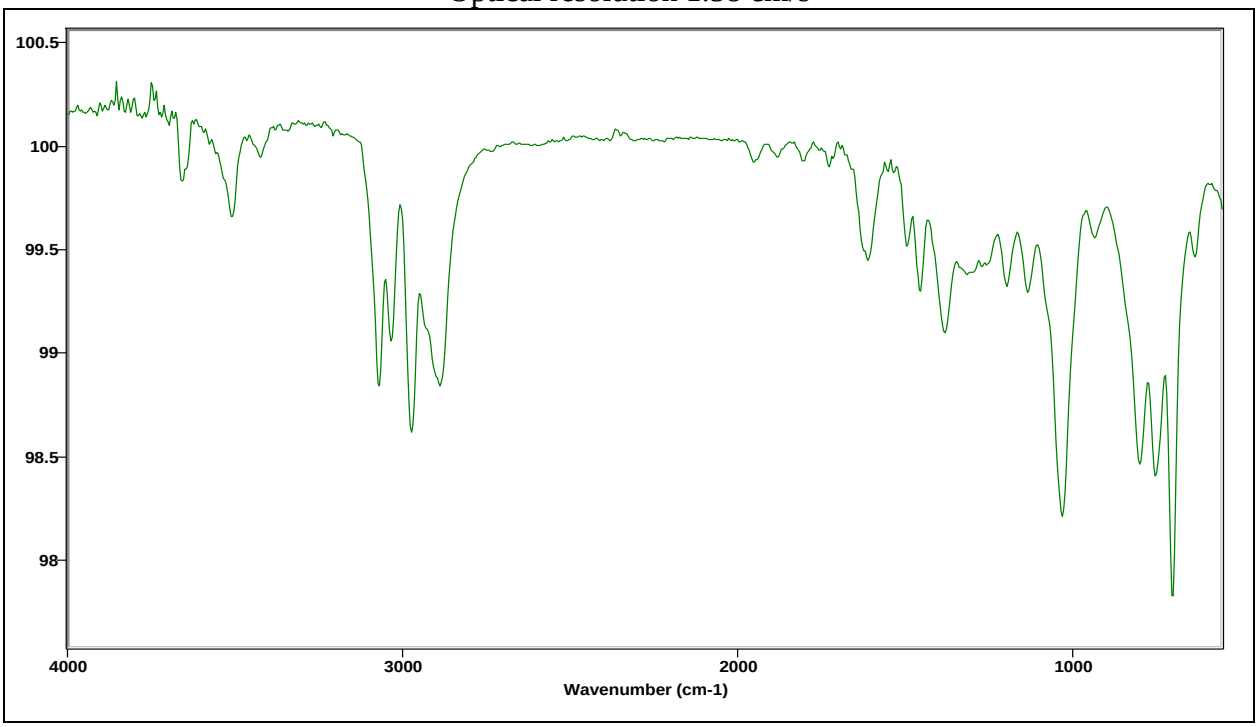
FTIR: Cathine HCl standard, KBr pellet.
16 scans, 2 cm^{-1} resolution



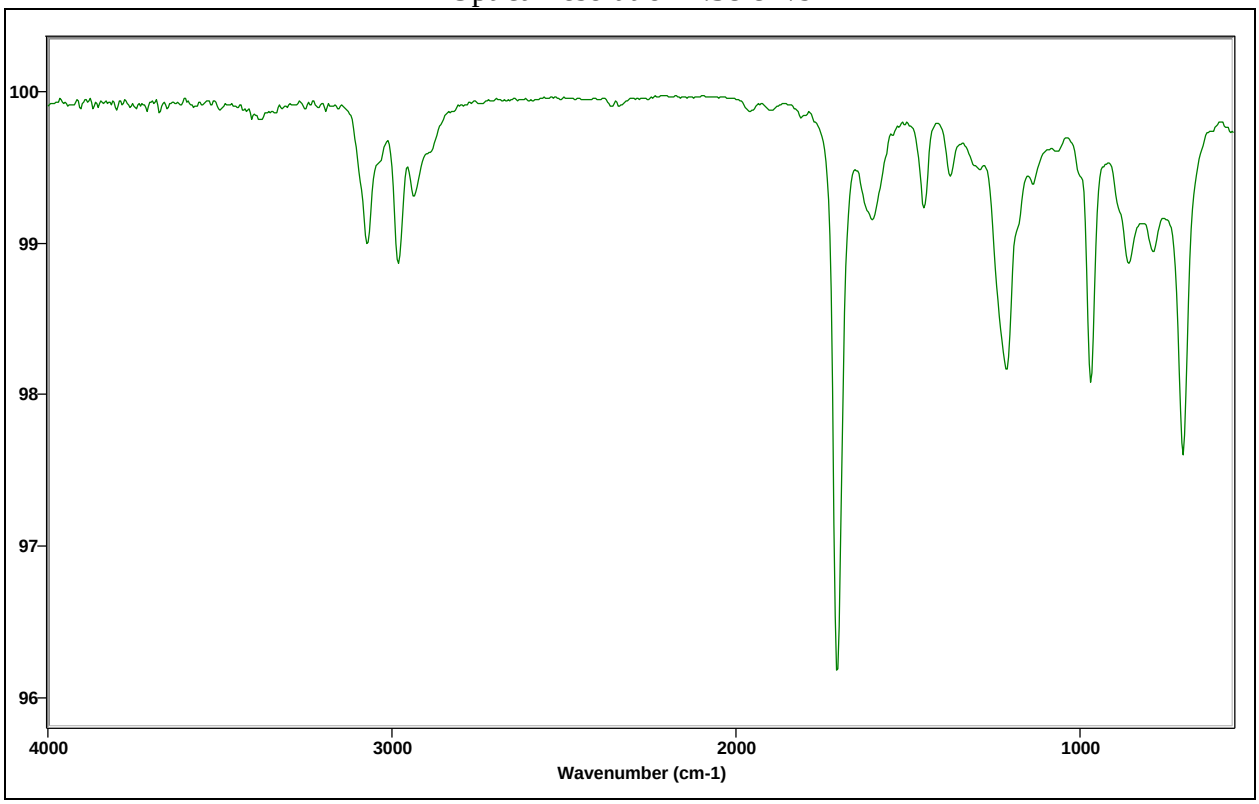
FTIR: Cathinone HCl standard, KBr pellet.
16scans, 2 cm^{-1} resolution



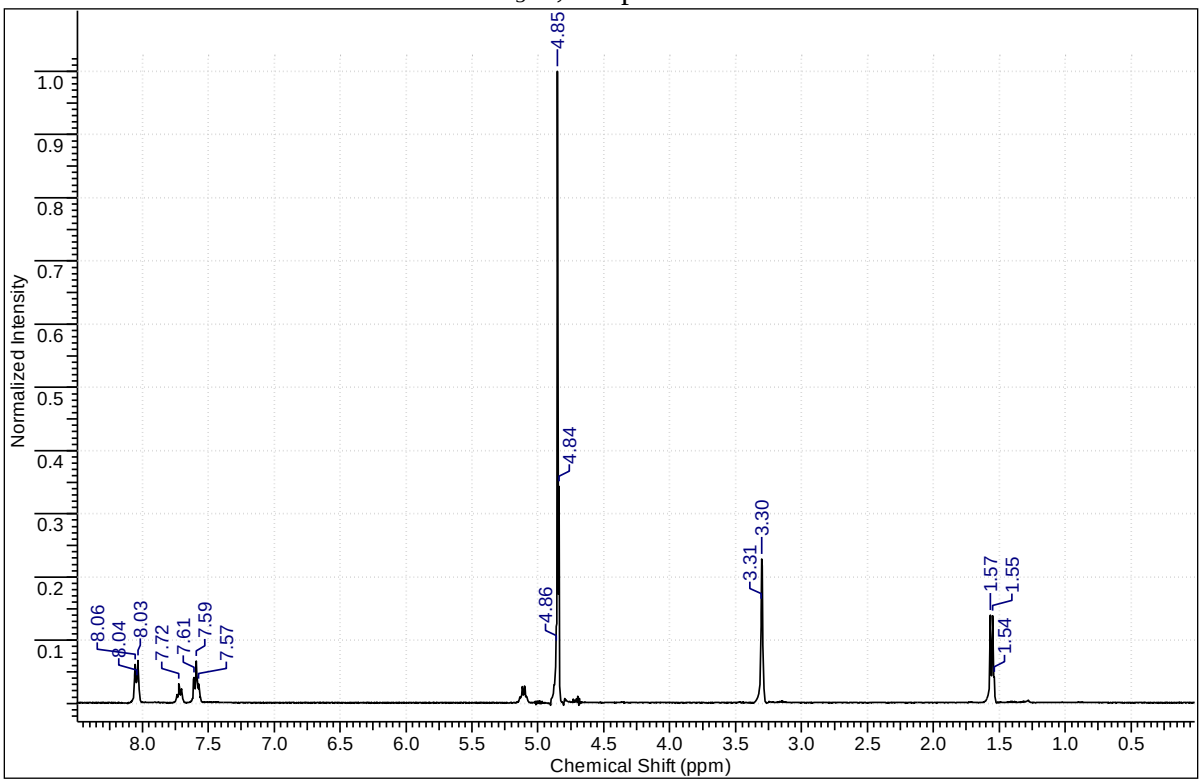
IR (Vapor Phase): Cathine
Optical resolution 1.58 cm/s



IR (Vapor Phase): Cathinone
Optical resolution 1.58 cm/s



NMR (Proton): Cathinone
CD_3Cl, 8 repetitions



NMR (Proton): Cathine hydrochloride

CD_3Cl, 8 repetitions