DETERMINATION OF NARCOTIC AND PSYCHOTROPIC SUBSTANCES BY USING INFRARED SPECTROSCOPY

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ABSTRACT

DETERMINATION OF NARCOTIC AND PSYCHOTROPIC SUBSTANCES BY USING INFRARED SPECTROSCOPY

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Narcotic and psychotropic substances are all chemicals that affect a person's mental activities, perceptual abilities, behavior and level of consciousness; they may cause physical and/or psychological dependence. For determination of narcotic and psychotropic substances, chromatographic techniques are usually preferred which are aimed to identify the target chemicals and require several extraction steps. In this study, an Infrared Spectrometric method has been developed for qualitative determination of most widely encountered substances (morphine, heroin, cocaine, MDMA (3,4-methylenedioxymethamhetamine) and amphetamine) and additives (caffeine, paracetamol and lactose). Standard reference materials and illicit samples have been analyzed in powdered form by using Fourier Transform Infrared-Attenuated Total Reflectance (FTIR-ATR) technique. In the first part, a spectral FTIR database was constituted from the standard references. Illicit samples containing drugs and additives in varying percentages were analyzed using the same method and their database forecast results were compared with results from Gas Chromatography and High Pressure Liquid Chromatography. In the second part of the study, the possibility of finding a

similarity between two samples just by comparing their spectra was investigated. For this purpose, all illicit sample spectra were collected in a new database, and then randomly selected samples were searched using this database. Most of the search attempts resulted in a correct match. Consequently, it has been observed that FTIR-ATR can be used as a priory detection step for classification studies; moreover with this technique pre-determination of narcotic and psychotropic substances can be done simply and rapidly.

Keywords: Narcotic and psychotropic substances, FTIR, drug, forensic chemistry.

ÖZ

NARKOTİK VE PSİKOTROPİK MADDELERİN İNFRARED SPEKTROSKOPİ YÖNTEMİ İLE TAYİNİ

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Narkotik ve psikotropik maddeler, kişilerin ruhsal durumunu, fiziksel ve düşünsel güçlerini etkileyen ve fiziksel ya da psikolojik bağımlılığa yol açan maddelerdir. Narkotik ve psikotropik maddelerin analizlerinde genellikle hedef bileşenlerin tayinlerine yönelik olarak, ekstraksiyon işlemleri ve uzun analiz süresi gerektiren kromatografik yöntemler kullanılmaktadır. Bu çalışmada, ülkemizde en sık rastlanan narkotik ve psikotropik maddeler (morfin, eroin, kokain, MDMA (3,4-metilendioksimetamfetamin) ve amfetamin) ve bu maddelerin bileşimlerinde bulunabilecek çeşitli katkı maddelerinin (kafein, parasetamol, laktoz) nitel tayinleri için Infrared Spektrometri yöntemi geliştirildi. Standart maddeler ve yasadışı yollarla üretilmiş örnekler toz halinde Fourier Transform Infrared-Attenuated Total Reflectance (FTIR-ATR) tekniği ile analiz edildi. Çalışmanın ilk aşamasında standart maddelerden sanal bilgisayar FTIR Kütüphanesi oluşturuldu ve kullanıldı. Bu yöntemle değişik oranlarda etken ve katkı maddeleri içeren yasadışı örnekler tanımlandı ve sonuçlar Gaz Kromatografi ve Yüksek Basınçlı Sıvı Kromatografi analizleri ile doğrulandı. İkinci aşamada ise, iki örnek arasındaki benzerliğin sadece spektrumlarının karşılaştırılması ile mümkün olup olmadığı araştırıldı. Bu

amaçla, yasadışı yollarla üretilen örneklerin spektrumları yeni bir kütüphane altında toplandı ve rasgele seçilen örneklerin spektrumları alınarak bu kütüphanede tarandı. Çalışma sonucunda, örneklerin büyük bölümünün kütüphanede bulunan kendi spektrumu ile eşleştiği görülmüştür. Sonuç olarak, FTIR-ATR tekniğinin narkotik ve psikotropik maddelerin sınıflandırma çalışmalarında bir ön eleme basamağı olarak kullanılabileceği; ayrıca bu maddeler için basit ve hızlı bir ön belirleme yöntemi olduğu belirlenmiştir.

Anahtar Kelimeler: Narkotik ve psikotropik maddeler, FTIR, drog, adli kimya.

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CHAPTER I

INTRODUCTION

1.1 DEFINITIONS OF NARCOTIC AND PSYCHOTROPIC SUBSTANCES

Narcotic and Psychotropic substances are all chemicals that has an affect upon the body and mind. Their use may lead to physical and/or psychological dependence [1].

In scientific publications, narcotics are usually distinguished from psychotropic substances as they are referred to opium alkaloids but for forensic purposes the term “DRUG” can be used to define all of the substances that have a risk of being abused.

1.2 HISTORY OF DRUGS

The history of drugs can be attributed to the beginning of the human race. Natural drugs were used by ancient medicine men to heal some diseases without considering any side effects. Today, it is known that there is no drug that is not harmful or even poisonous at high doses, and much of the scientific work on drugs has attempted to widen the gap between effective and toxic doses.

Ancient drugs, prepared from plants, were used for treatment of diseases as well as having power on the community. Sumerians had known opium and used it as a painkiller. Pre-Columbian Mexicans used many substances from tobacco to mind-expanding hallucinogenic plants in their medicinal treatments and religious ceremonies. Cocaine’s potential for addiction was known and used with evil intent by South American Indian chiefs hundred years ago. Tobacco, Cannabis, Opium Poppy, Coca bush, Khat and other drug containing plants has been chewed or smoked in many regions of the world as a traditional habit since those times [2].

Morphine has been used during World War I as a painkiller and anesthetics; cocaine has been used for a long time as a local anesthetic for eye and nose surgeries until they were replaced by less toxic synthetic counterparts.

After the developments in technology and drug industry, it became possible to produce the synthetic counterparts of these natural drugs. Especially, after 1930 several numbers of drugs had been synthesised for medicinal use. However, in all cultures there have always been a few individuals who have tendency to misuse drugs. Thus, both the non-medical use of drugs and problem of drug abuse are as old as civilization itself.

1.3 DRUG TRAFFICKING AND CONTROL MECHANISMS

It is important to realize that almost all drugs have been and should be isolated or synthesized for the benefit of human; however, for some of them, just during the research studies, or after using for a time, it has been understood that they have the potential of developing dependency and are liable to be abused. Therefore, it has been a necessity for the governments to constitute some national and international control systems in order to regulate the production, selling and use of these drugs.

Three important international conventions, under the United Nations provision, have been accepted by a large number of participant governments;

“Single Convention on Narcotic Drugs (1961)” [3]

“Convention on Psychotropic Substances (1971)” [4]

“UN Conventions Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988)” [5]

On the other hand, limitations of legal production resulted in an increase of the demand for illicit drugs, thus led to the growing problem of illicit productions. Today, illicit manufacture, trafficking and abuse of clandestinely produced drugs are serious global problems.

Illicit trafficking of drugs is a many-sided problem that creates a risk for public health because drugs produced in clandestine laboratories are usually not

hygienic and may contain several harmful impurities due to the lack of quality control steps. Another important aspect is the diversion of money, owned from drug trafficking, into several terrorist activities.

Illicit trafficking of drugs has a general distribution tendency that opiates are usually originated from Asia and dispersed through Europe and America, whereas cocaine and amphetamines are usually produced in European and American countries and dispersed through Asia and Africa. Along with this dispersion, Turkey covers a very important geographical location through which all trafficking ways pass over.

In this crucial location, Turkey has to take responsibility of struggling against illicit trafficking which will be successful only with the full collaboration of national and international law enforcement teams, governments, community and forensic laboratories.

1.4 TERMINOLOGY OF DRUGS

1.4.1 Drug Abuse

Drug abuse is the misuse of medicinal preparations without prescription and usually with increased doses or usage of illicitly produced drugs.

1.4.2 Drug Dependence

Drug dependence is the tendency to take drug with repeatedly and in increasing doses. There are two forms of dependence, namely Psychological and Physical.

1.4.2.1 Psychological Dependence

Psychological dependence on the effects of the drug related to a subjective and individual appreciation of those effects. It means there is a tendency to take the drug regularly or continuously either to obtain the specific effects it produces or to nullify certain unpleasant sensation.

1.4.2.2 Physical Dependence

Physical dependence on the drug is resulting from the adaptation of the body to the substance and leading to the appearance of severe physical and/or

psychological disorders when the person concerned stops taking the drug. These disorders constitute the withdrawal or abstinence syndromes. The complex of syndrome varies according to the type of drug.

1.4.3 Tolerance

In addition to one or both forms of dependence, the drug user may develop a tolerance to a particular drug. This means that he has to take larger doses to obtain the same result since the effect of a given quantity of the drug becomes progressively less [6].

1.5. CLASSIFICATION OF DRUGS

An effective classification of drugs can be done according to their effects on the human body; namely depressants, stimulants and hallucinogens. However, many substances have not strictly defined boundaries in that their effects may change according to the dose. Usually, the first impression is the sense of well being and large doses make the dominant effects become observable.

1.5.1 CNS (Central Nervous System) Depressants

CNS depressants slow down the central nervous system so that they create sedation. The popular drugs in this group are Narcotics and Hypnotic sedatives.

1.5.1.1 Narcotics

The term narcotic come from the Greek word for stupor, refers to induce sleep. In a legal context, narcotic refers to opium, opium alkaloids (morphine and codeine), opium alkaloid derivatives (heroin) and totally synthetic substituents with morphine-like effects (meperidine, methadone, and fentanyl).

Aside from their clinical use in the treatment of pain, cough suppression and acute diarrhea, narcotics produce a general sense of well being by reducing tension, anxiety and aggression. These effects are helpful in a therapeutic setting but contribute to their abuse. With repeated use of narcotics, tolerance and dependence develop quickly.

Opium

Opium is a natural product obtained from the *Papaver Somniferum L.* The plant was grown in the Mediterranean region as early as 3000 BC and opium was known and used as a painkiller until that times [7].

Opium is obtained by incision of the unripe poppy capsules. The milky latex that oozes from the incisions is scraped by hand and air-dried to produce the opium gum, which is known as raw opium. The major constituents of raw opium are plant fragments, resins, sterols, triterpenoid alcohols, fatty acids, polysaccharides and more than thirty alkaloids. These alkaloids are divided into two chemical classes; phenanthrene alkaloids (morphine, codeine and thebaine) and isoquinoline alkaloids (papaverine and narcotine). Papaverine and narcotine have no significant effect on Central Nervous System but they are found in the final morphine product as impurities.

The relative amounts of the different alkaloids can vary greatly depending on such factors as the climate, the altitude, the fertility of the soil, the moisture, age of the plant, the time of lancing and the variety of *Papaver Somniferum L.*

Morphine

Morphine is the principal alkaloid of opium, ranging in concentration of 4-21 %.It is one of the most effective drugs known for relief of pain but clinically it is used in only absolutely necessary cases due to rapid development of tolerance and dependency.

The crude morphine in illicit market can be of very high or very low quality, depending upon the purification procedures, the intended purpose of the material, habits, knowledge and professional skill of the illicit producer.

Final morphine product diverted into the illicit market contains codeine, thebaine, narcotine and papaverine as impurities.

Codeine

Codeine, which has effects similar to morphine, naturally founds in opium in concentrations ranging from 0.7-3 %. Its presence in crude morphine results in

the formation of acetyl codeine during the conversion of morphine to heroin. Codeine is prescribed as an analgesic, cough suppressant and hypnotic.

Papaverine

Papaverine is a non-addictive opium derivative, present at the 0.5-1.3 % level, used medicinally to relieve spasms of smooth muscle.

Narcotine

Narcotine is the second most abundant alkaloid, usually present in 2-8 % and sometimes is present in crude morphine as an impurity.

Heroin (Diacetylmorphine)

Heroin is derived from morphine by acetylating with acetic anhydride via a batch process. Pure heroin is a white powder with a bitter taste. Most illicit heroin is in powder form and may vary in color from white to dark brown due to the impurities (acetyl codeine, monoacetylmorphine, narcotine and papaverine) left from the manufacturing process or the presence of additives (caffeine, paracetamol, griseofulvin) and diluting agents like sugars, starch, powdered milk and quinine.

Heroin was first synthesized in 1874 as a safe, non-addictive substitute for morphine [7]. However, it was soon realized that severe dependency develops very quickly. Heroin is a highly addictive substance and can produce dependence within only a few days of regular use.

Heroin is a sedative and induces a euphoric, drowsy, warm and content feeling. It also relieves stress and discomfort by creating a relaxed detachment from pain, desires and activity.

As well as killing pain, moderate doses of pure opiates produce a range of mild effects. They depress the activity of the nervous system, including such reflexes as coughing, breathing and heart rate. At a higher dose sedation can be extreme and an overdose can result in unconsciousness, coma and often death from respiratory failure.

Synthetic Narcotics

Synthetic narcotics were marketed in order to replace with morphine and to treat heroin addictives. Most common drugs in this group are Meperidine, Methadone and Fentanyl. Although these drugs are used clinically, they have the potential of developing dependence, suffer from illicit production and abuse [6-8].

1.5.1.2 Hypnotic Sedatives

These groups of drugs are used to induce sleep, relieve stress and reduce anxiety by depressing central nervous system. Unlike most other classes of drugs of abuse, depressants are rarely produced in clandestine laboratories. Instead, legitimate pharmaceutical products are diverted into the illicit market.

Two major groups of depressants have dominated the licit and illicit market for near a century, first barbiturates and now benzodiazepines.

Barbiturates

Barbiturates are derivatives of barbituric acid and were first introduced for medicinal use in the early 1900s [6]. Barbiturates produce a wide spectrum of CNS depression, from mild sedation to coma, and have been used as sedatives, hypnotics, anesthetics and anticonvulsants. Barbiturates are classified according to how fast they produce an effect and how long those effects last, as ultra short (methohexital, thiamylal, thiopental), short and intermediate acting (pentobarbital, secobarbital, amobarbital) and long-acting (phenobarbital, mephobarbital). Ultra short-acting barbiturates produce anesthesia within about one minute after intravenous administration. Short and intermediate-acting barbiturates are used for sedation or to induce sleep, while long-acting barbiturates are used primarily for daytime sedation and the treatment of seizure disorders or mild anxiety. Depending on the dose, frequency and duration of use one can rapidly develop tolerance, physical dependence and psychological dependence on barbiturates. Barbiturates are only legal if prescribed and supervised by a doctor.

Abuse of barbiturates is very widespread but there is no indication of clandestine production, in that barbiturates in illicit market result from the diversion of legitimate sources [6, 8, 9].

Benzodiazepines

Benzodiazepines were first marketed in the 1960s [6]. It was claimed that they were much safer depressants with far less addiction potential than barbiturates. It has been recently realized that benzodiazepines share many of the undesirable side effects of the barbiturates. A number of toxic CNS effects are seen with chronic high dose benzodiazepine therapy.

The benzodiazepine family of depressants is used therapeutically to produce sedation, induce sleep, relieve anxiety and muscle spasms and to prevent seizures. In general, benzodiazepines act as hypnotics in high doses, anxiolytics in moderate doses and sedatives in low doses. Benzodiazepines differ from one another in how fast they take effect and how long the effects last. Shorter acting benzodiazepines (estazolam, flurazepam, quazepam, temazepam, triazolam) used to manage insomnia; longer duration benzodiazepines (alprazolam, chlordiazepoxide, clorazepate, diazepam, and oxazepam) are primarily used for the treatment of general anxiety.

Prolonged use can lead to physical dependence and even at recommended dosages withdrawal syndrome may be resulted [6, 8, 10].

1.5.2 CNS Stimulants

Stimulants have a long history of misuse. The well known less potent stimulants, which are nicotine and caffeine, relieve fatigue and increase alertness. More potent stimulant drugs are used medically and on prescription whilst others are made clandestinely and distributed on the illicit market.

The most popular drugs in this group are Cocaine and Amphetamines. They are used therapeutically only when it is necessary to stimulate mental or muscular activity or to treat obesity by reducing the appetite.

1.5.2.1. Cocaine

Cocaine is a unique chemical in that it is both a central nervous system stimulant and an anesthetic. It is obtained from the leaves of the *Erthroxylum* coca plant that is native to the mountains of South America. The traditional method of coca use is to chew the leaves. On the other hand, in illicit market cocaine is served as

powder cocaine or free-base (chemically purified cocaine) and produces much stronger effect than chewing the leaves.

While as early as 3000 BC, there is evidence of coca use in South America, pure cocaine was first isolated in the 1880's and used as a local anesthetics in eye, nose and throat surgery because of its ability to provide anesthesia as well as to constrict blood vessel and limit bleeding. In 1914 cocaine was banned in the U.S. under the Harrison Act, which controlled the sale of opium, opium derivatives and cocaine [6].

Cocaine increases alertness, wakefulness, elevates the mood, induces a high degree of euphoria, decreases fatigue, improves thinking, and increases concentration and energy. In large doses, users often display symptoms of psychosis with confused and disorganized behavior, irritability, fear and paranoia.

Cocaine is a highly addictive substance developing a strong tolerance and psychological dependence and moderate physical dependence.

Illicit Cocaine is usually distributed as a white crystalline powder in hydrochloride salt form or as an off white chunky material which is cocaine free base and commonly named as crack. Cocaine powder is often diluted with sugars and local anesthetics like lidocaine [6, 8, 11].

1.5.2.2 Amphetamine and Amphetamine Related Drugs

Amphetamine, dextroamphetamine and methamphetamine, are collectively referred to as amphetamines, while other members of the group, namely MDMA (3,4-methylenedioxy-N-methamphetamine), MDA (3,4-methylenedioxy-amphetamine), DOM (2,5-dimethoxy-4-methylamphetamine) and DOB (4-bromo-2,5-dimethoxyamphetamine) are the ring-substituted amphetamines.

Amphetamine

Amphetamine was first marketed in the 1930s as Benzedrine in an over-the-counter inhaler to treat nasal congestion. By 1937 amphetamine was available by prescription in tablet form and was used in the treatment of the narcolepsy (sudden sleep disorder) and Attention Deficit Hyperactivity Disorder [6].

During World War II, amphetamine was widely used to keep the fighting men going; both dextroamphetamine (Dexedrine) and methamphetamine (Methedrine) became readily available. As use of amphetamines spread, so did their abuse. Amphetamines became a cure-all for helping truckers to complete their long routes without falling asleep, for weight control, for helping athletes to perform better and train longer, and for treating mild depression. But with experience, it became evident that the dangers of abuse of these drugs outweighed most of their therapeutic uses. After 1965, limitations for amphetamines were initiated. Today, amphetamines have found a very limited therapeutical value whereas increasing demand of abusers lead to a huge number of illicit productions.

Methamphetamine

Methamphetamine is a central nervous system stimulant from the amphetamine family. It produces alertness, and elation, along with a variety of adverse reactions. First Synthesized in 1887, in the 1930s it was sold in the U.S. as a nasal spray for treatment of inflammation of nasal passages and as treatment for narcolepsy. During World War II, both sides used it to improve soldiers' performance. This became a major problem in Japan after World War II as they experienced the first known epidemic of methamphetamine abuse. In 1970, the Controlled Substances Act regulated the production of methamphetamine [6].

Today much of the methamphetamine available on the street is illicit and produced in clandestine laboratories.

Methamphetamine's effects include euphoria, hyper-excitability, extreme nervousness, accelerated heartbeat, sweating, restlessness, insomnia, tooth grinding and incessant talking. Users of large amount of methamphetamine over a long period can develop an amphetamine psychosis, which is a mental disorder similar to paranoid schizophrenia. Methamphetamine abuse develops moderate physical and psychological dependence as well as a strong tolerance. Withdrawal symptoms can occur when use of any amphetamines is stopped abruptly.

MDMA (3, 4-methylenedioxy-N-methamphetamine)

MDMA can be extracted from an essential oil of the sassafras tree. Its effects include euphoria, an increase in emotional openness and mild to moderate stimulant effect.

MDMA is commonly known as Ecstasy and was first patented in Germany in 1912 as a potential appetite suppressant though it was used as a psychotherapeutic tool in the late '70s and started to become available on the street. It gained wider popularity and at the time, it was banned by the DEA (Drug Enforcement Agency) in 1985 [6].

Mild to moderate doses of ecstasy produces a euphoric sense of well-being and a feeling of connectedness with and empathy for other people, an enhanced sense of pleasure and self-confidence and increased energy. In overdoses or misuses though, users can experience confusion, disorientation, anxiety, panic attacks, depression, insomnia, perceptual disorders and hallucinations, paranoia and psychosis. MDMA usage develops moderate psychological dependence and tolerance [6, 8, 12, 13].

1.5.3 Hallucinogens

Hallucinogen substances can be natural or synthetic origin and have no medicinal use because they have a violent effect on a person's mental activity, perceptual abilities and level of consciousness. The name is due to fact that they cause hallucinations, visions and on impression of depersonalization.

1.5.3.1 LSD (Lysergic Acid Diethylamide)

LSD is one of the potent hallucinogenic substances known. It was first discovered in 1938 while researching blood stimulants [6]. Because of its structural similarity to a chemical present in the brain and the similarity of its effects to certain aspects of psychosis, LSD was used for a time as a research tool to study mental illness.

There has been no licit use for LSD in over 20 years and LSD products encountered today on the illicit market are produced only in clandestine laboratories.

In its base form, LSD is a liquid and it is frequently served by dropping the liquid on to a small absorber like paper, sugar cubes or pharmacologically inert powders.

During the first hour after LSD ingestion, the user may experience visual changes with extreme changes in mood. In the hallucinatory state, the user may suffer impaired depth and time perception accompanied by distorted perception of the size and shape of objects, movements, color, sound, touch and user's own body image. Flashbacks have been reported days or even months after taking the last dose.

LSD creates no physical but moderate psychological dependence and tolerance [6, 8, 14].

1.5.3.2 Cannabis

Cannabis Sativa L., the hemp plant grows wild or cultivated in many areas of the world, with records dating back to at least the 9th century BC [6]. It's flowering or fruiting tops contain the psychoactive components delta-9-tetrahydrocannabinol (THC), cannabinol (CBN) and cannabidiol (CBD). Delta-9-tetrahydrocannabinol owns the most characteristic of psychoactive effects of the plant.

Cannabis is a very versatile plant; a strong fiber produced from the stem has been used to make rope, paper and cloth; the dried leaves and flowers are used as marijuana for their psychoactive or medicinal properties; the roots of the plant have been used medicinally; and the seeds are used for oil and animal feed.

In illicit market, cannabis is usually used as an herbal product (commonly known as marijuana), cannabis resin and liquid cannabis. Cannabis resin is formed by collecting the resin containing parts via some special methods to increase the THC content of the final product. On the other hand, liquid cannabis is produced by the extraction of THC from the plant by using chemical solvents.

Cannabis usage leads to time, color, and spatial perception distortions, a dreamy euphoria, excitement, laughter and increased appetite. Panic attacks and paranoia sometimes occur, particularly in new users. It develops no physical dependence but moderate psychological dependence and tolerance.

Marijuana has shown promise in many areas of medicine including as an anti-epileptic, as a treatment for nausea and other side effects of chemotherapy and AIDS drugs, as one of the only known treatments for glaucoma and as a treatment for asthma. Recently, the drug has also been used as an experimental treatment for anorexia nervosa [6, 8, 15].

1.6 THEORY OF THE METHOD USED IN THE STUDY

1.6.1 Infrared Spectrometry

The infrared spectrometry deals with the interaction of infrared (IR) radiation with matter. The infrared region of the electromagnetic spectrum covers the wavenumbers from 12800 cm^{-1} to 10 cm^{-1} and is further subdivided into near, mid and far-infrared regions in terms of applications and instrumental designs. The mid-infrared region extends from 4000 cm^{-1} to 200 cm^{-1} and covers most of the applications.

Absorption of infrared radiation causes transitions between vibrational energy levels of a molecule, which are also accompanied by several rotational motions. Vibrational energy corresponds to the vibrations of atoms about the mean center of their chemical bonds, whereas rotational energy changes occur due to tumbling motion of a molecule.

In order to absorb IR radiation, a molecule must undergo a net change in dipole moment as a consequence of its vibration. Homonuclear diatomic molecules do not absorb IR radiation. On the other hand, complex mixtures give rise to very crowded spectra in which assigning of bands to specific functional groups is very difficult. Therefore, IR Spectrometry is mostly useful for pure substances.

Absorption spectrum is a graph of wavelength (λ) vs. absorbance (A), but for IR region usually it is represented as wavenumber (in cm^{-1}) vs. percent transmittance (%T). Transmittance is the ratio of the radiant power (P) transmitted by a sample to the radiant power incident on the sample (P_0), i.e.

$$T = \frac{P}{Po}$$

Transmittance is related with absorbance as;

$$A = -\log T \ .$$

There are two types of molecular vibrations, stretching and bending. Stretching vibration is the movement along the bond axis and it causes the interatomic distance become increase or decrease. Bending motion, on the other hand, is the changing of bond angles.

When an IR spectrum is examined, three properties are considered. These are the number, the positions and the intensity of absorption bands resulted from a molecule.

The theoretical number of bands, i.e. fundamental vibrations, present for a molecule can be calculated from the formulas 3N-6 and 3N-5 for non-linear and linear molecules, respectively. The formulas are derived from the statement that, a molecule has three degrees of freedom on the x, y and z coordinates and molecules with N atoms have 3N degrees of freedom. However, in a non-linear molecule three of these motions translate the whole molecule on the x, y and z axes, while another three rotate the molecule on these axes, leaving 3N-6 motions for vibrational changes. On the other hand, for a linear molecule rotation around one of these axes does not affect the molecule and it has 3N-5 degrees of freedom for vibrations.

The spectrum of a molecule may contain fewer or more bands than expected. The reason for having fewer bands is due to the degenerate vibrations, resulted from the absorptions of common groups at the same wavenumber. In addition, some of the fundamental bands can be too weak to be observed or so close that they coalesce.

A greater number of bands can be present also when overtones, multiples of a given frequency, and combination bands, differences or sums of two other vibrations, are accompanied to the spectrum.

The position of absorption bands depends on the relative masses of the atoms; the force constants of the bonds and the geometry of the atom and it can be calculated from the Hooke's law.

For a diatomic molecule A-B, the wavenumber (in cm^{-1}) of the absorption is:

$$\bar{\nu} = \frac{1}{2\pi c}\sqrt{\frac{K}{\mu}} = 5.3x10^{-12}\sqrt{\frac{K}{\mu}} \qquad [16]$$

$\bar{\nu}$: wavenumber (cm^{-1})

c: the velocity of light (cm/s)

K: force constant of the bond (N/m)

μ: the reduced atomic mass of the atoms A and B (kg) ($\mu = \frac{MaMb}{Ma + Mb}$)

In practice, however, specific groups do not absorb at a definite wavenumber due to the effects of local environment of the group, but their band positions are given over a range of wavenumbers.

There are two useful regions in the IR spectrum. The group frequency region encompasses 3600 to 1200 cm^{-1} region, where the identical functional groups absorbs in a defined range of wavenumbers. Other important part is called fingerprint region from 1200 to 700 cm^{-1} and it reflects the absorptions from the skeletal structure of the molecule. Small differences in the structure result in significant changes in fingerprint region so it leads to great evidence for the identity of the compounds yielding the spectra. Only stereoisomers absorb exactly in the same way in this region [16-18].

1.6.2 Fourier Transform Infrared (FTIR) Spectrometry

There are several instrumental designs for IR absorption measurements. Dispersive instruments employ monochromator; nondispersive instruments employ filters for wavelength selection. Another design is the multiplex type, which employs an interferometer and uses Fourier Transform for signal encoding. In multiplex designs, many sets of information are transported simultaneously through a single channel.

An interferometer splits a beam of radiation into two and causes them to travel different distances, which is called optical path difference. Thereafter, two beams are combined in destructive and nondestructive means; by changing the optical path difference an interferogram is measured. Therefore interferogram is a plot of detector response versus optical path difference that is then Fourier transformed to give infrared spectra.

FTIR has several advantages over other IR designs. The first one is the *Fellgett* or *multiplex advantage* that is based on the fact that in FTIR instruments all wavelengths reach to the detector simultaneously. Therefore multiple scans of the sample can be done in a very short time and signal to noise ratio is improved. In addition, FTIR has high resolution, wavelength accuracy and precision so that signal averaging from multiple scans are possible and the result is the improved signal to noise ratio.

The second advantage is the *Jaquinot* or *throughput advantage*; FTIR systems have no limitations of entrance slit to reduce the radiation; as a result, the power of radiation reaching to the detector is much greater and hence the signal to noise ratio is improved.

The final advantage is the lack of interference from stray radiation since each IR frequency is modulated at a different frequency in an interferometer.

On the other hand, FTIR has a disadvantage. Since it is a single beam instrumental system, background measurement is done at a different time from the sample measurement; therefore a change in the environment can affect the final spectrum [16, 19].

1.6.3 Attenuated Total Reflectance Technique

FTIR spectra can be obtained from the transmission or reflection of IR radiation from the sample. In transmission measurements, the IR beam passes through the sample and it is applicable to solids, liquids, gases and polymers that allow transmission of source light. Reflectance measurements are based on the reflection of IR radiation on the sample. Reflectance techniques are classified as diffuse reflectance and Attenuated Total Reflectance (ATR).

ATR is especially useful for opaque solid samples regardless of thickness with a minimum time of preparation. Thin films, pastes, powders, suspensions, paper, coatings, and fibers can easily be analyzed with ATR technique.

The technique depends on the fact that when a beam of radiation passes from a denser medium to a less dense medium, reflection occurs. The fraction of the incident beam that is reflected increases as the angle of incidence becomes larger and beyond a critical angle, total radiation is internally reflected. However, the radiation penetrates somehow into the less dense medium before being totally reflected at the interface. The extent to which the radiation penetrates to less dense medium is called as *depth of penetration* and it is given by the following equation:

$$DP = \frac{1}{2\pi W N_C (\sin^2\theta - N^2{}_{sc})^{1/2}} \qquad [19]$$

DP: Depth of penetration, cm

W : Wavenumber of the radiation, cm^{-1}

N_c : Refractive index of crystal

Θ : Angle of incidence at the interface

N_{sc} : Ratio of refractive indices of sample and crystal (N_{sample} / $N_{crystal}$)

The penetrating radiation is named as evanescent radiation. If the less dense medium absorbs the evanescent radiation, attenuation of the beam occurs at wavelength of absorption bands, which is so called *Attenuated Total Reflection*.

According to above phenomenon, in ATR measurements sample is pressed against an internal reflection element with a high refractive index and the absorption of evanescent radiation occurs.

In order to obtain ATR effect, the refractive index of the internal reflection element should be greater than that of sample. Commonly used materials with high refractive indices are thallium bromide/iodide (KRS-5), zinc selenide, germanium and diamond crystals; their properties are shown in Table 1.1.

Table 1.1 Properties of Commonly Used ATR Crystal Materials. [17]

ATR Crystal Material	IR Transmission Range (cm^{-1})	Refractive Index at 2000 cm^{-1}
KRS-5 (Thallium Bromide/Iodide)	5000-250	2.38
Ge	5000-600	4.01
ZnSe	5000-500	2.40
Diamond	5000-10	2.40

When ATR spectrum of a sample is compared with its transmission spectrum, it is seen that bands in high wavenumbers (shorter wavelengths) are less intense. This occurs because depth of penetration is directly proportional with wavelength and at shorter wavelengths penetration decreases. Therefore, ATR spectrum is usually corrected when it is necessary to compare it with a transmission spectrum [16-19].

1.7 LITERATURE SURVEY

Levy et al. (1996) studied illicit heroin samples by FTIR with KBr pellet technique. Among the 2977 samples, they have distinguished five major groups according to having different additives. They also grouped the samples into the five districts of the country where each area has a different distribution of additives [20].

Koulis et al. (2000) collected spectra of 455 controlled and non-controlled drug standards with FTIR–ATR technique and they constituted a spectral library [21].

Ravbery (1987) proposed method for the quantitative determination of heroin and cocaine samples by using FTIR-ATR technique. Standard samples and prepared synthetic mixtures were quantitatively studied as KBr pellets.

For cocaine, two strong carbonyl absorption bands at 1730.9 cm^{-1} and 1712.8 cm^{-1} were selected and the effects of base and salt form and additives like procaine, mannitol, and lactose on the shape of the peaks were investigated. For heroin, on the other hand, the carbonyl peaks at 1763.0 cm^{-1} and 1736.0 cm^{-1} were selected and same variables were studied [22].

Ryder (2002) studied 85 solid samples containing illegal drugs by using Near Infrared and Raman Spectroscopy. Samples were prepared from the standard materials to reflect the real illicit drugs. The results were evaluated with chemometric methods and classification had been done according to type of the drug [23].

Ryder et al. (1999) studied cocaine, MDMA and heroin samples by near-IR and Raman Spectroscopy in order to make a discrimination between them. In addition, effect of various diluents and additives on Raman Spectra was investigated and the results were evaluated with Partial Least Square algorithm [24].

Beckstead and Neville (1988) investigated the ethyl acetate complex formation of O^6-acetylmorphine during the basic extraction of heroin samples. By examining the IR spectra of extracts, it is concluded that complex formation lead to the additional peaks that are closely similar to that of heroin and may lead to misidentification of the samples [25].

Heagy (1970) proved that infrared spectra could be used as an easy and rapid method to differentiate the optical isomers of amphetamine. It is observed that in the 800-600 cm^{-1} region of the spectrum d-, dl- and l- forms of amphetamine shows distinguishable absorbance characteristics [26].

Sondermann and Kovar (1999) studied ecstasy tablets with near infrared spectroscopy and applied partial least square regression models to differentiate main ingredients (MDMA or MDA), diluents and additives [27].

1.8 AIM OF THE STUDY

From the forensic science point of view, drug analysis is referred as the identification of contents and determination of percent amounts of active ingredients. In addition, sophisticated works on additives, diluents, specific impurities and some physical properties give very valuable information about drugs. It is known that chemical processes applied in clandestine production show close similarity around the same geographical regions, besides similar precursors and additives are usually used. Thus, identification of specific characteristics of drugs can help for making correlations between separate seizures, thereafter drug

trafficking ways can be followed, and furthermore the origin of drugs may be identified.

There are so many articles in the literature about drugs. Although, TLC and GC-MS for qualitative analysis and GLC and HPLC for quantification are commonly used ones, new drugs and the increasing number of samples have forced the scientist to employ powerful hyphenated and fast techniques like LC-MS, LC-MS-MS, GC-FTIR and Capillary Electrophoresis.

When working with chromatographic methods, specific extraction methods should be used for the identification of active ingredient and for each of other substances. In addition, chromatography is usually limited with the solubility of target compounds. Moreover, it is relatively time consuming and expensive.

In this study, the advances of FTIR technique have been exploited for the identification of drugs as for being a fast method and requiring almost no preparation work. It has been aimed to form an IR spectral database that could be used in differentiating various drugs and their additives by means of a simple method. Another scope of the study was to create another spectral database for illicit drugs seized in recent years; thus by comparing a newly handled drug with this database might indicate a correlation between them.

The drugs covered in this study have been the ones that most widely encountered in Turkey, namely morphine, heroin, amphetamine, MDMA and cocaine. Despite, cannabis is the most commonly cultivated drug; it has not been included because it can be simply identified by the detection of specific microscopic characters. In addition, the commercially available depressant drugs like benzodiazepines and barbiturates were not included because they are not produced illicitly.

CHAPTER II

EXPERIMENTAL

2.1 Chemicals and Reagents

2.1.1 Standards

Standards were supplied from Lipomed and Sigma-Aldrich and their catalog numbers are indicated in the Table 2.1.

Table 2.1 Specifications of Reference Standards

Reference Standard	Producer	Catalog Number
Heroin ($C_{21}H_{23}NO_5.HCl.H_2O$)	Lipomed (Certificated HPLC Purity 89.33 %)	M-29-HC
Cocaine ($C_{17}H_{21}NO_4.HCl$)	Lipomed (Certificated HPLC Purity 99.89 %)	COC-156-HC
d,l-amphetamine ($C_{18}H_{26}N_2.H_2SO_4$)	Sigma-Aldrich	A 1263
d,l-MDMA ($C_{11}H_{15}NO_2.HCl$)	Lipomed (Certificated HPLC Purity 99.66 %)	MDM-94-HC
d,l-methamphetamine ($C_{10}H_{15}N.HCl$)	Lipomed (Certificated HPLC Purity 99.44 %)	AMP-301-HC
Morphine Base ($C_{17}H_{19}NO_3$)	TMO (Toprak Mahsülleri Ofisi) Bolvadin Plant Alkaloid Factory	> 95 % (Private discussion)
Morphine Sulfate ($C_{34}H_{40}N_2O_{10}S.5H_2O$)	Sigma-Aldrich	M 8777
Morphine Hydrochloride ($C_{17}H_{19}NO_3.HCl.H_2O$)	Lipomed	M 35-HC
Narcotine ($C_{22}H_{23}NO_7.HCl$)	Sigma-Aldrich	N 9007
Papaverine ($C_{20}H_{21}NO_4.HCl$)	Sigma-Aldrich	P 3510
Paracetamol ($C_8H_9NO_2$)	Sigma-Aldrich	A 7085
Caffeine ($C_8H_{10}N_4O_2$)	Sigma-Aldrich	C-7731
Lactose ($C_{12}H_{22}O_{11}.H_2O$)	Sigma-Aldrich	L-3625

2.1.2 Samples

During the study, a total of 76 illicit drug samples, containing several additives and active drugs in varying percent amounts, were analyzed. Illicit samples were obtained from the Gendarme Criminal Laboratory Chemistry Branch. They were selected in order to reflect a wide range of variety in terms of their compositions.

However, as for the active drugs only heroin, morphine, cocaine, amphetamine and MDMA were studied because they are the most commonly encountered drugs in Turkey. On the other hand, although these drugs can contain many other additives, only the presence of caffeine, paracetamol and lactose were examined, again due to the same reason of having a wide usage.

2.2 Instrumentation and Apparatus

All drug standards and samples were analyzed with FTIR-ATR System. Quantitative analyses of the samples were done by HPLC (High Pressure Liquid Chromatography) and GC-FID (Gas Chromatography-Flame Ionization Detector). Qualitative analyses of the samples were done by GC-MSD (Gas Chromatography-Mass Selective Detector).

2.2.1 FTIR

Perkin Elmer FTIR Spectrometer, Model Spectrum One was used to collect the spectra of drug standards and illicit drug samples. Method parameters are shown in Table 2.2.

Table 2.2 Parameters of FTIR

Detector	MIR-TGS (Mid Infrared- Triglycerine Sulphate)
Source	Silicon Carbide (Globar)
IR Accessory	Universal ATR
Resolution	4 cm^{-1}
Scan Range	4000-650 cm^{-1}
Scan Number	32
Force applied onto samples	145-150 Newton (Corresponding pressure is $5.13x10^6$ – $5.31x10^6$ N/m^2)
Diameter of pressure arm	6.0 mm

All spectra were obtained by using an ATR accessory. A schematic representation of the ATR used in the study is shown in Figure 2.1.

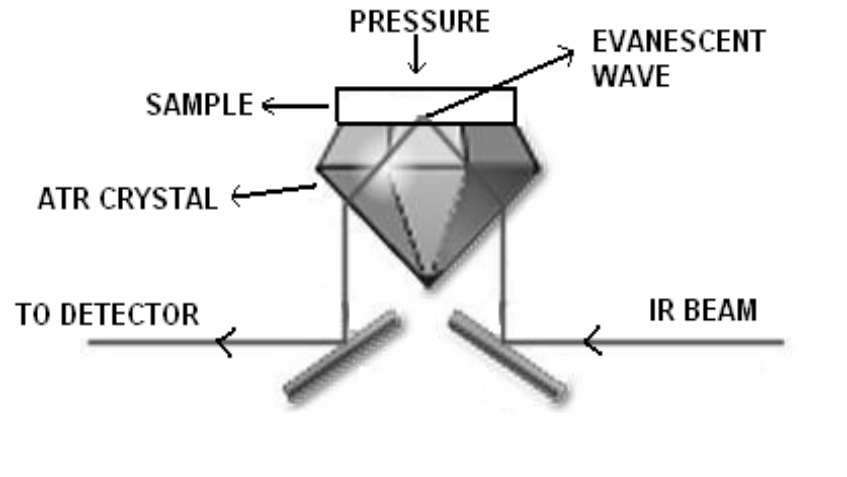

Figure 2.1 Schematic representation of ATR technique [28].

The ATR accessory composed of a single reflection Diamond crystal with a refractive index of 2.40 and reflection angle of 45^0. A composite of ZnSe is covered at the bottom of crystal to prevent the radiation loss. [29].

2.2.2 GC-MSD

Qualitative analyses of the samples were done with Agilent Technologies 6890 N GC-MSD System. Method parameters are shown in Table 2.3.

Table 2.3 Parameters of GC-MSD Method.

Column	Cross-linked %5 phenyl %95 dimethylpolysiloxane (Hewlett-Packard HP-5MS) 0,25 mm in internal diameter, 30 m in length and 0.25 µm in film thickness
Carrier Gas	Helium with 1.0 mL/min constant flow rate
Injection Port T	265 ^{0}C
MSD transfer line T	280 ^{0}C
MS Quad T	150 ^{0}C
MS Source T	230 ^{0}C
Solvent Delay	4.00 min.
Column T	Initial T:100 , initial time:1 min., ramp 20 ^{0}C /min , final T:280 ^{0}C, hold time:20 min
Injection volume	1.0 µL
Split Ratio	70:1
Mass Range	40.0-550.0 amu

2.2.3 HPLC

Quantitative analyses of Morphine, Heroin, Amphetamine and MDMA were done with Agilent 1100 Series Reverse phase HPLC system. Parameters of the method are shown in Table 2.4.

Table 2.4 Parameters of HPLC Method

Column	Waters bondapak C-18, 30 cm in length, 3.9 internal diameter
Detector	UV Diode Array Detector
Wavelength	218 nm (selected for best absorbance)
Flow rate	1 ml / min.
Mobile phase	A: Phosphate buffer (pH 2.26), B: Methanol
Gradient conditions (for morphine and heroin)	Time % Methanol % Buffer 0 5 95 20 40 60 27 40 60 32 60 40 37 60 40 42 5 95
Gradient conditions (for amphetamine and MDMA)	Time % Methanol % Buffer 0 5 95 20 40 60 25 5 95 30 5 95
Injection solution	Water, Acetonitrile, Acetic Acid (89:10:1) pH:3,71
Injection volume	20 μL

2.2.4 GC-FID

Quantitative analyses of cocaine samples were done with Agilent 5890 GC System. Parameters of the method are shown in Table 2.5

Table 2.5 Parameters of GC-FID Method

Detector	Flame Ionization detector (FID)
Carrier Gas	Helium
Column	5% Phenyl 95% dimethylpolysiloxane (HP-5), 30 m in length, 0.32 mm internal diameter, 0.25 μm film thickness
Injection port T	265 ^{0}C
Column T	Initial T: 100 ^{0}C, Initial Time : 1.0 min., ramp: 20 ^{0}C / min, final T:280 ^{0}C, hold time 20.0 min.
Detector T	280 ^{0}C
Internal Standard	n-octacosane
Injection volume	1.0 μL

2.3. Procedures

2.3.1 FTIR

In IR spectrometry; solid samples are usually sampled as KBr disc or Nujol mull techniques, which give good spectra and compensate inhomogeneity problems. However, both techniques require time for preparation and do not practical as compared to ATR sampling.

In the study, powdered samples were directly applied onto ATR crystal. During ATR sampling one of the most important parameters is the particle size of the sample. Samples should be finely powdered to get the best contact with the crystal and obtain the best homogeneity.

All standards and samples were ground by using an agate mortar and pestle for about 2 minutes that was an adequate time for obtaining a fine powder.

With the help of the pressure arm on the ATR accessory, 145-150 N force was applied onto samples to get a good contact with the crystal surface. The application of force leads to a thin film that the final thickness of the samples was not greater than 1.0 mm.

IR spectra were obtained in % transmission mode, however when the comparison of band intensities were needed then they were transformed to absorbance mode by using the software.

Background spectra were collected for every 5 samples.

The crystal surface was cleaned with isopropyl alcohol by using a piece of cotton.

IR searches of spectra were done by using an Euclidian search, which is one of the possible searching tool in the software and it is based on the comparison of spectra shapes. The best spectrum shape match appears on the top of the hit list.

Hit lists can also be generated in other criterions like Possible Structural Unit score and Peak match score [30].

However, the best results were obtained by using Euclidian search.

CHAPTER III

RESULTS AND DISCUSSIONS

3.1 Optimization of FTIR Parameters

3.1.1 Scan Number and Holding Time

In order to optimize the scan number, standard Heroin Hydrochloride salt in powder form was studied by applying different scan numbers and for each of them four replicate measurements were done. Results are shown in Table 3.1

Table 3.1 Variation of %T with Number of Scans

Scan Number	% T at 1759 cm^{-1}	Evaluation of Results	% T at 1735 cm^{-1}	Evaluation of Results
8 (1)	71.66	Mean: 70.82 Standard Deviation:1.22	54.06	Mean: 53.74 Standard Deviation:2.22
8 (2)	71.72		56.73	
8 (3)	70.79		52.42	
8 (4)	69.10		51.75	
16 (1)	69.02	Mean: 71.54 Standard Deviation:2.19	51.58	Mean: 54.96 Standard Deviation:3.22
16 (2)	73.11		57.94	
16 (3)	70.43		52.85	
16 (4)	73.62		57.47	
32 (1)	71.65	Mean: 70.28 Standard Deviation:1.62	54.21	Mean: 51.88 Standard Deviation:2.76
32 (2)	70.28		51.70	
32 (3)	71.18		53.54	
32 (4)	68.01		48.05	
64 (1)	68.17	Mean: 71.46 Standard Deviation:4.07	51.06	Mean: 54.39 Standard Deviation:5.39
64 (2)	71.07		53.10	
64 (3)	69.32		51.06	
64 (4)	77.30		62.35	
124 (1)	75.91	Mean: 72.94 Standard Deviation:2.75	60.45	Mean: 56.00 Standard Deviation:4.02
124 (2)	69.32		50.86	
124 (3)	72.74		55.38	
124 (4)	73.80		57.33	

Another parameter in relation with the percent transmittance value is the time elapsing under pressure; this parameter will be called as *holding time*. As the time is prolonged under pressure, particles come closer and a better contact with the crystal is obtained. To investigate the time needed to obtain the best intensities, the spectra of standard Heroin Hydrochloride salt in powder form were collected at every 5 minutes up to 20 minutes using the same scan number and with four replicate measurements. Results are shown in Table 3.2.

Table 3.2 Variation of % T with Holding Time, Number of Scans is 32.

Holding time	% T at 1759 cm^{-1}	Evaluation of results	% T at 1735 cm^{-1}	Evaluation of results
5 min (1)	73.19	Mean: 72.82 Standard deviation:1.49	57.25	Mean: 55.92 Standard deviation:2.39
5 min (2)	72.19		54.91	
5 min (3)	71.21		53.08	
5 min (4)	74.70		58.42	
10 min (1)	73.18	Mean: 72.80 Standard deviation:1.52	57.23	Mean: 55.90 Standard deviation:2.46
10 min (2)	72.17		54.93	
10 min (3)	71.14		52.96	
10 min (4)	74.70		58.51	
15 min (1)	73.15	Mean: 72.79 Standard deviation:1.52	57.23	Mean: 55.86 Standard deviation:2.45
15 min (2)	72.17		54.87	
15 min (3)	71.13		52.92	
15 min (4)	74.71		58.40	
20 min (1)	73.17	Mean: 72.79 Standard deviation:1.53	57.34	Mean: 55.89 Standard deviation:2.47
20 min (2)	72.17		54.90	
20 min (3)	71.11		52.90	
20 min (4)	74.71		58.41	

In order to see the differences between the data sets for various scan numbers and holding time statistical evaluation was applied according to the following relation;

$$\left| \overline{X}_1 - \overline{X}_2 \right| < \pm \, t\, s_{pooled} \sqrt{\frac{N_1 + N_2}{N_1 N_2}} \qquad [31]$$

$\overline{X_1}$ and $\overline{X_2}$ are the mean values of two sets to be compared, N_1 and N_2 are respective number of measurements.

If the difference between the mean values of two experimental data sets is smaller than the calculated value on the right side of the equation, then there is no significant difference between the two mean values.

s_{pooled} is the combined standard deviation for two data sets and can be calculated from the formula;

$$s_{pooled} = \sqrt{\frac{\sum_{i=1}^{N_1} \left(X_i - \overline{X}_1\right)^2 + \sum_{j=1}^{N_2} \left(X_j - \overline{X}_2\right)^2}{N_1 + N_2 - 2}} \qquad [31]$$

Comparison of the scan numbers of 32 and 124 and holding time of 5 and 20 minutes are shown in the Table 3.3. These were selected as the sets with lowest and highest mean values.

Table 3.3 Statistical Evaluations of the Results.

	For scan numbers of 32 and 124		For holding time of 5 min and 20 min.	
	At 1759 cm^{-1}	At 1735 cm^{-1}	At 1759 cm^{-1}	At 1735 cm^{-1}
t (for 95% confidence level and 6 degree of freedom)	2.45	2.45	2.45	2.45
S_{pooled}	2.26	4.21	1.51	2.41
$t\, s_{pooled} \sqrt{\frac{N_1 + N_2}{N_1 N_2}}$	3.91	7.29	2.62	4.18
$\left\| \overline{X}_1 - \overline{X}_2 \right\|$	2.66	4.12	0.03	0.03

As it can be seen in the table, all mean value differences are smaller than the calculated values which indicates variations in scan number and holding time do not result in any improvement in band transmittances. Therefore, it was decided to use an average scan number of 32 with zero holding time.

On the other hand, during the preliminary studies it was observed that the regime of tightening has a notable effect on the band intensities; i.e. increasing the applied force slowly up to 150 Newton, and then immediately relaxing the pressure arm till 100 Newton and thereafter rapidly rising the applied force again to 150 Newton gave the best results. It can be suggested that during the relaxation process, air between the particles is forced to come out further and subsequent force application ensures that the particles get together closer leading to a better contact with the crystal surface.

All IR spectra were obtained so that minimum transmittance was not less than 25 % to ensure a healthy signal to noise ratio.

3.1.2 Particle Size

It was observed that particle size has a great effect on FTIR-ATR spectra. Naturally, smaller particle sizes result in better contact with ATR crystal; sensitivity is better.

It could be suggested to sift the samples in order to decrease the particle size, however these drug samples consist of several components with their respective particle size distributions; consequently a sifting procedure would result in a mixture that may not be representative of the original sample. In other words, the component with the smallest particle size would be present in the final sample with an enriched concentration; the final sample will not be representative.

The most convenient way to decrease the particle size was grinding the samples until a fine powder is obtained using a minimal period that is 2 minutes for this study. A grinding procedure that is excessively long would result in several undesired effects. It has been reported that grinding may alter the composition of the sample and may result in a phase transformation from crystalline to amorphous state due to pressure applied or direct frictional heating [32]. Besides, extensive grinding would make the procedure longer that is in contrast with the general purpose of the study.

3.1.3 Effect of Humidity on Spectra

Water contributes to the spectra with O-H stretching bands in 3600-3200 cm^{-1} region. The effect of humidity and crystal water on the spectra of drugs in accordance with IR search results was examined with several samples by collecting the spectrum before and after drying (2 hours at 100 ^{0}C in oven) the sample. It was observed that although water causes an obvious change in spectrum regarding visual examination, its presence does not cause any significant influence on the computer search results. Therefore, it was decided that there is no need to dry the samples before collecting the spectra. Effect of humidity on heroin spectrum is shown in Figure 3.1. The searching software decided both spectra as Heroin base.

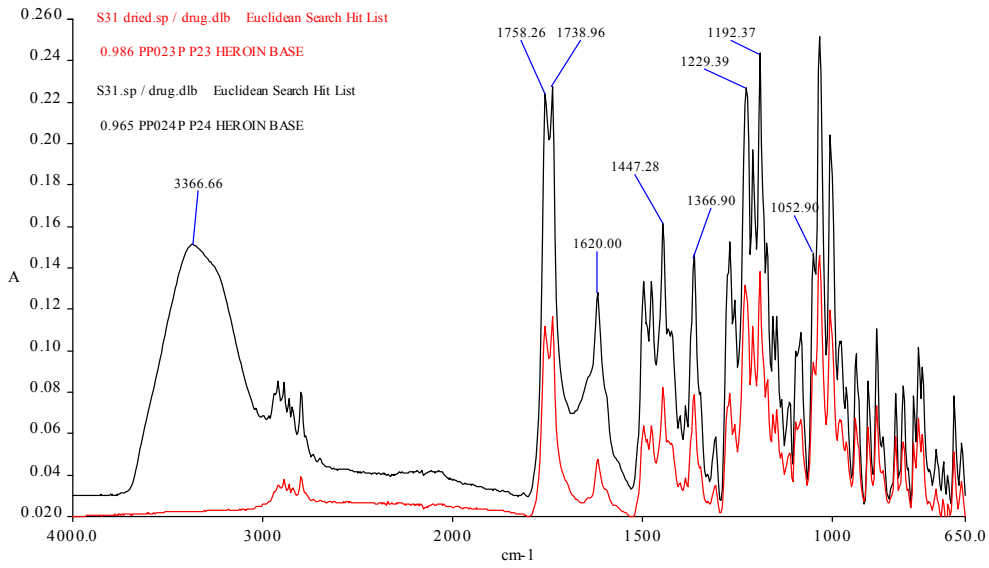

Figure 3.1 Effect of humidity on IR spectrum of Heroin (Black: IR-ATR Spectrum of S31 before drying, Red: IR-ATR Spectrum of S31 after drying)

3.2. Constitution of Spectral ATR Database for Drug Standards

In the first part of the study, an FTIR-ATR spectral database was constituted to identify the compositions of illicit samples.

Illicit samples contain active drug and additives in varying percent amounts. Therefore, a successful IR database should comprise possible alternatives of different compositions as well as the pure standards.

In order to constitute the database for standards, pure standards and secondary standards with known percent concentrations were used. The mixtures of standards were prepared to simulate the illicit samples.

3.2.1 Relation Between Percent Concentration and Band Intensity

In order to find a correlation between percent concentration of the drug in the sample and its characteristic absorption bands, several sets of samples with varying percent amounts of drugs were examined. It was expected that increasing the percent amount of the drug should enhance its absorption, and it was thought

that identification of the samples in known concentration ranges might be possible, but the results were not as expected.

The first set contained three heroin samples with different heroin percent amounts, i.e., 0.4 %, 19.9 % and 63.7 %, shown in Figure 3.2.

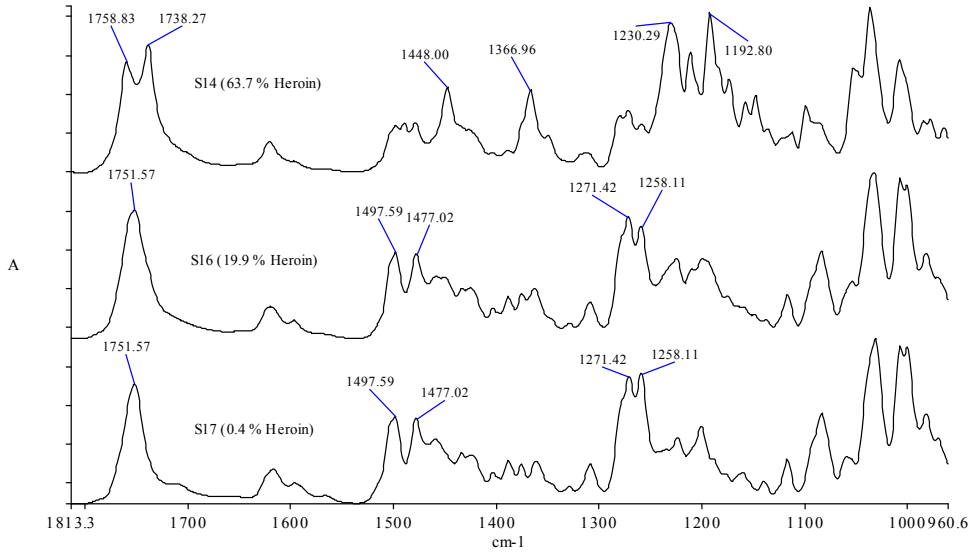

Figure 3.2 Effect of Heroin concentration on the appearance of carbonyl peaks.

It was observed that percent amount of heroin in the sample has a direct effect on the appearance of carbonyl stretching bands; low concentrations (0.4 %) result in a single peak at 1751 cm^{-1} as a significant contribution from narcotine only and spectrum resembles naturally to that of narcotine, which is the second most abundant component in the sample. On the other hand, when the heroine concentration is large (63.7 %), both peaks appear as contribution from heroine at 1759 cm^{-1} and 1738 $cm^{-}1$. However, for sample 16 (S16) although concentration of heroin is large enough (19.9 %), carbonyl stretching of narcotine is still very dominant and it shields the heroin peaks.

Consequently, it could not be possible to make a direct correlation between the percent amount and intensity because other components of the sample have a great influence on the spectra.

Besides, in another set of samples the effect of percent amount of caffeine was investigated by successively increasing the caffeine concentration in heroin sample. It was expected that an increase in caffeine concentration would enhance its absorbance bands with a direct correlation. However, again no relation between concentration and characteristic band intensities could be made.

As a result, for the database it was decided to include different percent combinations of drugs and additives so as to cover all possible alternatives of illicit samples but their respective percent concentrations were not noted in the final form of the database. Consequently, it was just aimed to detect whether the sample contains an additive or not in any amount.

3.2.2 FTIR Spectral Database Content

Final form of the database is shown in Table 3.4 in which Drug standards were labelled as “R”, prepared mixtures and secondary standards as “P”. All spectra in the database are shown in the Appendix B from Figures B-3 to B-44. Compositions of secondary standards below have been determined by HPLC.

Table 3.4 Database Content.

Label	Drug	Composition (w/w %)
R1	Heroin Hydrochloride	100.0 %
R2	Acetyl Codeine Base	100.0 %
R3	Caffeine	100.0 %
R4	Cocaine Hydrochloride	100.0 %
R5	Codeine Base	100.0 %
R6	d,l-amphetamine Sulfate	100.0 %
R7	d,l- MDMA Hydrochloride	100.0 %
R8	d,l-methamphetamine Hydrochloride	100.0 %
R9	Morphine Base	100.0 %
R10	Narcotine Hydrochloride	100.0 %
R11	Papaverine Hydrochloride	100.0 %

Table 3.4 (Continued)

R12	Paracetamol	100.0 %
R13	Morphine Hydrochloride	100.0 %
R14	Morphine Sulfate	100.0 %
P1	Heroin, Caffeine	52.2 % Heroin, 15.2 % Caffeine
P2	Heroin, Caffeine	55.7 % Heroin, 10.1 % Caffeine
P3	Heroin, Caffeine	58.6 % Heroin, 5.4 % Caffeine
P4	Heroin, Caffeine	60.0 % Heroin, 3.2 % Caffeine
P5	Heroin, Caffeine	61.1 % Heroin, 1.5 % Caffeine
P6	Heroin, Caffeine	34.9 % Heroin, 3.0 % Caffeine
P7	Heroin, Caffeine	34.1 % Heroin, 5.3 % Caffeine
P8	Heroin, Caffeine	32.4 % Heroin, 10.0 % Caffeine
P9	Heroin, Caffeine	30.3 % Heroin, 15.8 % Caffeine
P10*	MDMA, Caffeine	30.7 % MDMA, 26.9 % Caffeine
P11*	MDMA, Paracetamol	29.5 % MDMA, 29.5 % Paracetamol
P12*	MDMA, Lactose	29.2 % MDMA, 30.5 % Lactose
P13*	MDMA, Caffeine, Paracetamol	24.0 % MDMA, 23.3 % Caffeine, 19.5 % Paracetamol
P14*	MDMA, Caffeine, Lactose	23.9 % MDMA, 21.4 % Caffeine, 21.6 % Lactose
P15	Amphetamine, Caffeine	66.4 % Amphetamine, 33.5 % Caffeine
P16	Amphetamine, Paracetamol	66.8% Amphetamine, 33.1 % Paracetamol
P17	Amphetamine, Lactose	71.4 % Amphetamine, 28.6 % Lactose
P18	Amphetamine, Caffeine, Paracetamol	62.2 % Amphetamine, 17.9 % Caffeine, 19.7 % Paracetamol
P19	Amphetamine, Caffeine, Paracetamol, Lactose	42.4 % Amphetamine, 18.8 % Caffeine, 16.4 % Paracetamol, 22.4 % Lactose
P20	Amphetamine, Caffeine, Lactose	46.6 % Amphetamine, 22.7 % Caffeine, 30.6 % Lactose
P21	Heroin, Caffeine, Paracetamol	43.5 % Heroin, 14.7% Caffeine, 15.0 % Paracetamol
P22	Heroin, Caffeine, Paracetamol	24.7 % Heroin, 18.2 % Caffeine, 13.1 % Paracetamol
P23 [a]	Heroin Base	62.6 % Heroin
P24 [b]	Heroin Base	36.5 % Heroin
P25	Caffeine, Paracetamol	41.4 % Caffeine, 47.6 % Paracetamol
P26	Caffeine, Griseofulvin	12.9 % Caffeine, Griseofulvin
P27 [c]	Morphine Base	10.8 % Morphine

* P10, P11, P12, P13 and P14 were prepared by mixing the powder of an illicit MDMA tablet, containing 42.0 % MDMA, with respective amounts of caffeine, paracetamol and lactose standards.

[a] P23 is an illicit heroin sample containing 62.6 % Heroin, 1.9 % Monoacetylmorphine, 5.1 % Acetyl codeine, 2.3 % Papaverine and 20.6 % Narcotine. It was used to prepare P1, P2, P3, P4, P5 and P21.

[b] P24 is an illicit heroin sample containing 36.5 % Heroin, 9.2 % Monoacetylmorphine, 3.1 % Acetyl codeine, 1.9 % Papaverine and 30.6 % Narcotine. It was used to prepare P6, P7, P8, P9 and P22.

[c] P27 is an illicit morphine sample containing 10.8 % Morphine, 3.5 % Codeine, 1.6 % Papaverine and 7.6 % Narcotine.

3.3 Interpretation of the Spectra

Drug standards have characteristic absorptions, which are very helpful to identify them.

3.3.1 Heroin Spectrum

The major peaks in heroin base spectrum are 1759 and 1738 cm^{-1} (carbonyl stretching), 1447 cm^{-1}, 1366 cm^{-1}, 1230 and 1211 cm^{-1} (acetate C-O stretching), 1192 cm^{-1} and 1052 cm^{-1}.

In heroin hydrochloride spectrum small shifts occur in the peak positions as; 1759 cm^{-1}, 1735 cm^{-1}, 1444 cm^{-1}, 1369 cm^{-1}, 1244 cm^{-1}, 1198 cm^{-1}, 1176 cm^{-1}, 1155 cm^{-1}, and hydrochloride salt formation results in N-H band at around 2600 cm^{-1}.

3.3.2 Cocaine Spectrum

Spectrum of cocaine hydrochloride has absorption peaks at 1728 and 1711 cm^{-1} (carbonyl stretching), 1264 cm^{-1}, 1230 and 1105 cm^{-1} (acetate C-O stretching), 1071 cm^{-1}, 1025 and 729 cm^{-1} (mono substituted benzene stretch) and hydrochloride salt formation is also identical due to the N-H stretching bands around 2530 cm^{-1}.

For cocaine base the major peaks are 1734 cm^{-1}, 1706 cm^{-1}, 1272 cm^{-1}, 1253 cm^{-1}, 1106 cm^{-1}, 1035 and 711 cm-1.

3.3.3 Amphetamine Spectrum

The major peaks in Amphetamine Sulfate spectrum are 1550 cm^{-1}, 1144 cm^{-1} (ionic SO4 stretch), 1050 cm^{-1}, 729 and 698 cm-1 (mono substituted benzene stretch) and N-H stretching of amine salt at 2800-3000 cm^{-1} region.

3.3.4 MDMA Spectrum

In the MDMA Hydrochloride spectrum important peaks are 2710 cm^{-1} (N-H stretching of amine salt), 2458 cm^{-1} (C-H stretching of CH_3 group), 1488 cm^{-1} (C-H bend), 1244 and 1030 cm^{-1} (C-O-C stretching of methoxy group), 930 cm^{-1} (C-O stretching).

3.3.5 Morphine Spectrum

Morphine has characteristic peaks at around 3200 cm^{-1} (O-H stretching), 1471 cm^{-1} (O-H bend), 1442 cm^{-1} (C-C stretch) 1241 cm^{-1}, 1117 cm^{-1}, 1086 cm^{-1}, 941 cm^{-1}, 800 cm^{-1} and 757 cm^{-1}.

3.3.6 Caffeine Spectrum

Caffeine has important peaks at 1693 and 1644 cm^{-1} (carbonyl stretch), 1547 cm^{-1}, 1237 cm^{-1}, 758 cm^{-1} and 743 cm^{-1}.

However, it was observed that when caffeine exists is heroin, its peak positions change as 1698 cm^{-1}, 1656 cm^{-1}, 1550 cm^{-1}, 1230 cm^{-1}, 764 $cm^{-1}$and 745 cm^{-1}.

3.3.7 Paracetamol Spectrum

The major peaks in paracetamol spectrum are 3321 cm^{-1} (N-H stretching), 3108 cm^{-1} (O-H stretching), 1650 cm^{-1} (carbonyl stretching), 1609 cm^{-1} (N-H bend), 1561 cm^{-1}, 1505 cm^{-1}, 1433 cm^{-1}, 1258 $cm^{-1}$and 1224 cm^{-1}.

3.3.8 Lactose Spectrum

Lactose has important peaks at 3260 cm-1 (O-H stretching), 1140 cm^{-1}, 1114 cm^{-1}, 1070, 1018 cm^{-1}, 987 $cm^{-1}$and 875 cm^{-1}.

3.4 Investigating the Effects of Additives on Drug Spectra

Caffeine, paracetamol and lactose when exist in the sample can be identified with the addition of extra bands.

When caffeine exists in the sample its carbonyl absorption bands at 1698 cm^{-1} (or 1693) and 1656 cm^{-1} (or 1644) can easily be identified. The spectra of heroin, amphetamine and MDMA containing caffeine are shown in Figure 3.3, Figure 3.4 and Figure 3.5, respectively.

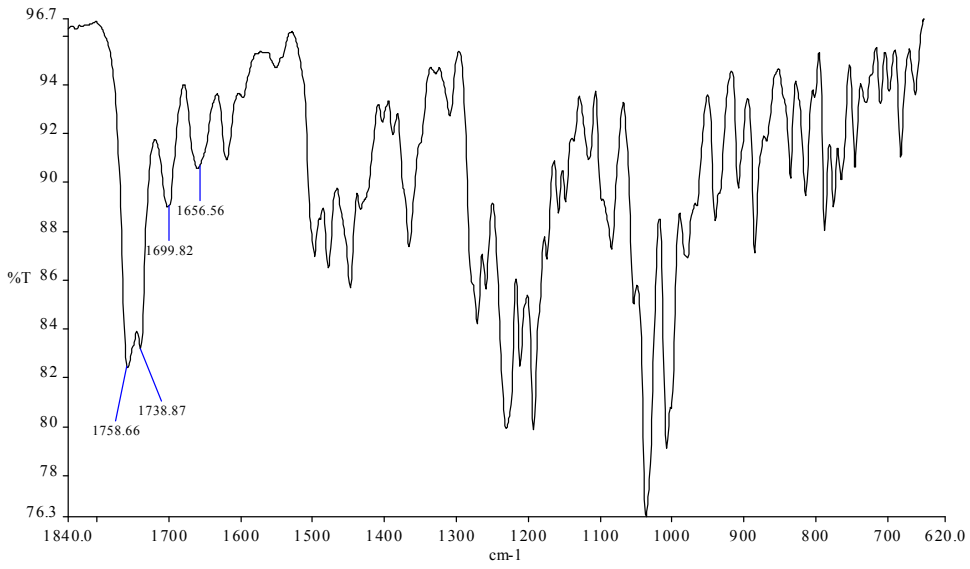

Figure 3.3 IR-ATR Spectrum of Heroin with Caffeine (additional caffeine peaks at 1699 cm^{-1} and 1656 cm^{-1})

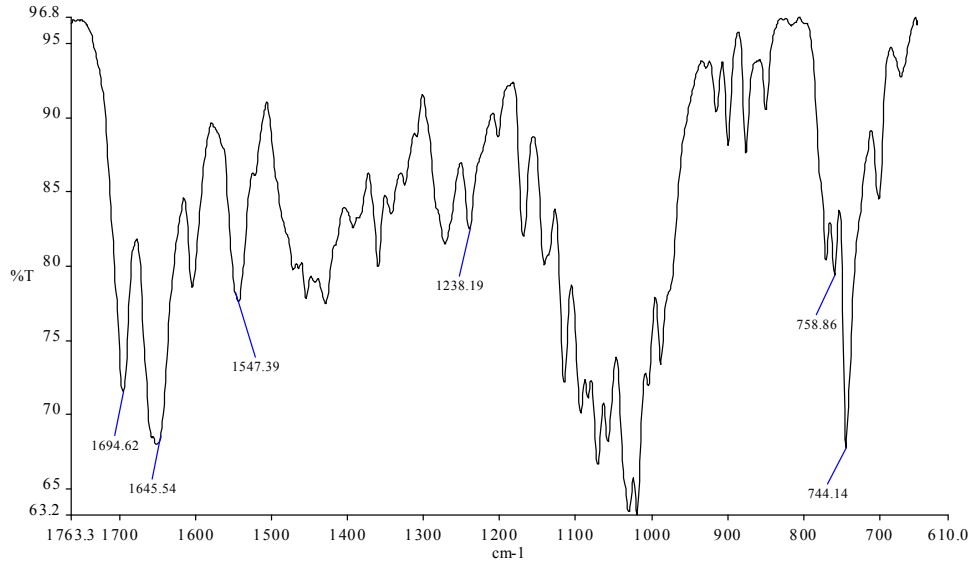

Figure 3.4 IR-ATR Spectrum of Amphetamine with Caffeine (additional caffeine peaks at 1694 cm^{-1} and 1645 cm^{-1})

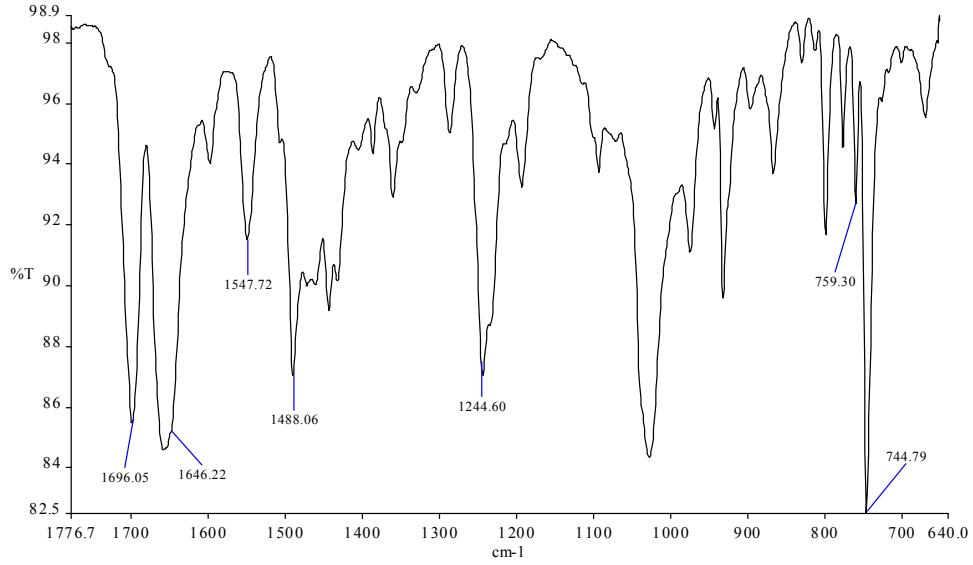

Figure 3.5 IR-ATR Spectrum of MDMA with Caffeine (additional caffeine peaks at 1696 cm^{-1} and 1646 cm^{-1})

Addition of paracetamol into sample also gives identical bands at 1651 cm^{-1}, 1610 cm^{-1}, 1561 cm^{-1} and 1433 cm^{-1}. This is shown in Figure 3.6.

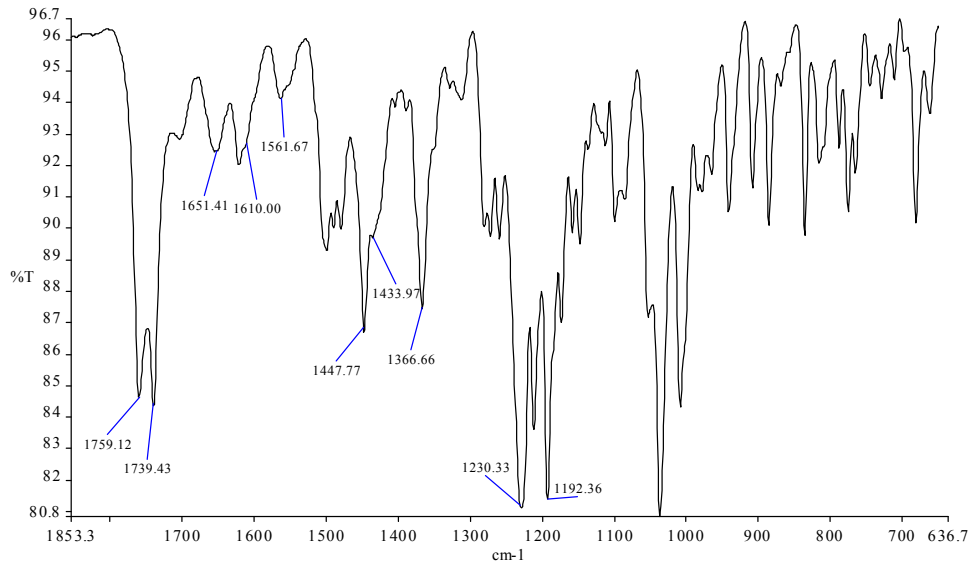

Figure 3.6 IR-ATR Spectrum of Heroin with Paracetamol (additional paracetamol peaks at 1651 cm^{-1}, 1610 cm^{-1}, 1561 cm^{-1} and 1433 cm^{-1})

However, when the sample contains both caffeine and paracetamol identification of them separately is impossible due to their close absorption bands in 1700-1650 cm^{-1} region. This is shown in Figure 3.7. In the spectrum, caffeine peaks at 1699 cm^{-1}, 1657 cm^{-1} and 1548 cm^{-1} are evident; on the other hands paracetamol peaks at 1650 cm^{-1}, 1610 cm^{-1}, 1561 cm^{-1} and 1432 cm^{-1} exist as shoulders, hence they could not be identified by the searching software.

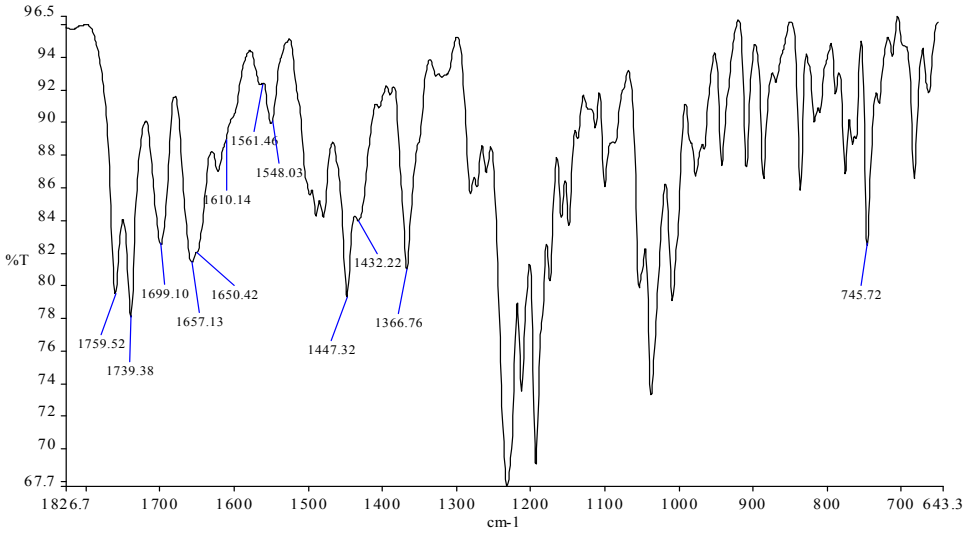

Figure 3.7 IR-ATR Spectrum of Heroin containing Caffeine and Paracetamol

Existence of lactose in the amphetamine and MDMA tablets is evident from the additional peaks at 1140 cm^{-1}, 1114 cm^{-1}, 1070 cm^{-1} and 1018 cm^{-1}. This is shown in Figure 3.8.

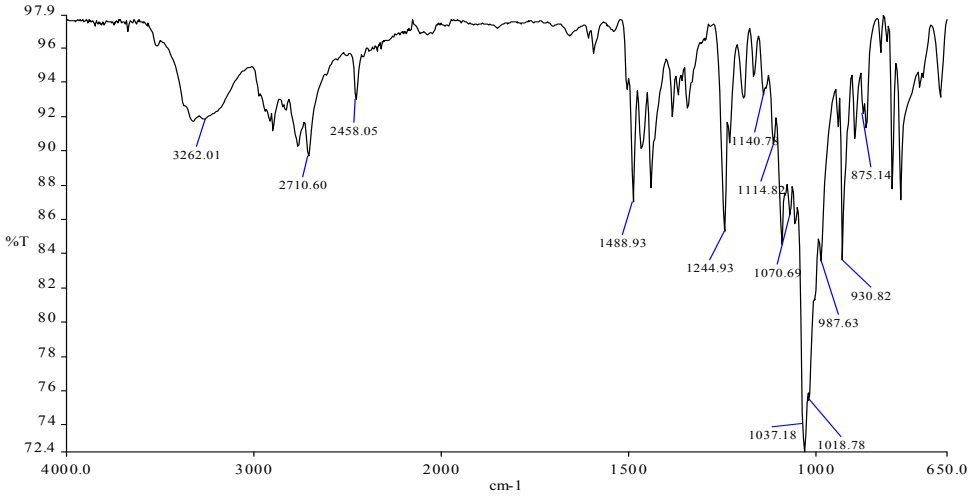

Figure 3.8 IR-ATR Spectrum of MDMA containing lactose. (additional lactose peaks at 1140 cm^{-1}, 1114 cm^{-1}, 1070 cm^{-1} and 1018 cm^{-1})

3.5 Comparison of the IR Forecasts with HPLC and GC Results

After constitution of the database of standards, 76 illicit drug samples were studied with the same method and they were searched against this database by means of Euclidian search. Only the first search result was taken in account. The IR forecasts for 76 illicit drugs were compared with their HPLC and GC results and are shown in Table 3.5

Table 3.5 Comparison of IR Forecasts with HPLC and GC Results.

Sample No	IR Forecast	HPLC or GC-FID Results
S1	Cocaine	89.3 % Cocaine
S2	Cocaine	90.4 % Cocaine
S3	Cocaine	58.1 % Cocaine
S4	Cocaine	63.6 %Cocaine
S5	Cocaine	80.1 % Cocaine
S6	Morphine	11.6 % Morphine
S7	Morphine	10.8 % Morphine
S8	Morphine	73.3 % Morphine
S9	Morphine	27.2 % Morphine
S10	Morphine	42.7 % Morphine
S11	Morphine	51.2 % Morphine
S12	Morphine	54.3 % Morphine
S13	Morphine	50.6 % Morphine
S14	Heroin	63.7 % Heroin, 26.7 % Narcotine
S15	Heroin	63.7 % Heroin, 27.4 % Narcotine
S16	Narcotine	19.9 % Heroin, 49.6 % Narcotine
S17	Narcotine	0.4 % Heroin, 58.4 % Narcotine
S18	Heroin	17.5 % Heroin, 49.6 % Narcotine
S19	Narcotine	0.2 % Heroin, 55.5 % Narcotine
S20	Heroin, Caffeine	27.8 % Heroin, 13.7 % Caffeine, 35.4 % Narcotine
S21	Heroin, Caffeine	29.6 % Heroin, 13.7 % Caffeine, 34.8 % Narcotine
S22	Narcotine	30.6 % Heroin, 45.8 % Narcotine
S23	Heroin, Caffeine	43.5 % Heroin, 8.2 % Caffeine, 26.9 % Narcotine
S24	Heroin, Caffeine	58.8 % Heroin, 3.3 % Caffeine, 20.1 % Narcotine

Table 3.5 (Continued)

S25	Heroin, Caffeine	27.0 % Heroin, 13.0 % Caffeine, 33.3 % Narcotine
S26	Narcotine	26.7 % Heroin, 0.4 % Caffeine, 1.4 % Paracetamol, 40.9 % Narcotine
S27	Narcotine	25.1 % Heroin, 4.6 % Caffeine, 0.9 % Paracetamol, 42.8 % Narcotine
S28	Narcotine	27.0 % Heroin, 5.3 % Caffeine, 1.0 % Paracetamol, 40.7 % Narcotine
S29	Heroin, Caffeine	35.5 % Heroin, 13.9 % Caffeine, 12.8 % Paracetamol, 24.3 % Narcotine
S30	Heroin, Caffeine	35.9 % Heroin, 14.4 % Caffeine, 14.4 % Paracetamol, 23.1 % Narcotine
S31	Heroin	51.3 % Heroin, 26.2 % Narcotine
S32	Heroin	55.2 % Heroin, 25.3 % Narcotine
S33	Heroin	62.6 % Heroin, 20.6 % Narcotine
S34	Heroin	62.3 % Heroin, 22.2 % Narcotine
S35	Heroin	61.2 % Heroin, 20.3 % Narcotine
S36	Heroin, Caffeine	32.2 % Heroin, 5.1 % Caffeine, 43.4 % Narcotine
S37	Heroin, Caffeine	35.9 % Heroin, 3.9 % Caffeine, 44.2 % Narcotine
S38	Heroin	55.2 % Heroin, 30.8 % Narcotine
S39	Heroin	54.8 % Heroin, 29.9 % Narcotine
S40	Heroin	43.6 % Heroin, 26.6 % Narcotine
S41	Heroin	36.5 % Heroin, 30.6 % Narcotine
S42	Paracetamol	90.5 % Paracetamol
S43	Caffeine, Paracetamol	41.4 % Caffeine, 47.6 % Paracetamol
S44	Griseofulvin, Caffeine	16.9 % Caffeine, Griseofulvin
S45	Griseofulvin, Caffeine	12.9 % Caffeine, Griseofulvin
S46	Paracetamol	88.3 % Paracetamol
S47	Amphetamine, caffeine, lactose	3.5 % Amphetamine, 14.2 % Caffeine, Lactose
S48	Caffeine	1.6 % Amphetamine, 19.5 % Caffeine, Lactose
S49	Amphetamine, caffeine, lactose	8.6 % Amphetamine, 20.2 % Caffeine, Lactose
S50	Amphetamine, lactose	14.3 % Amphetamine, 0.9 % Caffeine, Lactose
S51	Amphetamine, caffeine, lactose	11.2 % Amphetamine, 2.2 % Caffeine, Lactose
S52	Amphetamine, caffeine, lactose	19.9 % Amphetamine, 3.8 % Caffeine, Lactose
S53	Amphetamine, lactose	15.1 % Amphetamine, 0.4 % Caffeine, Lactose
S54	Amphetamine, caffeine, lactose	18.6 % Amphetamine, 5.6 % Caffeine, Lactose

Table 3.5 (Continued)

S55	MDMA, lactose	15.0 % MDMA, lactose
S56	Caffeine	5.5 % Amphetamine, 33.4 % Caffeine, Lactose
S57	MDMA, lactose	33.0 % MDMA, lactose
S58	MDMA lactose	35.1 % MDMA, lactose
S59	MDMA, lactose	22.6 % MDMA
S60	MDMA, lactose	38.9 % MDMA, 2.1 % Caffeine
S61	Amphetamine, caffeine, lactose	17.1 % Amphetamine, 15.8 % Caffeine, Lactose
S62	Caffeine	2.4 % Amphetamine, 18.2 % Caffeine, Lactose
S63	MDMA	31.5 % MDMA
S64	MDMA, lactose	34.5 % MDMA, lactose
S65	MDMA, lactose	29.2 % MDMA, lactose
S66	MDMA, lactose	32.9 % MDMA, lactose
S67	MDMA	41.5 % MDMA
S68	MDMA, lactose	20.7 % MDMA, lactose
S69	MDMA, lactose	31.6 % MDMA, lactose
S70	MDMA	26.2 % MDMA, 1.8 % Caffeine
S71	MDMA, lactose	25.6 % MDMA, 0.6 % Caffeine
S72	MDMA	35.9 % MDMA
S73	MDMA, lactose	60.4 % MDMA, lactose
S74	MDMA	55.9 % MDMA, lactose
S75	MDMA	40.3 % MDMA, lactose
S76	MDMA	39.1 % MDMA, lactose

3.5.1 Evaluation of the Comparison

The IR forecasts of the samples can be evaluated as satisfactory except for a few deviating results. There is no completely wrong result, but some of them are incomplete, which means some of the components in the sample could not be identified.

For cocaine samples, S1 through S5, there was no problem and all of them were identified correctly. Illicit cocaine samples are usually served in high purity, usually greater than 80 %. Some of them may contain sugar or carbonates, but during the study, additives of cocaine were not examined. In addition, it was observed that

base and hydrochloride salt form of the cocaine could easily be differentiated from the IR spectra due to the shifts in the peak positions. This is true for S5, which is in base form and shown in the Appendix C-5.

Similarly, for morphine samples, S6 through S13, no problem was encountered because morphine almost never contains additives. During the conversion of morphine to heroin, additives are included to increase the total amount.

Illicit heroin samples can be found in many different compositions due to several impurities coming from the morphine (like meconine, thebaine, narcotine and papaverine) and conversion steps (like calcium carbonate) and other substances (such as caffeine, griseofulvin, paracetamol, procaine) included into the final product. Therefore, it was not easy to predict the influence of each component on to the spectra.

One criterion for the heroin samples was the percent amount of heroin in the sample, when the heroin is in low amounts then the second most abundant component narcotine becomes dominant on the spectra, this was the case for samples S17 and S19.

Another factor is the significant contribution from narcotine peak at 1751 cm^{-1}, which is shielding the carbonyl bands of heroin at 1759 and 1738 cm-1 and resulting the spectra resembles to that of narcotine. For samples S16, S22, S26, S27 and S28 this can be an explanation for the IR forecasts giving narcotine, although all samples contained a notable amount of heroin.

On the other hand, when we examine the narcotine concentration in above samples, it was seen that all have narcotine greater than 40 %, which is very high and makes the narcotine major ingredient of the sample. Consequently, we can conclude that IR forecasts are accurate, although the existence of heroin is not detected. Besides, the presence of narcotine is also an indication of an opium product.

Existence of caffeine in heroin was identified easily even when it is present in small amounts, such as in S23, S24, S36 and S37. Caffeine peaks at 1698, 1656, 1550 and 1230 cm^{-1} are still observable in the spectra.

Samples containing both caffeine and paracetamol, S26, S27, S28, S29 and S30, were not identified correctly. Three of them, S26, S27 and S28, suffer from great narcotine contribution at 1751 cm^{-1}, consequently, the forecast results were narcotine only; whereas for other two, S29 and S30, although caffeine peaks at 1698, 1656, 1550 1230, 764 and 745 cm^{-1} are clear, paracetamol peaks exist in the shoulders at 1650, 1609, 1561 and 1430 cm^{-1}; consequently IR forecasts indicated the composition as heroin plus caffeine.

Amphetamine tablets numbered as S47, S49, S51, S52, S54 and S61 were correctly identified.

In the samples S50 and S53, caffeine concentrations are very low (0.9 % and 0.4 %), therefore caffeine was not detected. On the other hand, in the samples S48 and S56, amphetamine concentrations are low (1.6 % and 5.5 %) and caffeine is the major component, naturally IR forecasts were caffeine and not amphetamine.

MDMA tablets numbered as S58, S59, S63, S64, S65, S66, S67, S68, S69, S72 and S73 were correctly identified.

Caffeine content in the MDMA tablets (S60, S70 and S71) was not detected because the concentration of caffeine was low in all of them (2.1 %, 1.8 % and 0.6 %, respectively). However, small absorption band of caffeine at 1694 cm^{-1} is visually observable in the spectra.

Finally, for MDMA tablets S57, S74, S75 and S76 the searching software did not detect lactose, although existence of lactose was visually evident from the IR spectra.

3.6 FTIR Spectral Database for Illicit Samples

In the first part of the study, the identification of illicit samples was tried by searching them against a database constituted from drug standards.

In this part, the aim was rather different in that the comparison of illicit sample spectra were done by searching them against a database constituted from only real illicit samples, not the synthetically formed ones.

As it is known, all components of the sample contribute to the IR spectrum so that small variations are identical in IR analyses of the samples. Besides, two samples having identical spectra should be very similar to each other.

Keeping this statement in mind, it was investigated whether it would be possible to detect presence of samples that was included in database just by comparing their IR spectra. This is important because in case of success, the procedure will constitute a simple way of grouping the illicit samples. In other words, some samples can be differentiated in several defined groups having the same properties so that this can be used as a pre-selection step in profiling studies before other detailed analyses are performed.

3.6.1 Blind Study

In order to test the comparison power of the FTIR-ATR method, a blind study was designed.

All illicit sample spectra were collected in a new database. Then some of the illicit samples labeled as unknowns were analyzed again and their spectra were searched against this new database. The aim was to examine whether all blind samples would match with their own spectrum in the database.

In the blind study, 26 illicit samples were selected randomly from a total of 76; using some of them two or three times, the total number was raised to 45. The search results of blind study are presented in Table 3.6.

Table 3.6 Result of Blind Study

Sample No	IR Forecast	Forecast Result	True Sample
1	MDMA, lactose	S69	S69
2	Caffeine	S62	S62
3	Caffeine, griseofulvin	S45	S45
4	MDMA, lactose	S60	S60
5	Caffeine	S48	S48
6	MDMA, lactose	S69	S69
7	MDMA, lactose	S59	S59
8	MDMA, lactose	S59	S59

Table 3.6 (Continued)

9	Heroin, caffeine	S20	S20
10	Caffeine	S62	S62
11	Cocaine	S1	S1
12	Cocaine	S2	S4
13	Heroin, caffeine	S36	S20
14	Narcotine	S17	S19
15	Cocaine	S2	S4
16	Heroin	S14	S14
17	MDMA, lactose	S59	S59
18	Caffeine, griseofulvin	S45	S45
19	MDMA, caffeine, lactose	S57	S57
20	Amphetamine, lactose	S50	S50
21	Narcotine	S17	S19
22	MDMA	S63	S63
23	Caffeine	S56	S56
24	Heroin, Caffeine	S24	S24
25	MDMA	S60	S60
26	Cocaine	S2	S1
27	Heroin	S14	S14
28	Amphetamine, caffeine, lactose	S53	S54
29	Caffeine	S48	S48
30	Heroin, caffeine	S24	S24
31	MDMA	S57	S57
32	Heroin	S18	S18
33	MDMA	S75	S75
34	MDMA, lactose	S66	S66
35	MDMA	S67	S70
36	Heroin, caffeine	S20	S20
37	Morphine	S9	S9
38	Narcotine	S26	S26
39	Amphetamine, lactose	S50	S50
40	Narcotine	S26	S28
41	Amphetamine, lactose	S50	S50
42	MDMA, lactose	S58	S58
43	MDMA, lactose	S58	S58
44	Caffeine,	S49	S49
45	MDMA, lactose	S60	S60

3.6.2 Evaluation of Blind Study

Almost all the blind samples were correctly matched with their counterparts in the database, which indicates that similar samples can also be found with the same way.

Blind samples numbered as 12, 14, 15, 21, 28 and 40 were matched with different samples but examination of the results pointed out that the real sample and the forecast sample did belong to the same seizure. Therefore, it is highly probable that they are the same substances in different packages.

Blind samples numbered as 13, 26 and 35 gave totally irrelevant results using IR spectra. But when their spectra compared visually with that of forecasted spectra, it was seen that they are identical. Therefore, it may be considered that they have a great similarity.

In addition, the identification of the sample composition was not a limiting factor in this blind study. For example, for the samples S62, S60, S59 and S50, the IR search results did not exactly identifie the true composition; however, in the blind study these samples were correctly match with their counterparts. In contrast, S1, S4 and S20 were identified correctly with IR search but they were not matched with their own spectra in the blind study.

As a consequence of this blind study, it can be concluded that FTIR-ATR is a very powerful technique for comparison purposes; small variations in sample compositions can easily be observed and similar samples can be found from the IR analyses and classification of the drugs can be possible with this simple way.

CHAPTER IV

CONCLUSION

The applicability of the FTIR-ATR technique for illicit drugs was investigated. Unlike KBr and Nujol mull techniques, working with ATR requires no complicated sample preparation and this makes the technique very advantageous for the identification of huge numbers of captured material.

Illicit drugs are not pure substances but they contain several chemicals. Therefore, it is impossible to identify all the components and to prepare a totally representative working sample in order to include into the IR database. Therefore, although secondary standards were used, some of the components of the sample should be still out of control. However, the technique has been applied on the real samples and can be utilized satisfactorily for the studied group of drugs.

This technique can be used as an alternative to pre-determination techniques such as color tests, TLC and GC-MS. It can be used conveniently in crucial points like customs, where a rapid decision is needed about a suspicious material. In addition, for chemical profiling studies, it can be used as a fast pre-detection step to determine the similarities between new samples and those from previous seizures. Correlations between separate seizures may also be detected.

As future aspects of the study, work on larger number of additives and different compositions should be performed to widen the content of the standard database to identify more drugs. Number of illicit samples in the sample database should be increased and multivariate statistical methods can be employed to improve the power of the technique.

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* The publications of United Nations can be accessed on the website http:// www.unodc.org under the title "news and publications / publications / scientific support".

APPENDIX A

CHEMICAL AND PHYSICAL PROPERTIES OF DRUGS

Table A.1 Chemical and Physical Properties of Drugs [33, 34]

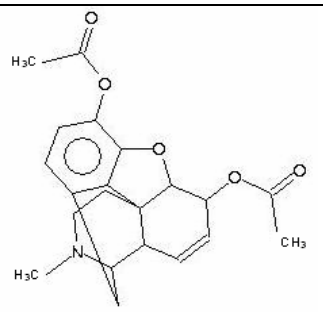
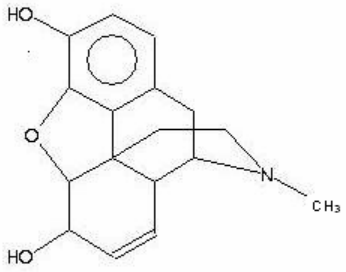
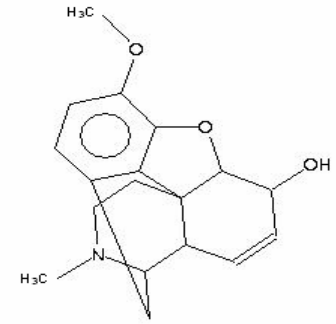
Names	Molecular Structure & Molecular Formula	Physical Properties
Heroin Diacetylmorphine (5α,6α)-7,8-Didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol diacetate (ester)	 $C_{21}H_{23}NO_5$	Solid mol wt. 369.4 mp. 173 ^{0}C
Morphine (5α,6α)-7,8-Didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol	 $C_{17}H_{19}NO_3$	Solid mol wt. 285.3 mp. 197 ^{0}C
Codeine (5α,6α)-7,8-Didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ol	 $C_{18}H_{21}NO_3$	Solid mol wt.299.4 mp. 154-156 ^{0}C

Table A.1 (Continued.)

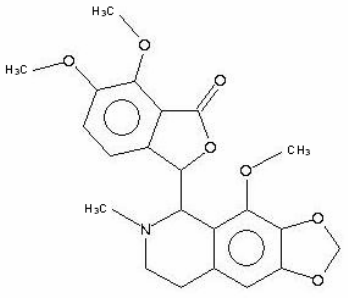
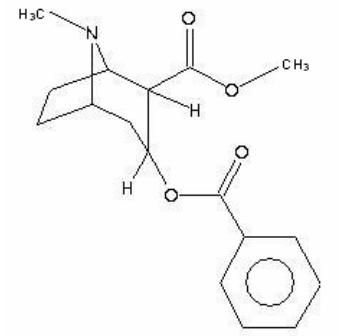
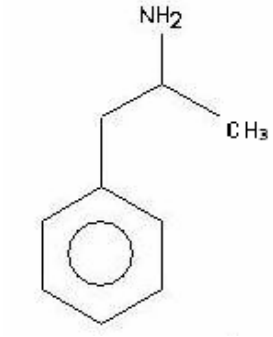
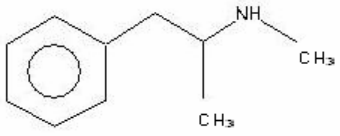
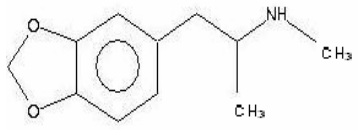
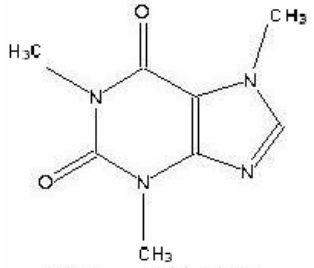
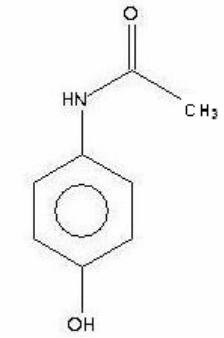
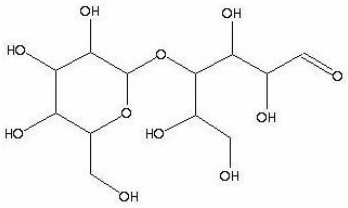
Narcotine [S-(R*,S*)]-6,7-dimethoxy-3-(5,6,7,8-tetrahydro-4-methoxy-6-methyl-1,3-dioxolo[4,5-g]isoquinolin-5-yl)-1(3H)-isobenzofuranone	 $C_{22}H_{23}NO_7$	Solid mol wt. 413.4 mp. 176 ^{0}C
Cocaine [1R-(exo,exo)]-3-(Benzoyloxy)-8-methyl-8-azabicyclo[3.2.1]-octane-2-carboxylic acid methyl ester	 $C_{17}H_{21}NO_4$	Solid mol wt. 303.6 mp. 98 ^{0}C
Amphetamine (±)-α-methylbenzene-ethanamine	 $C_9H_{13}N$	Mobile liquid mol.wt. 135.2 bp_{760}. 200-203 ^{0}C
Methamphetamine (S)-N,α-dimethylbenzene-ethanamine	 $C_{10}H_{15}N$	Solid mol wt. 149.2 mp. 170-175 ^{0}C

Table A.1 (Continued.)

MDMA 3,4-methylenedioxy-methamphetamine N,α-dimethyl-1,3-benzodioxole-5-ethanamine	 $C_{11}H_{15}NO_2$	Oil mol wt. 193.2 $bp_{(0.4)}$ 100-110 ^{0}C
Caffeine 3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione	 $C_8H_{10}N_4O_2$	Solid mol wt. 194.2 mp. 238 ^{0}C
Paracetamol Acetaminophen N-(4-hydroxyphenyl)-acetamide	 $C_8H_9NO_2$	Solid mol wt. 151.2 mp. 169 ^{0} C
Lactose 4-(β-D-galactosido)-D-glucose	 $C_{12}H_{22}O_{11}$	Solid mol wt. 342.3 mp.201-202 ^{0}C

APPENDIX B

IR-ATR SPECTRA OF STANDARDS

(R: Reference Standards, P: Prepared Standards)

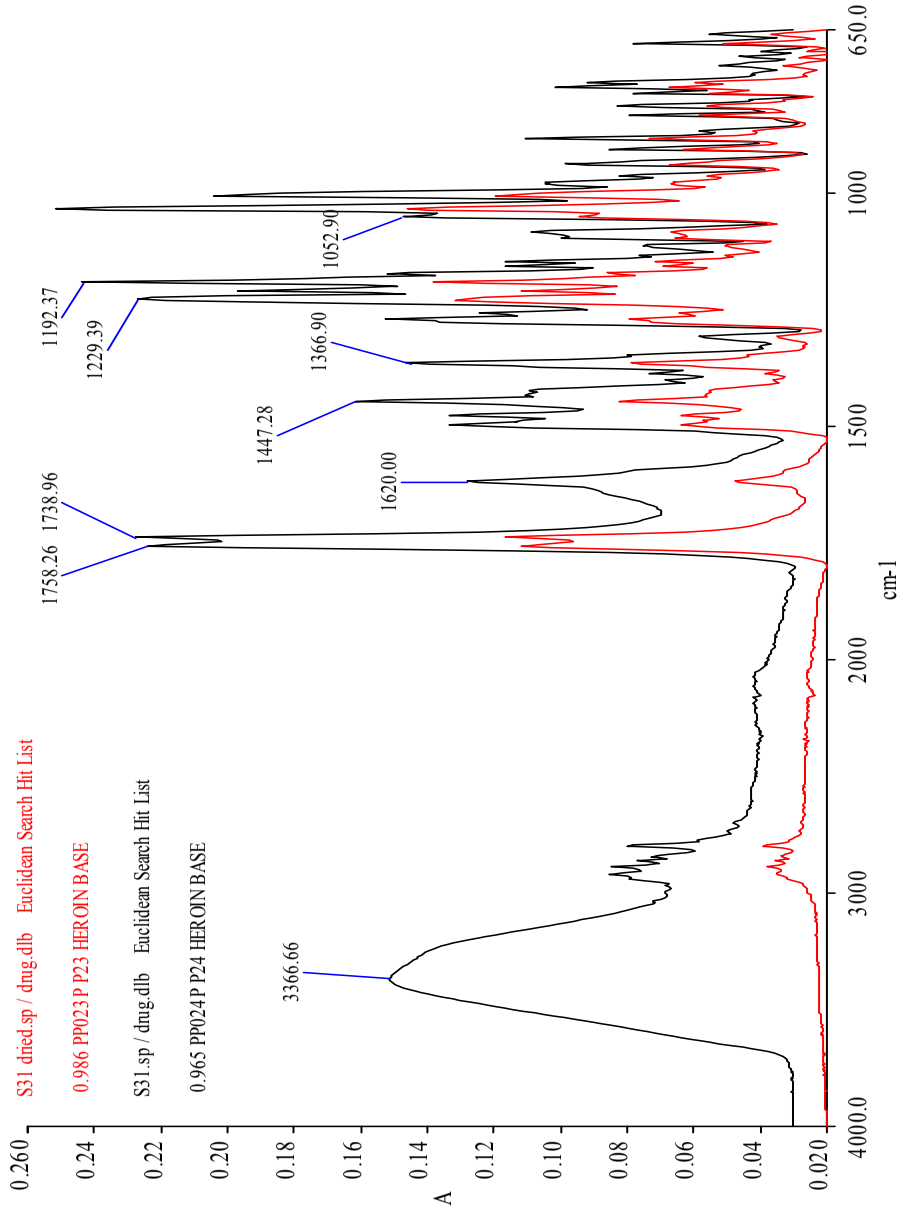


Figure B-1 Effect of humidity on IR spectrum (Black: IR Spectrum of S31before drying, Red: IR Spectrum of S31 after drying)

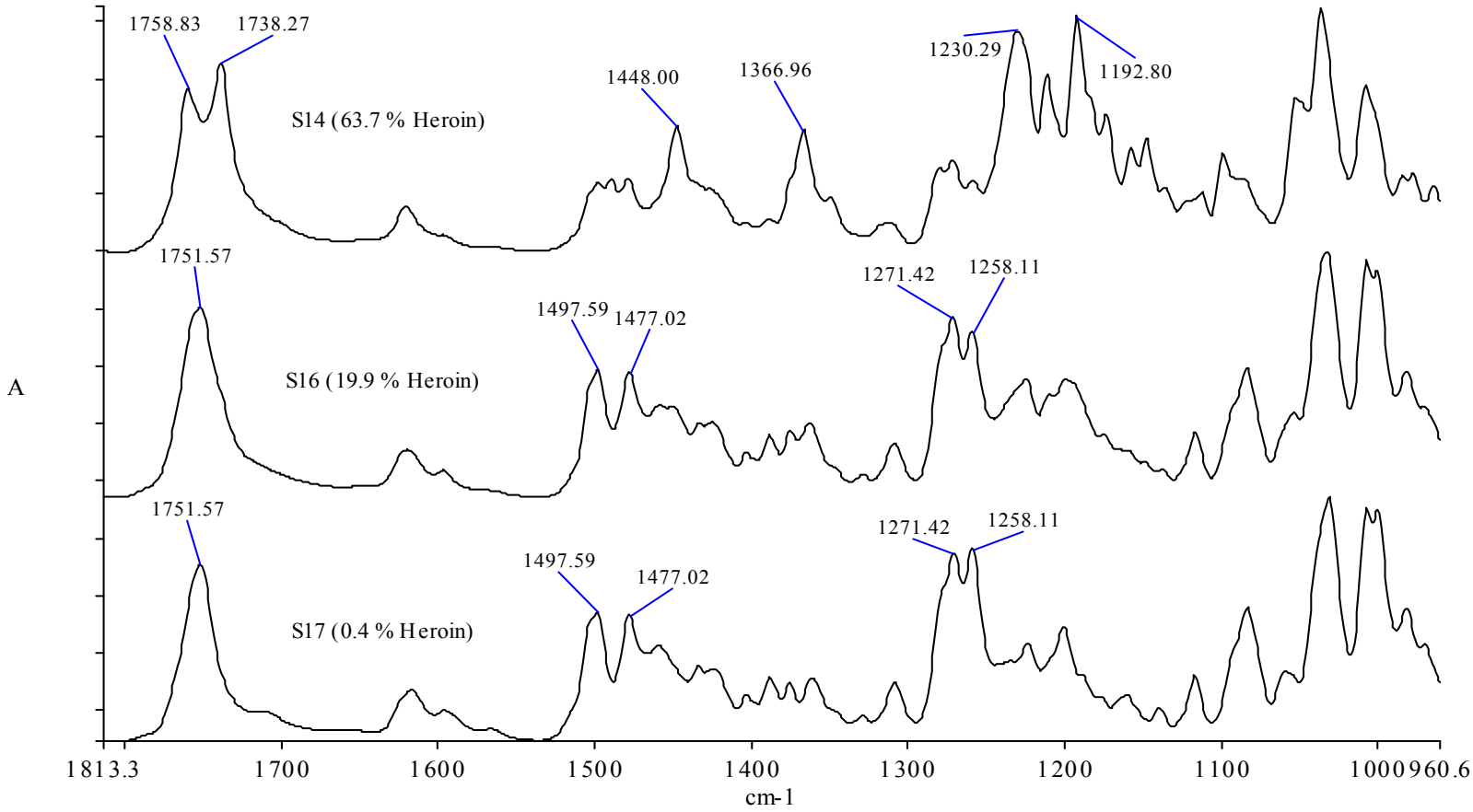


Figure B-2 The effect of Heroin concentration on the appeareance of carbonyl peaks at 1758 cm^{-1} and 1738 cm^{-1}.

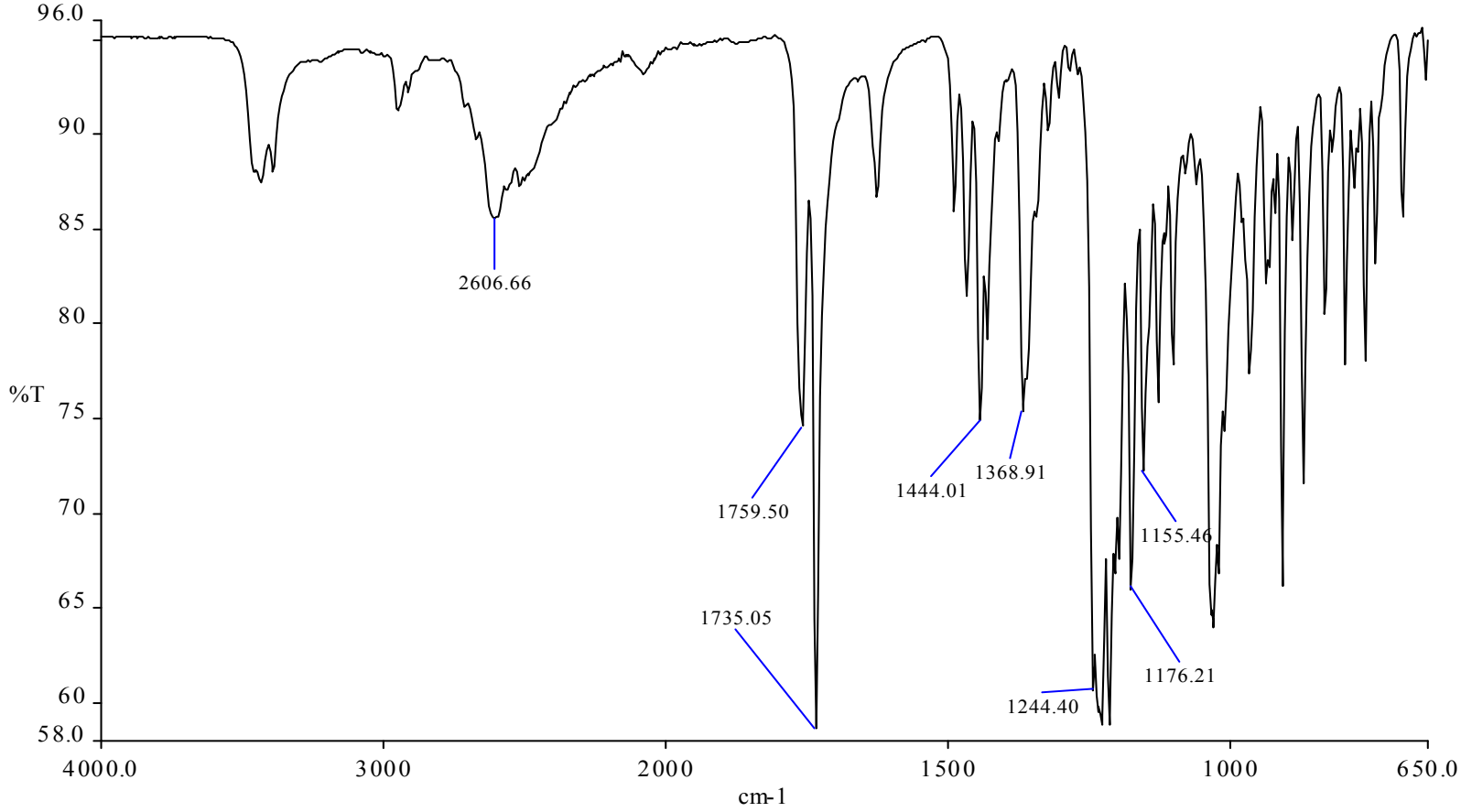


Figure B-3 IR-ATR Spectrum of Heroin HCl (R1)

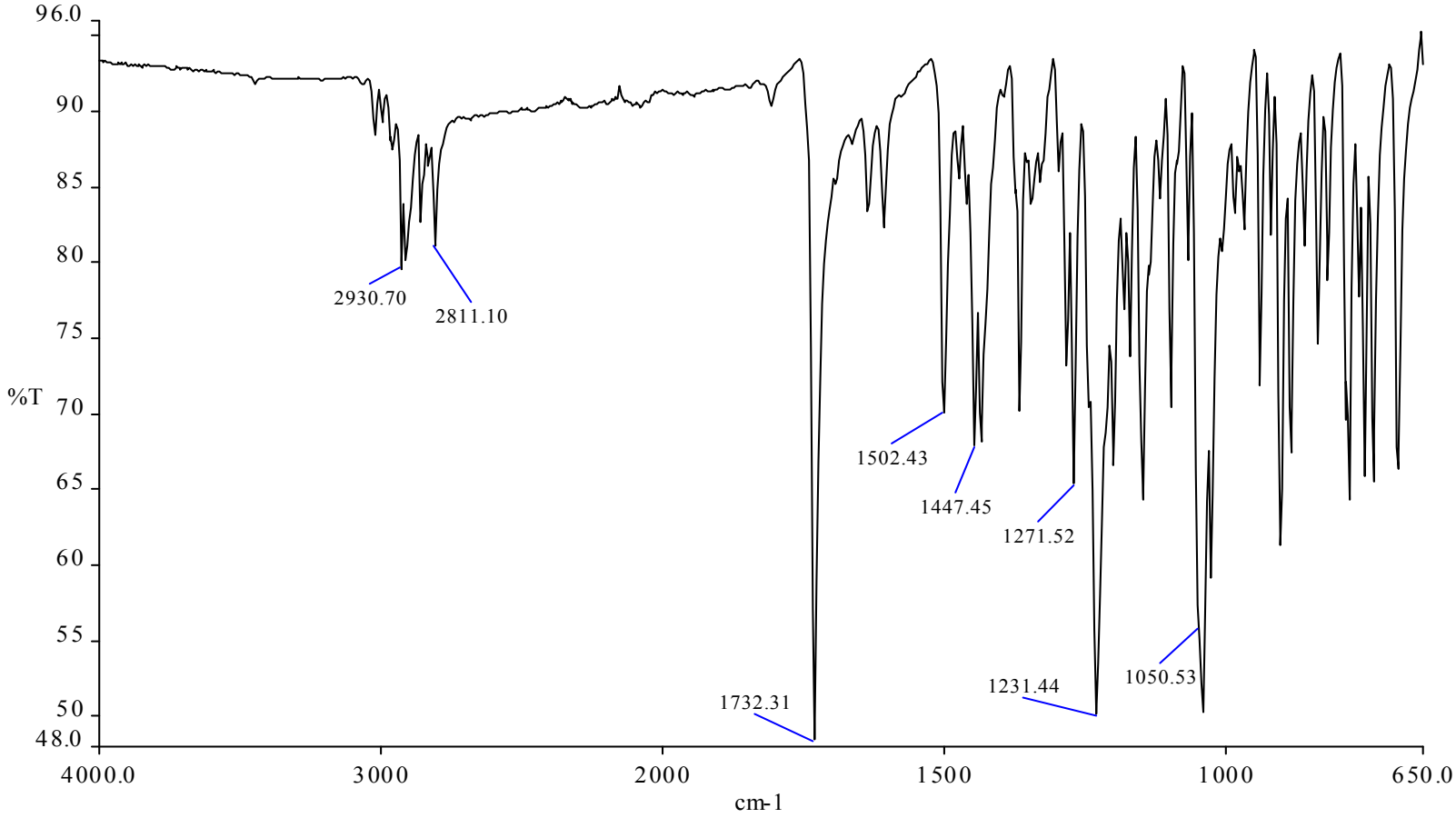


Figure B-4 IR-ATR Spectrum of Acetyl Codeine (R2)

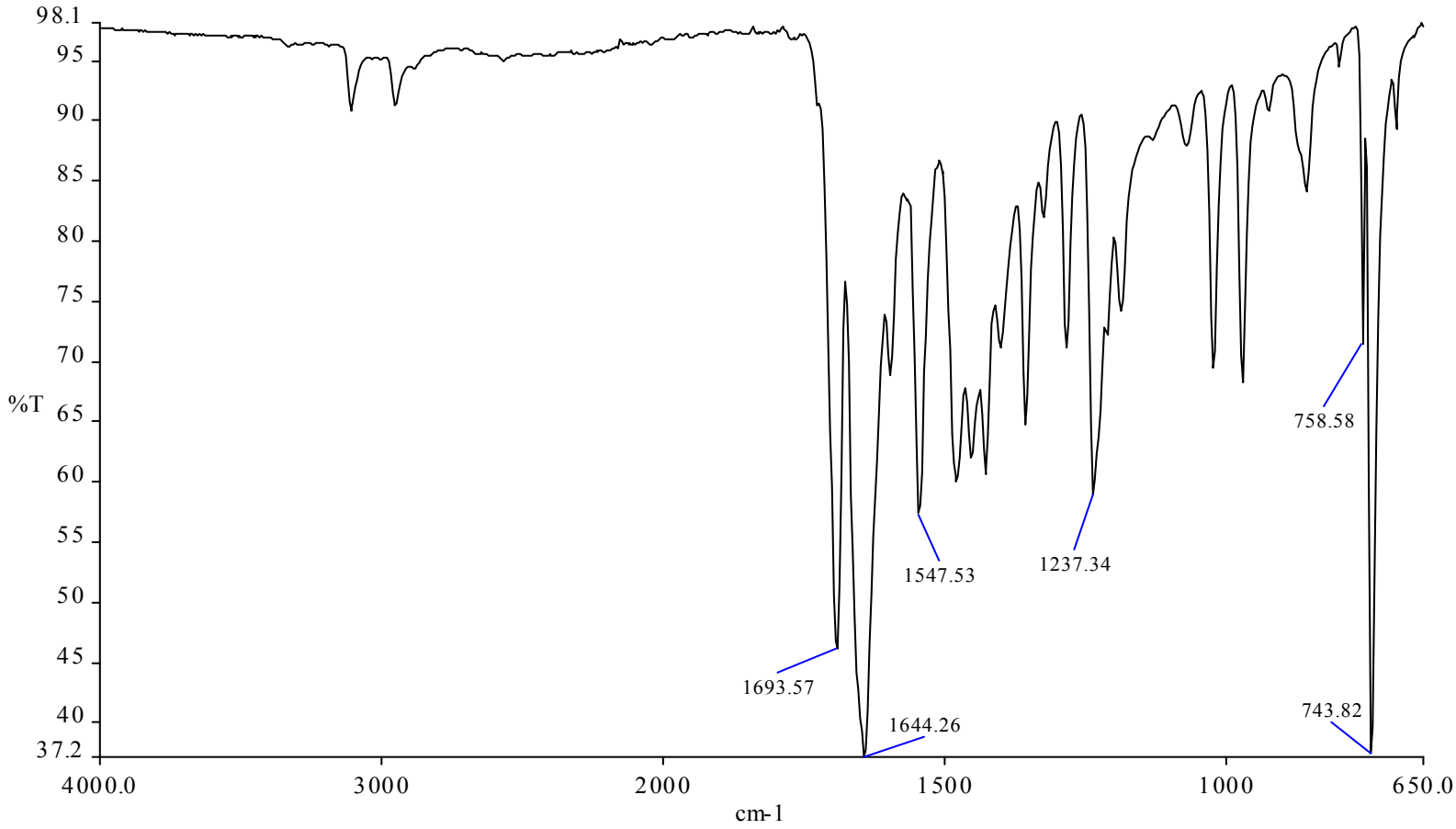


Figure B-5 IR-ATR Spectrum of Caffeine (R3)

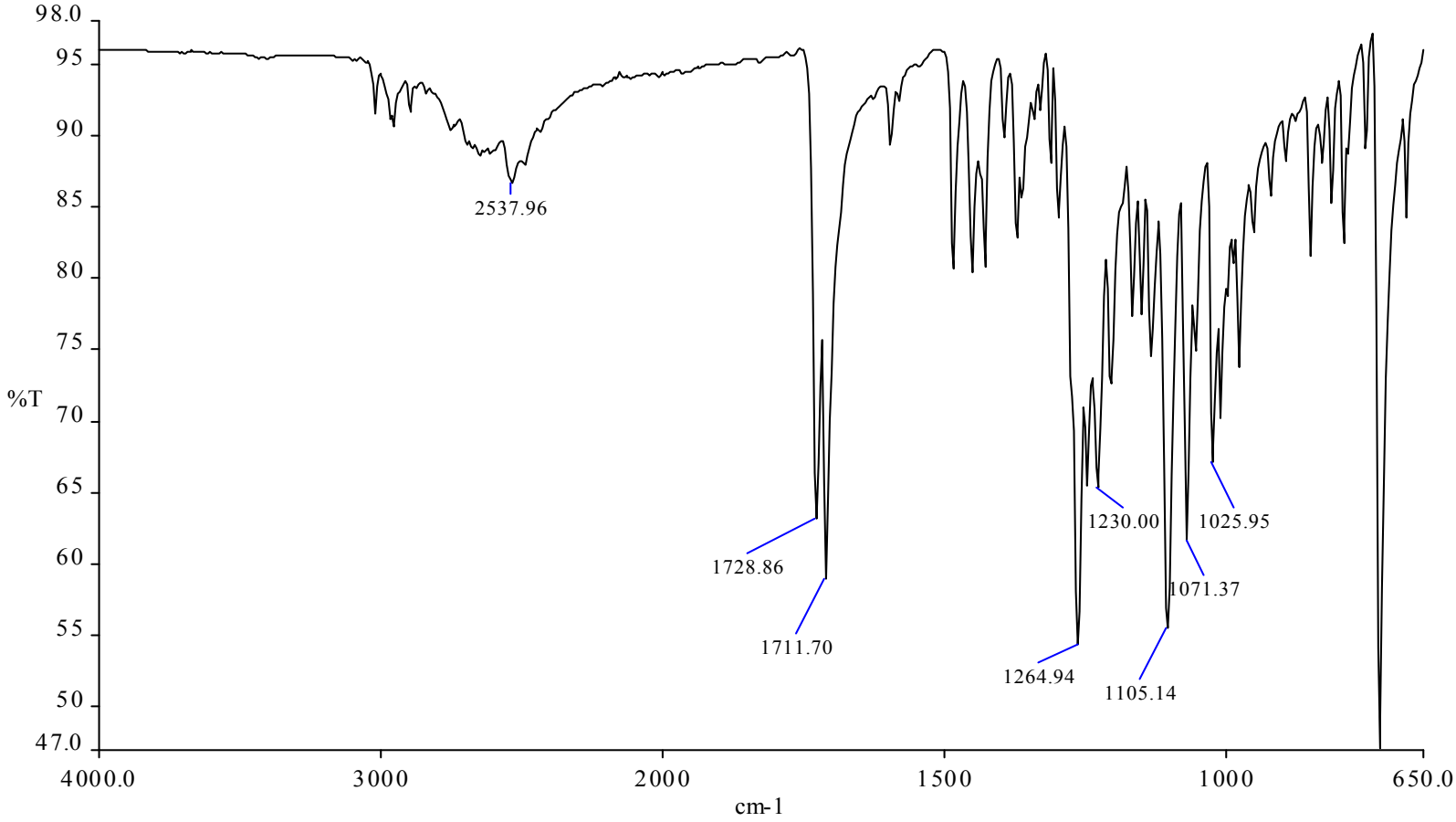


Figure B-6 IR-ATR Spectrum of Cocaine HCl (R4)

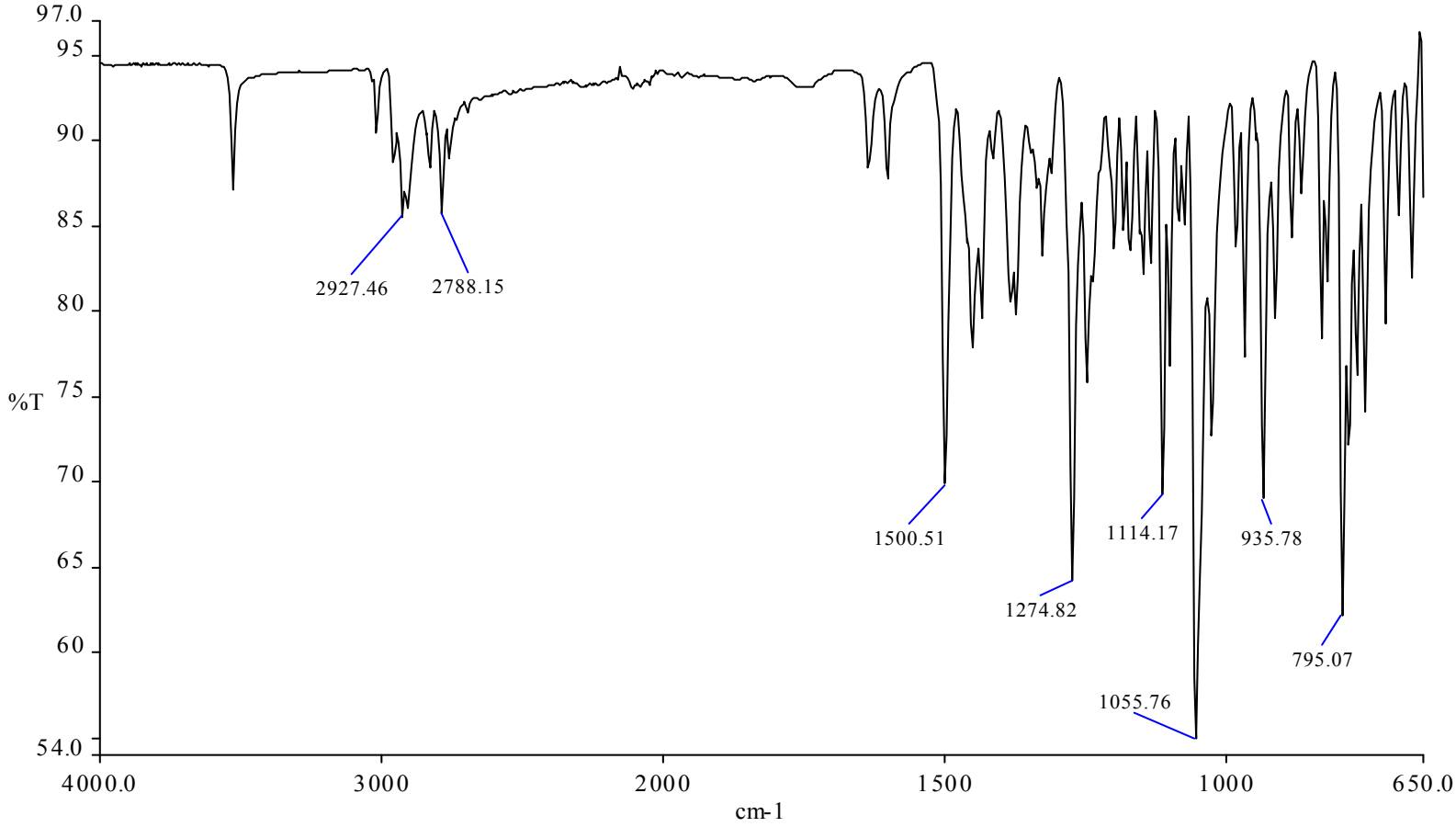


Figure B-7 IR-ATR Spectrum of Codeine (R5)

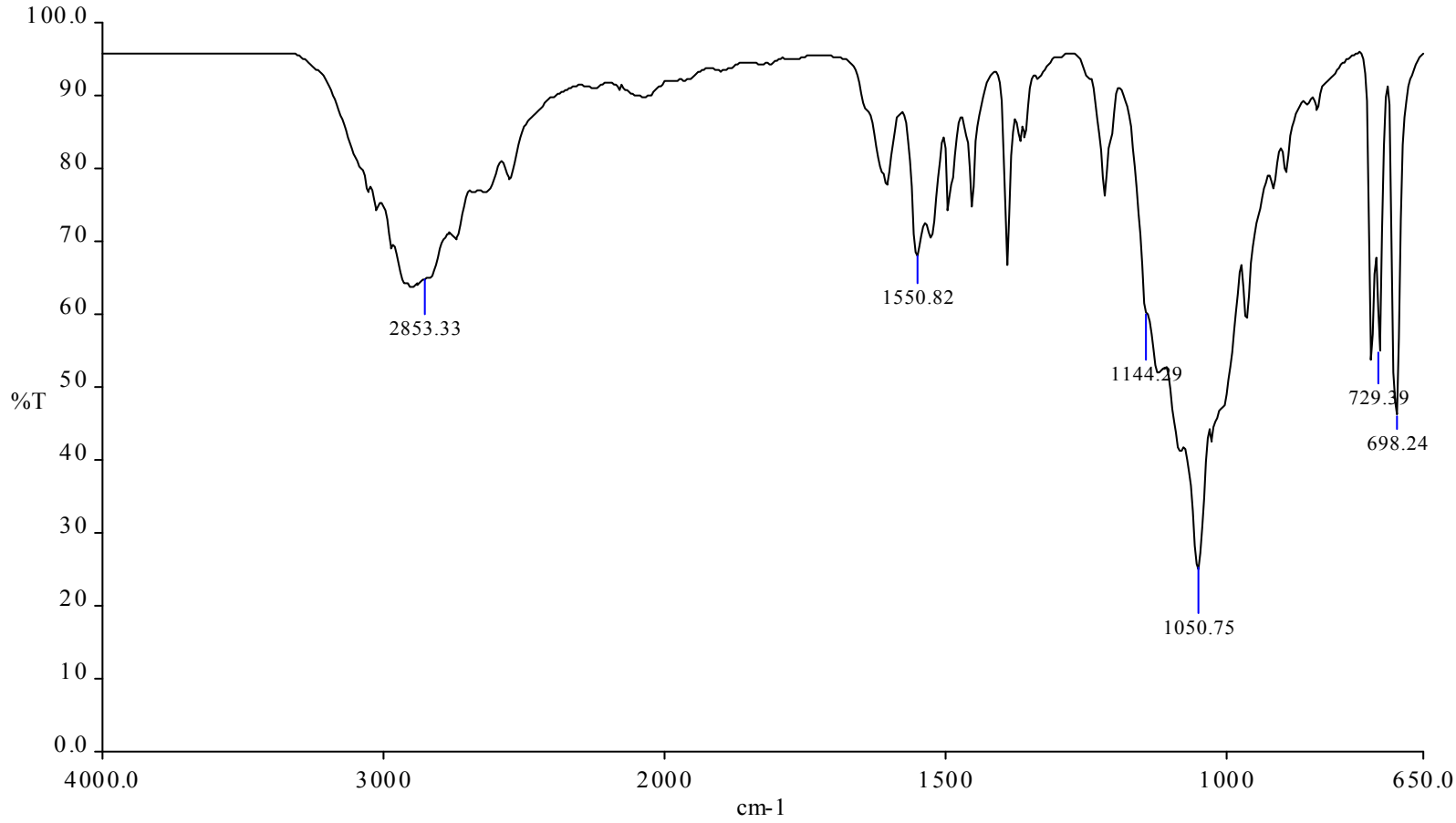


Figure B-8 IR-ATR Spectrum of d,l-Amphetamine SO_4 (R6)

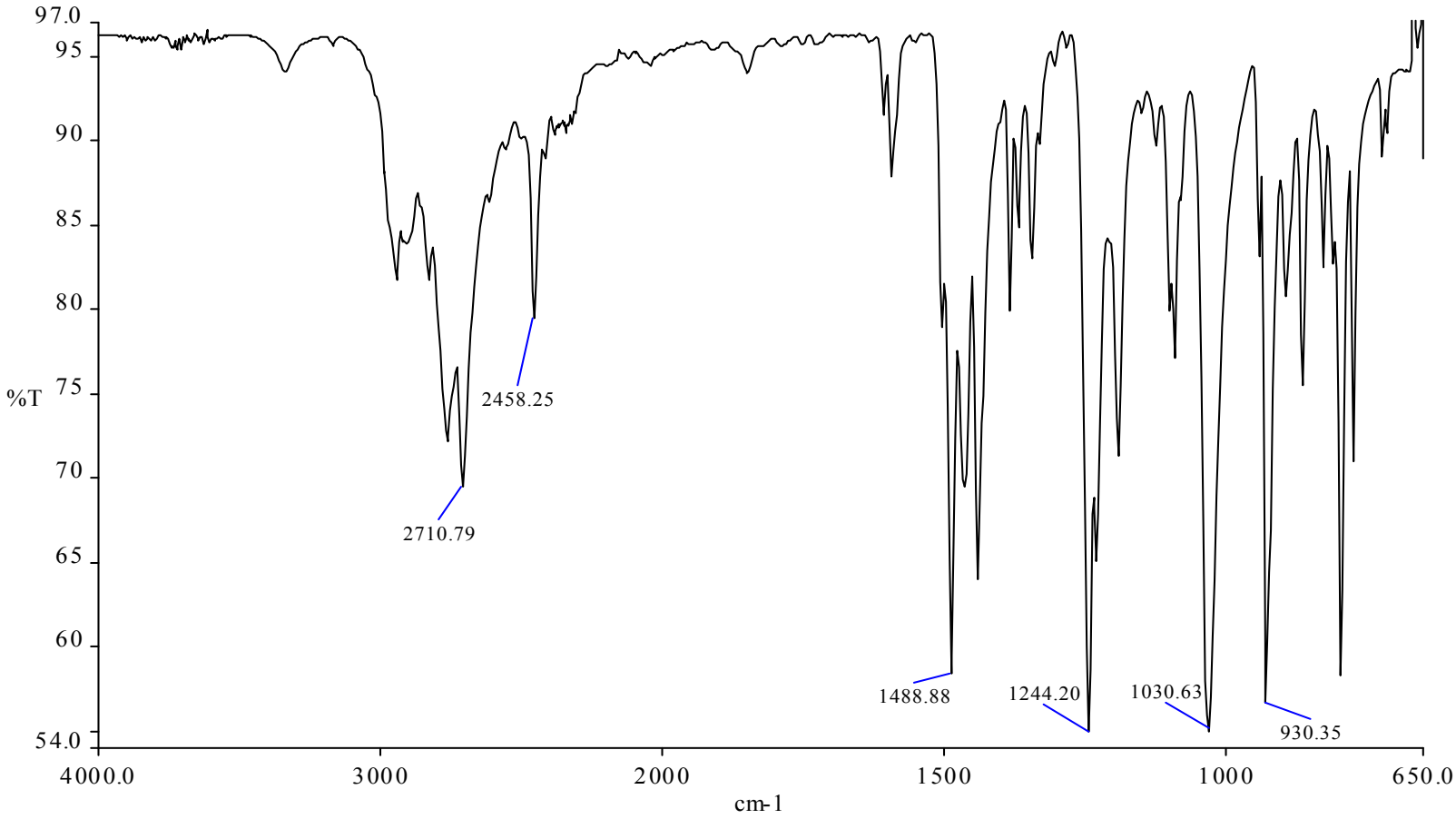


Figure B-9 IR-ATR Spectrum of d,l-MDMA HCl (R7)

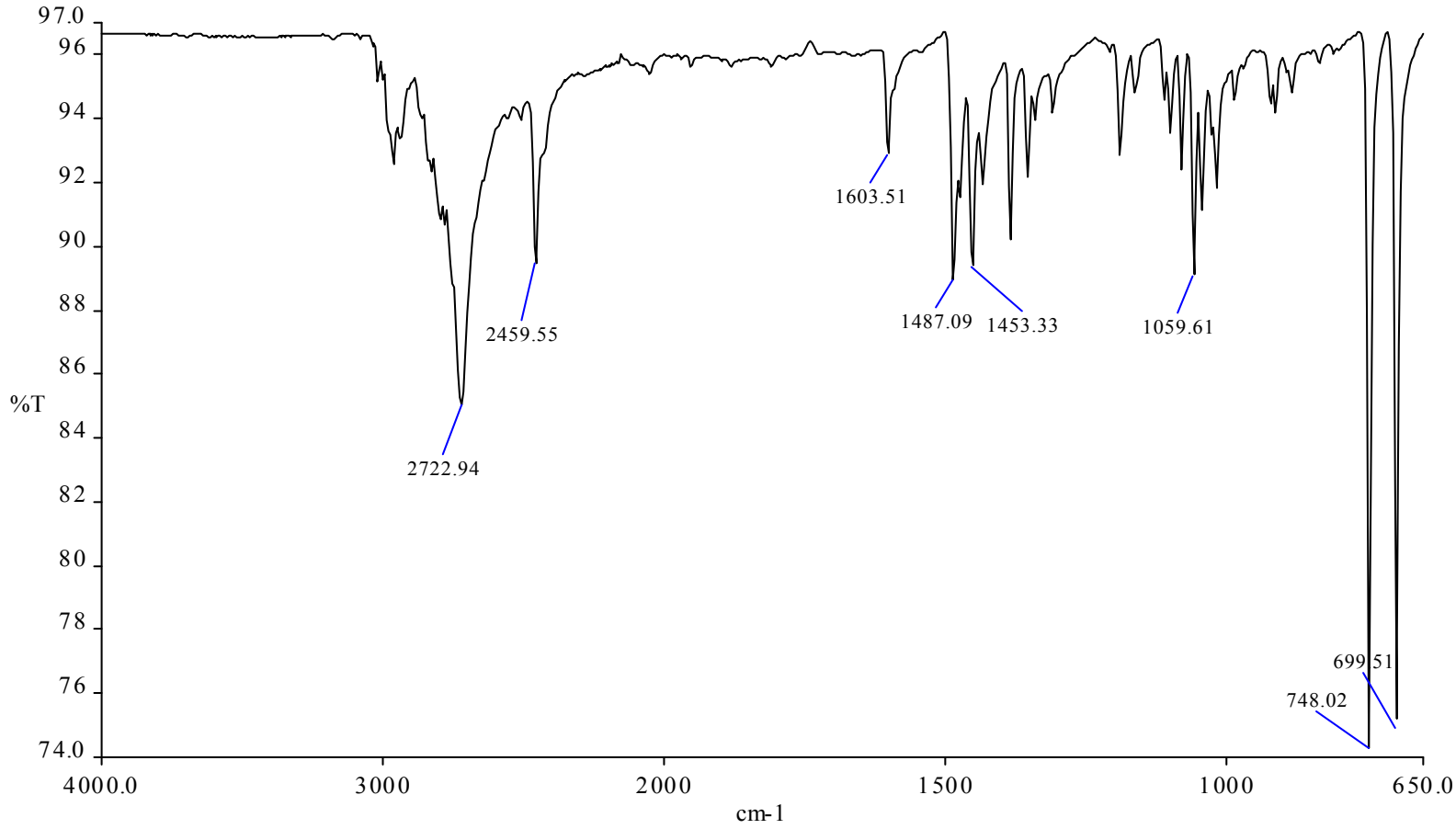


Figure B-10 IR-ATR Spectrum of d,l-methamphetamine HCl (R8)

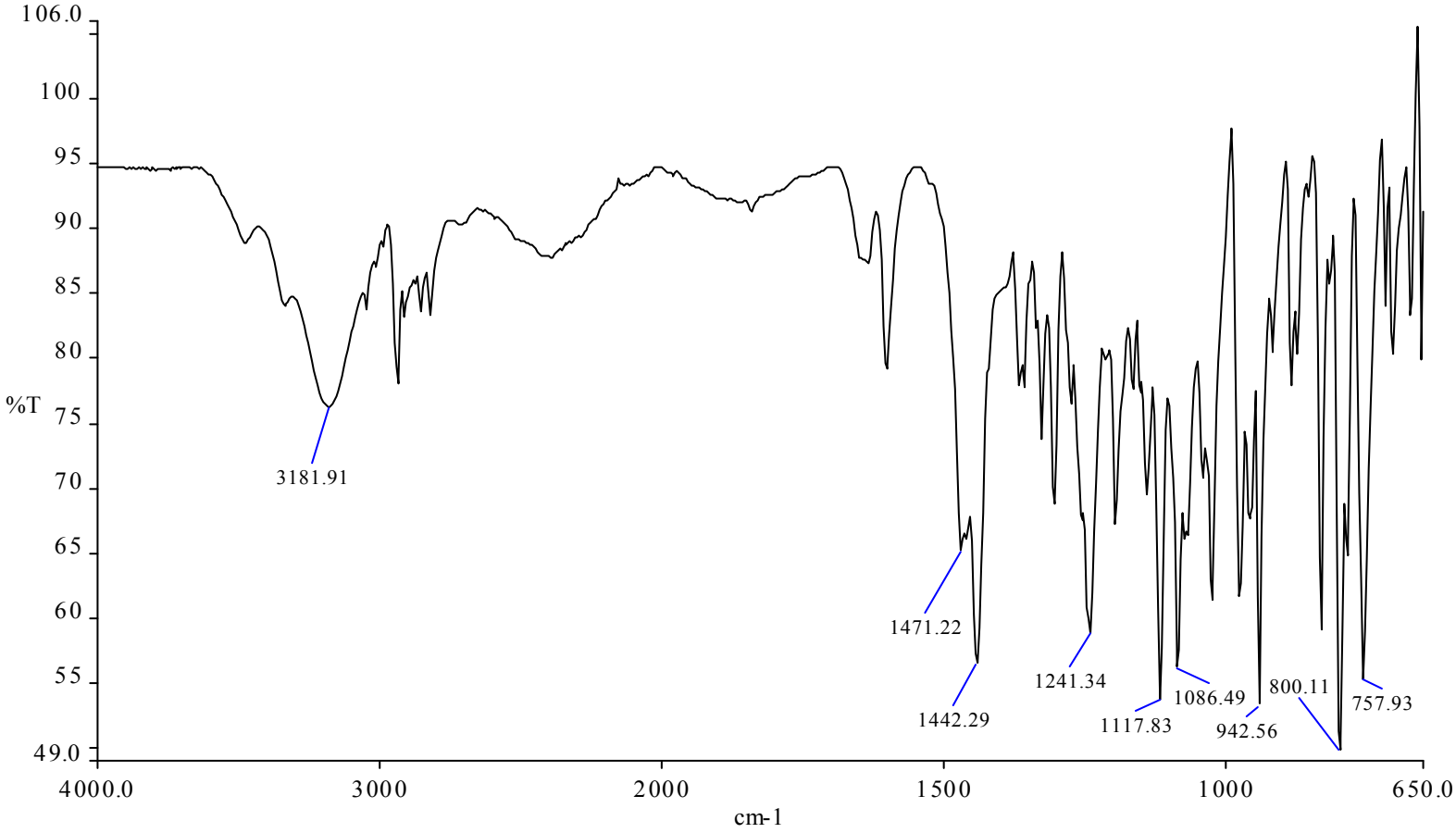


Figure B-11 IR-ATR Spectrum of Morphine Base (R9)

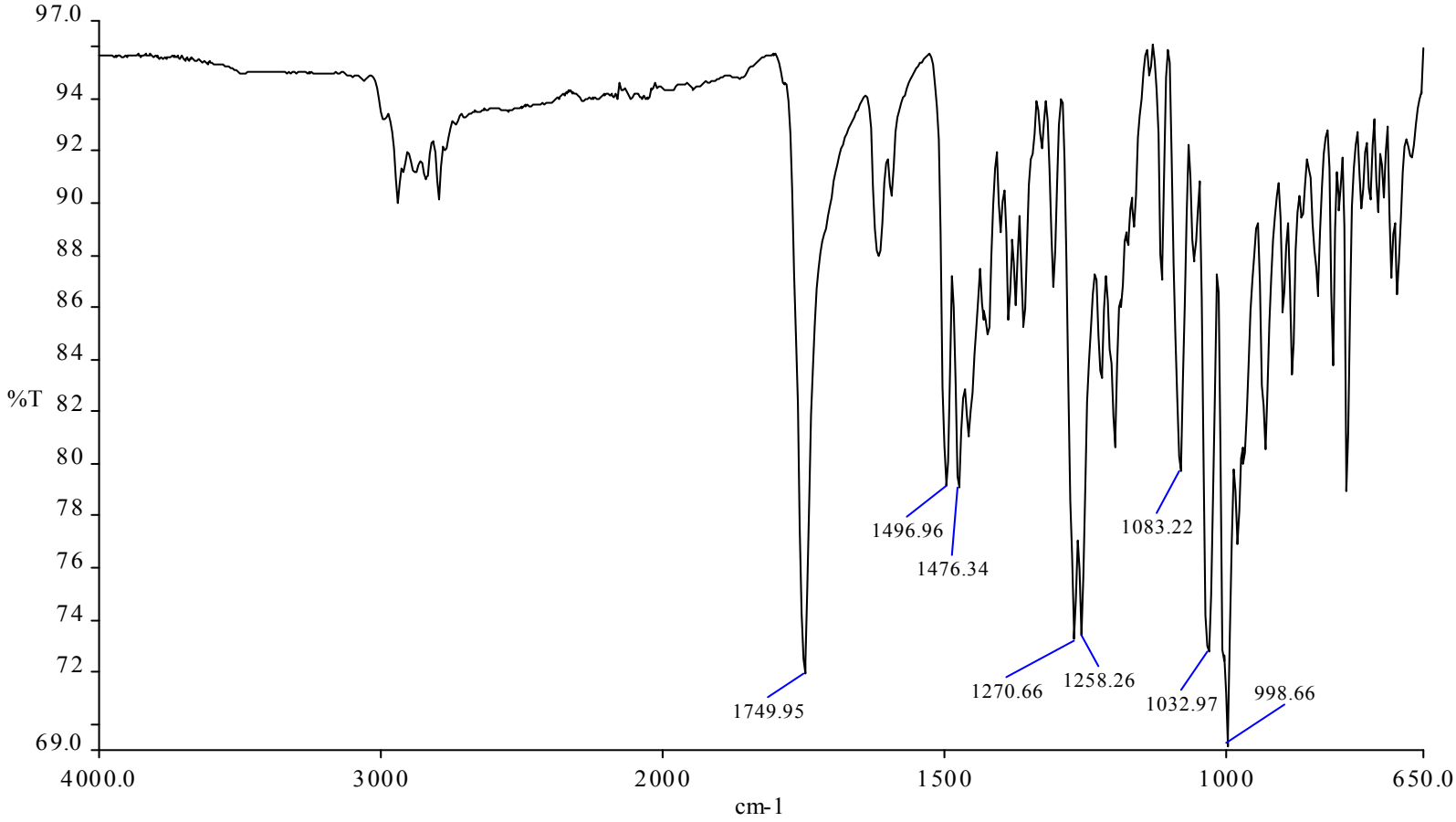


Figure B-12 IR-ATR Spectrum of Narcotine HCl (R10)

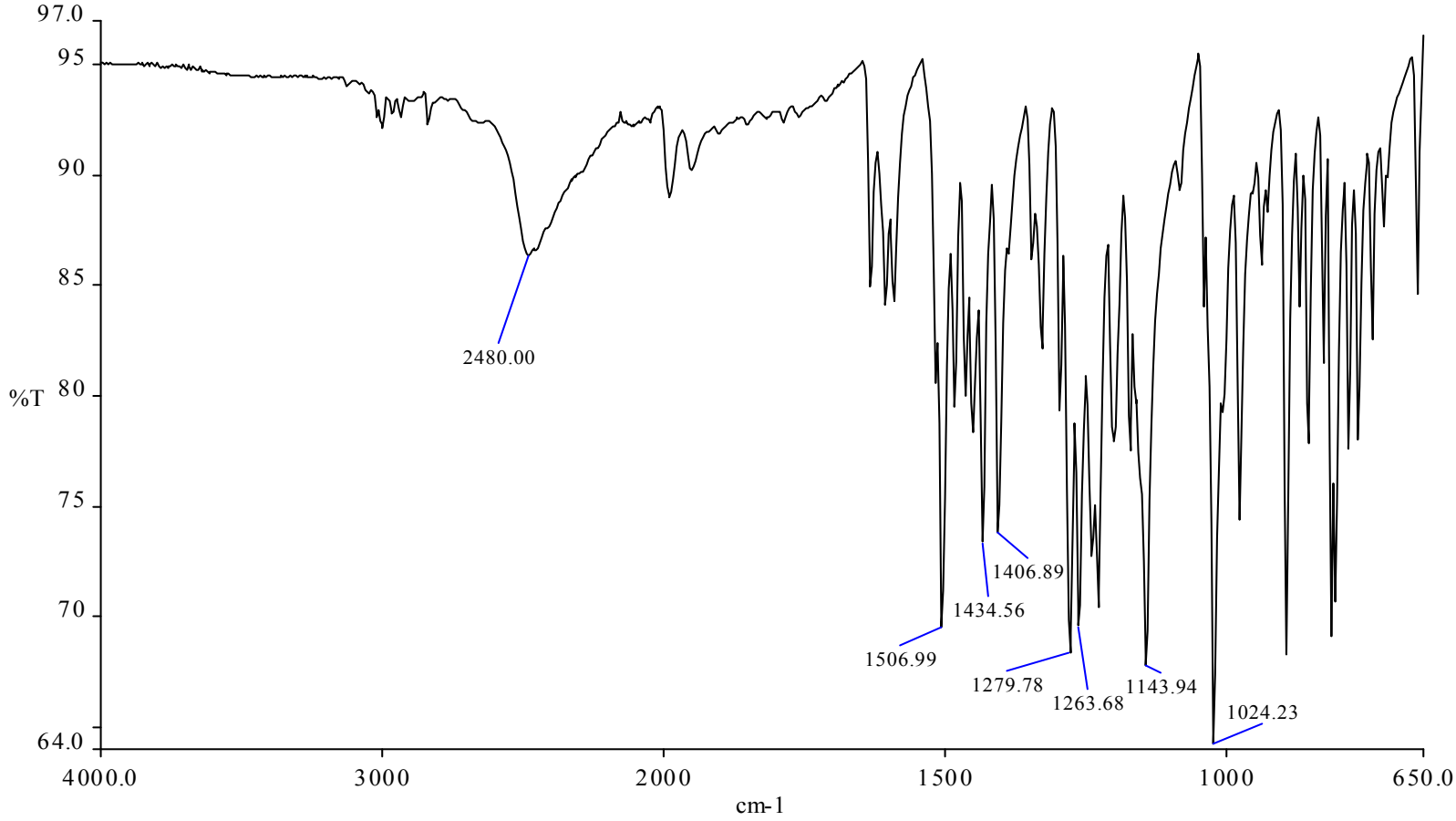


Figure B-13 IR-ATR Spectrum of Papaverine HCl (R11)

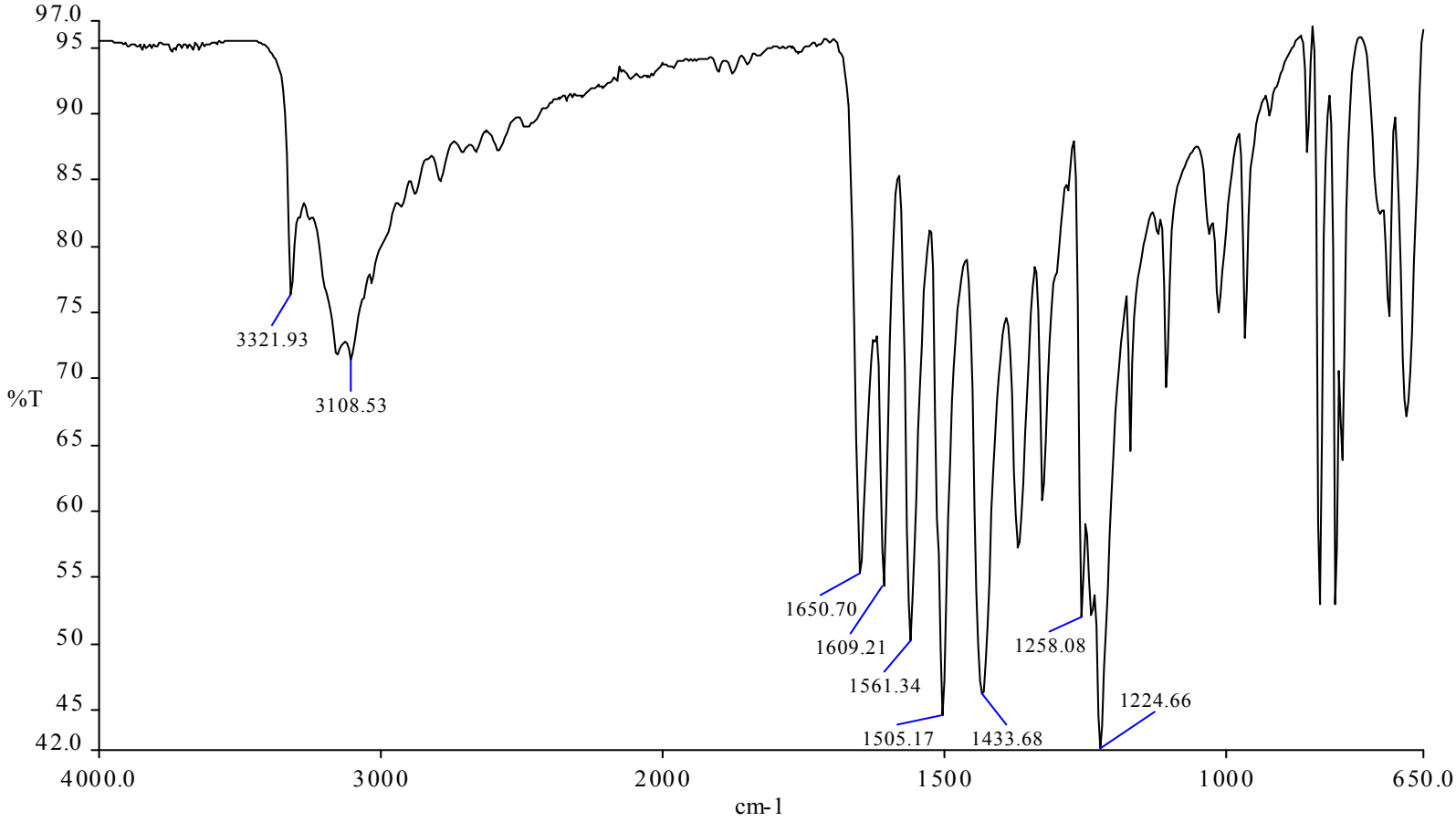


Figure B-14 IR-ATR Spectrum of Paracetamol (R12)

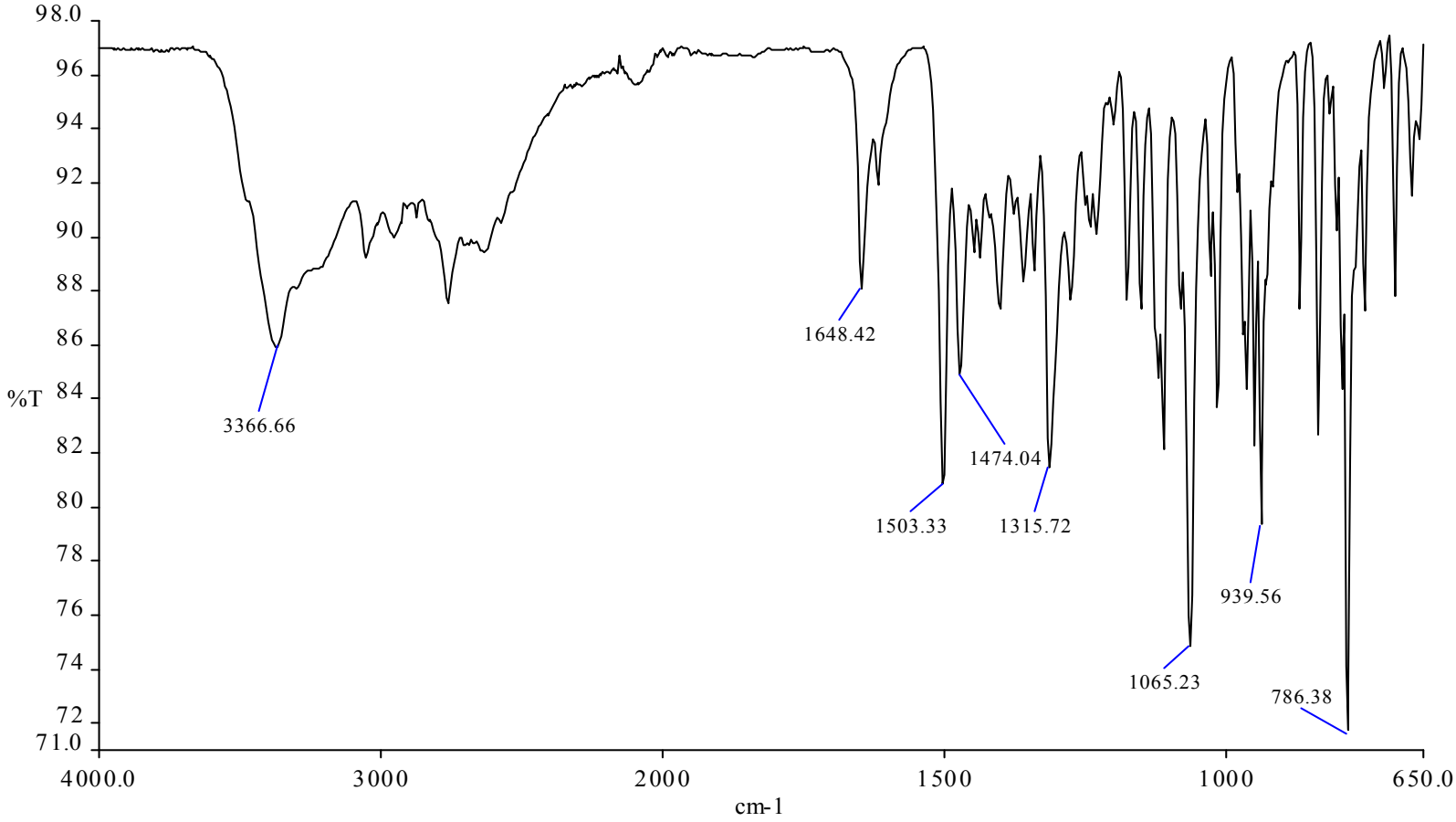


Figure B-15 IR-ATR Spectrum of Morphine HCl (R13)

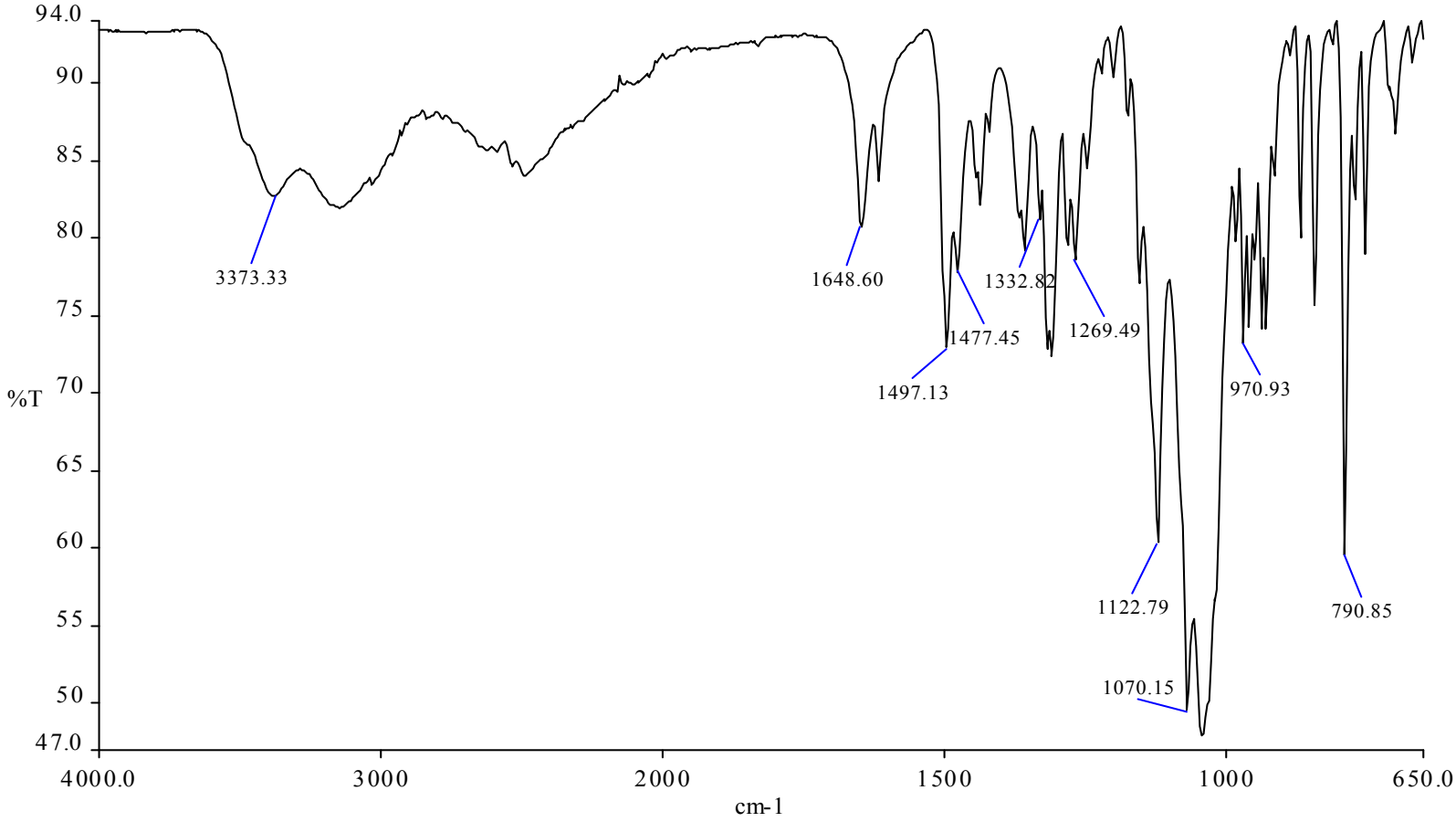


Figure B-16 IR-ATR Spectrum of Morphine H_2SO_4 (R14)

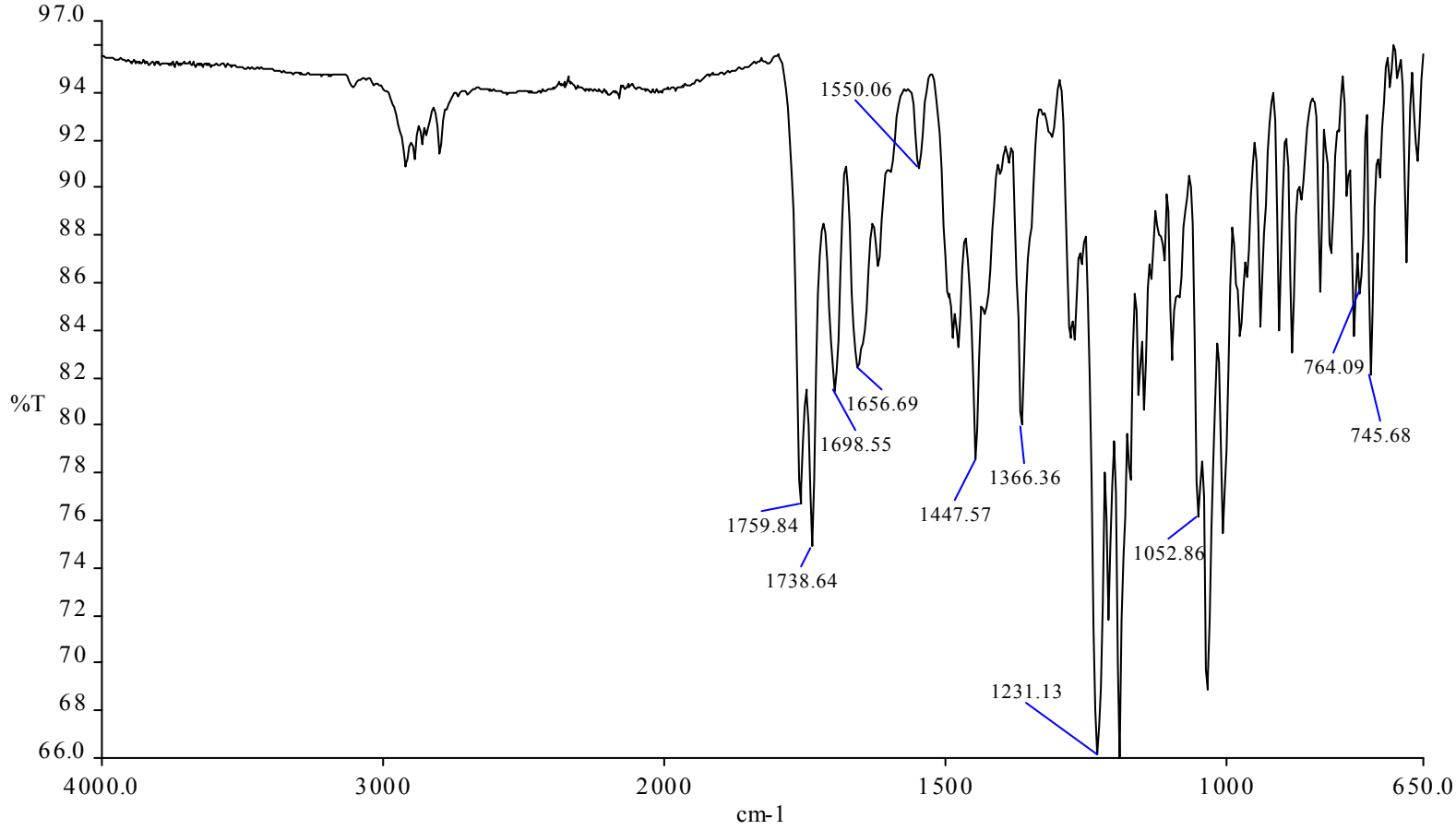


Figure B-17 IR-ATR Spectrum of Heroin containing Caffeine (P1)
(52.2 % Heroin, 15.2 % Caffeine)

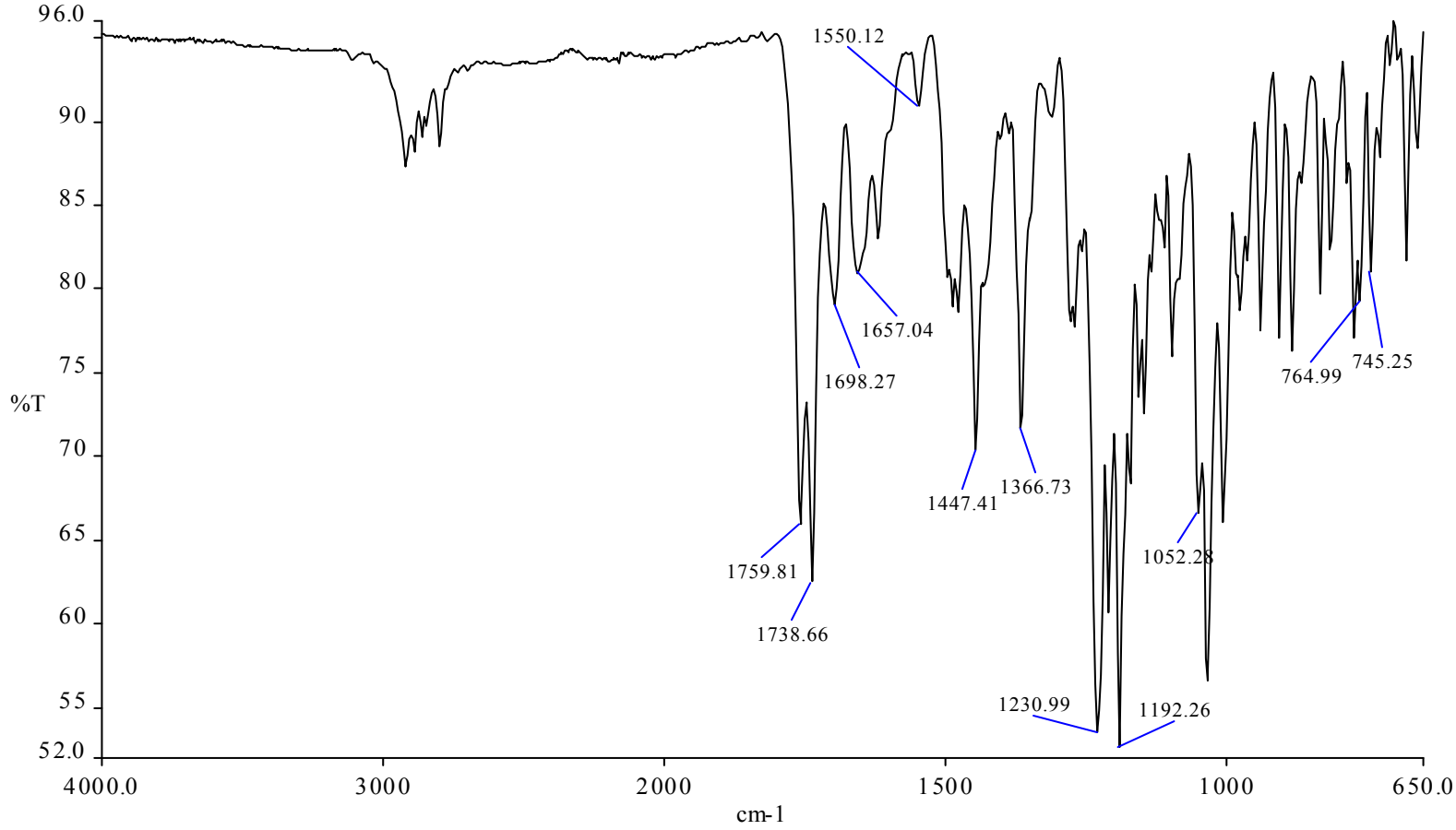


Figure B-18 IR-ATR Spectrum of Heroin containing Caffeine (P2)
(55.7 % Heroin, 10.1 % Caffeine)

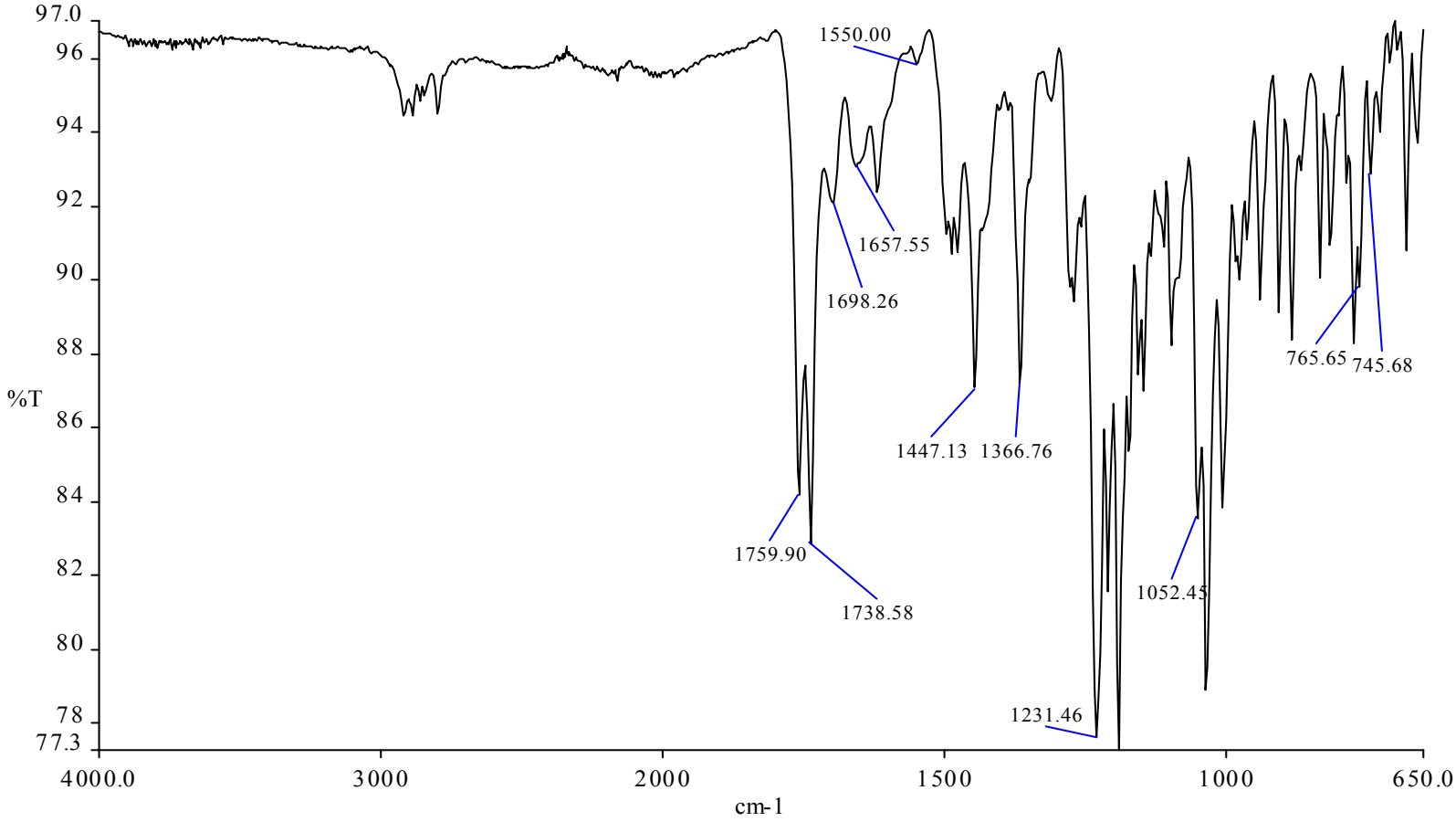


Figure B-19 IR-ATR Spectrum of Heroin containing Caffeine (P3)
(58.6 % Heroin, 5.4 % Caffeine)

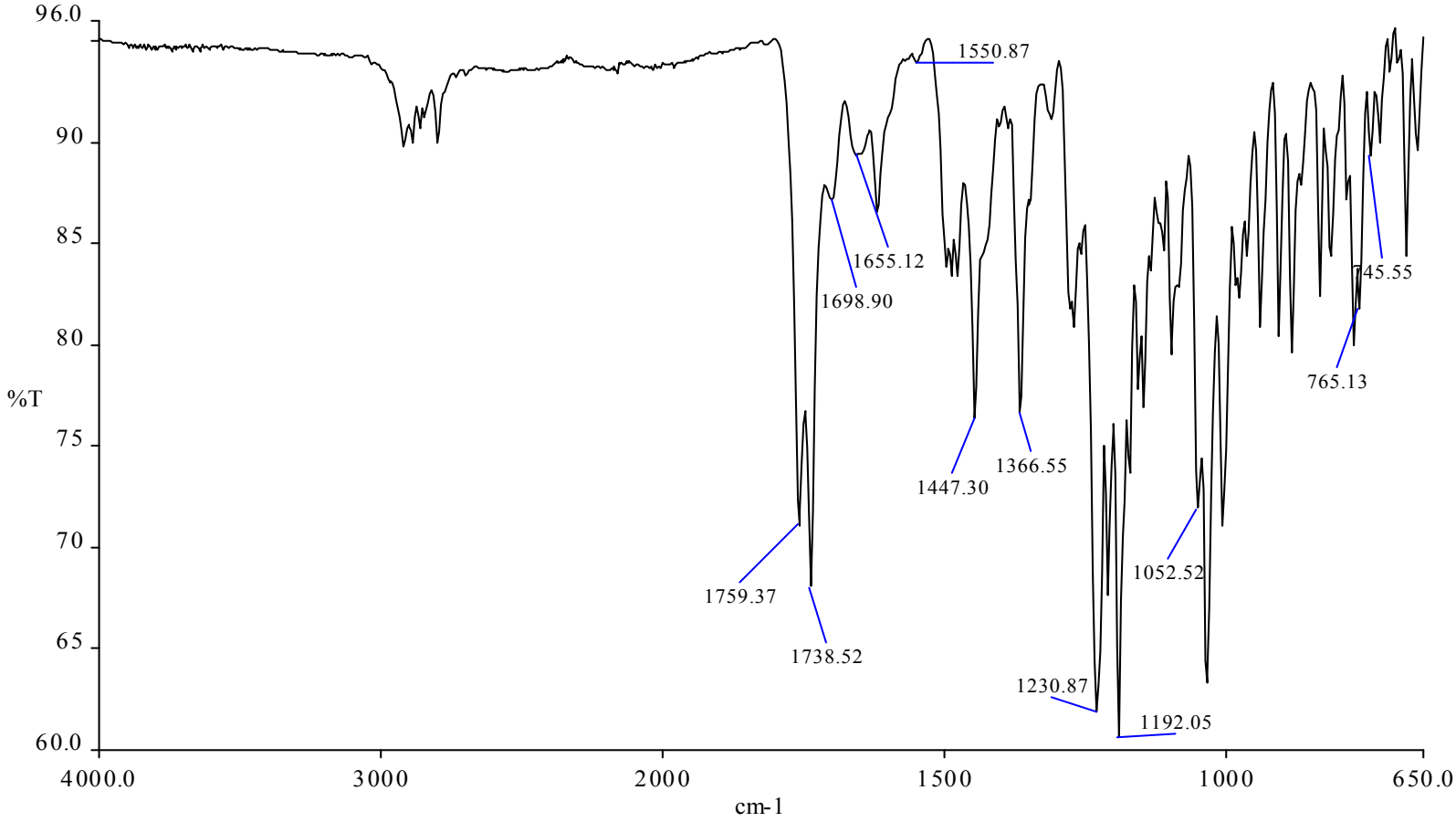


Figure B-20 IR-ATR Spectrum of Heroin containing Caffeine (P4)
(60.0 % Heroin, 3.2 % Caffeine)

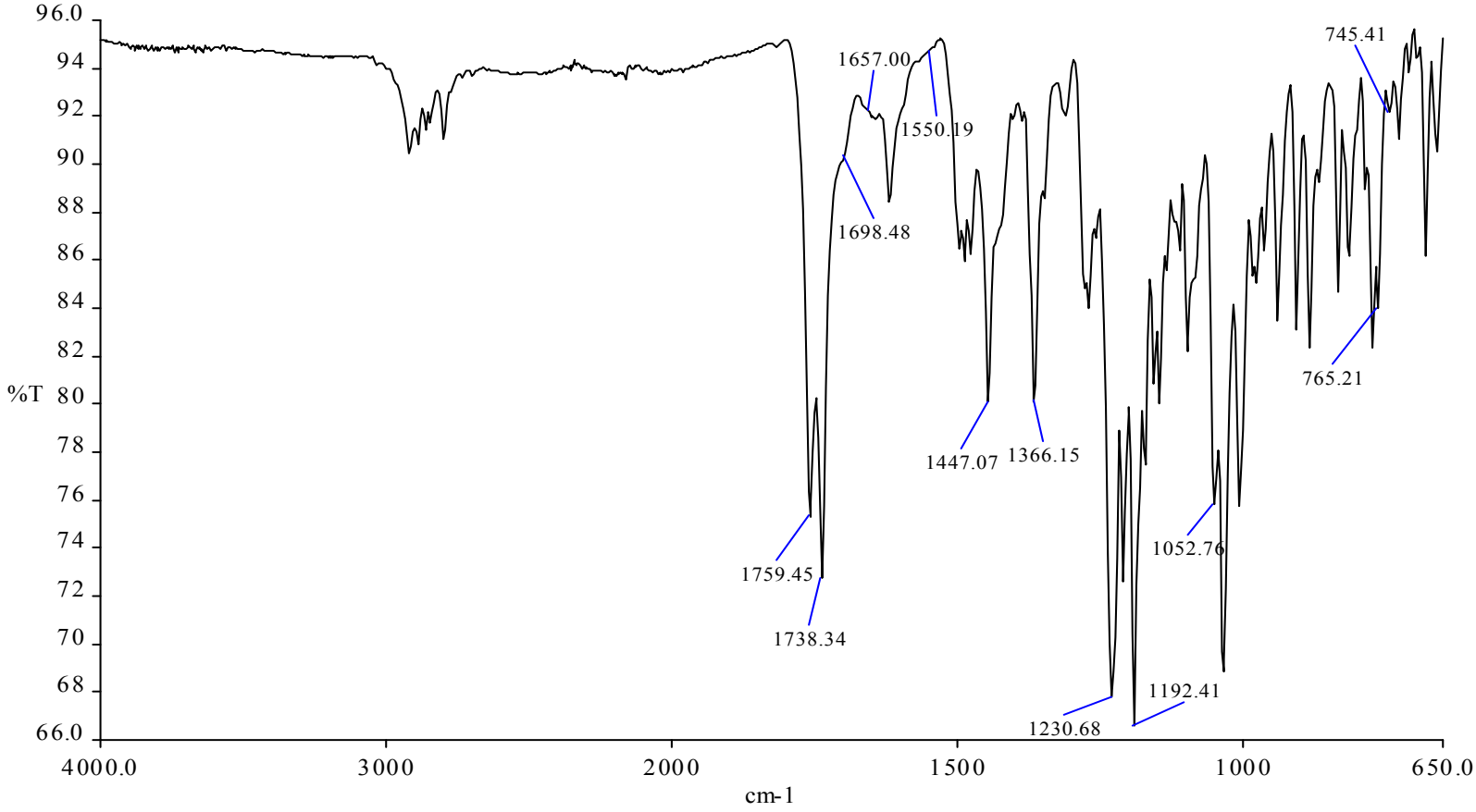


Figure B-21 IR-ATR Spectrum of Heroin containing Caffeine (P5)
(61.1 % Heroin, 1.5 % Caffeine)

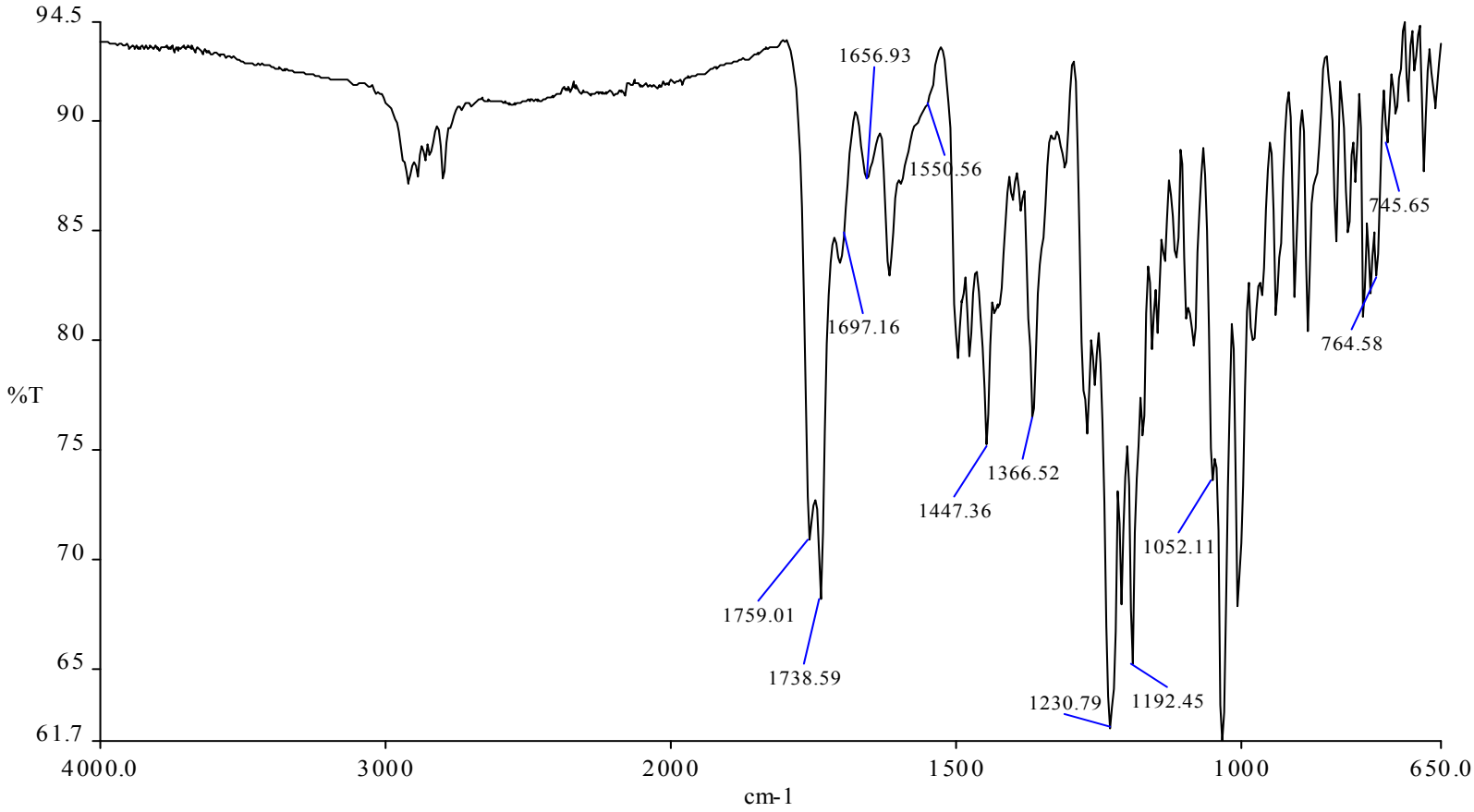


Figure B-22 IR-ATR Spectrum of Heroin containing Caffeine (P6)
(34.9 % Heroin, 3.0 % Caffeine)

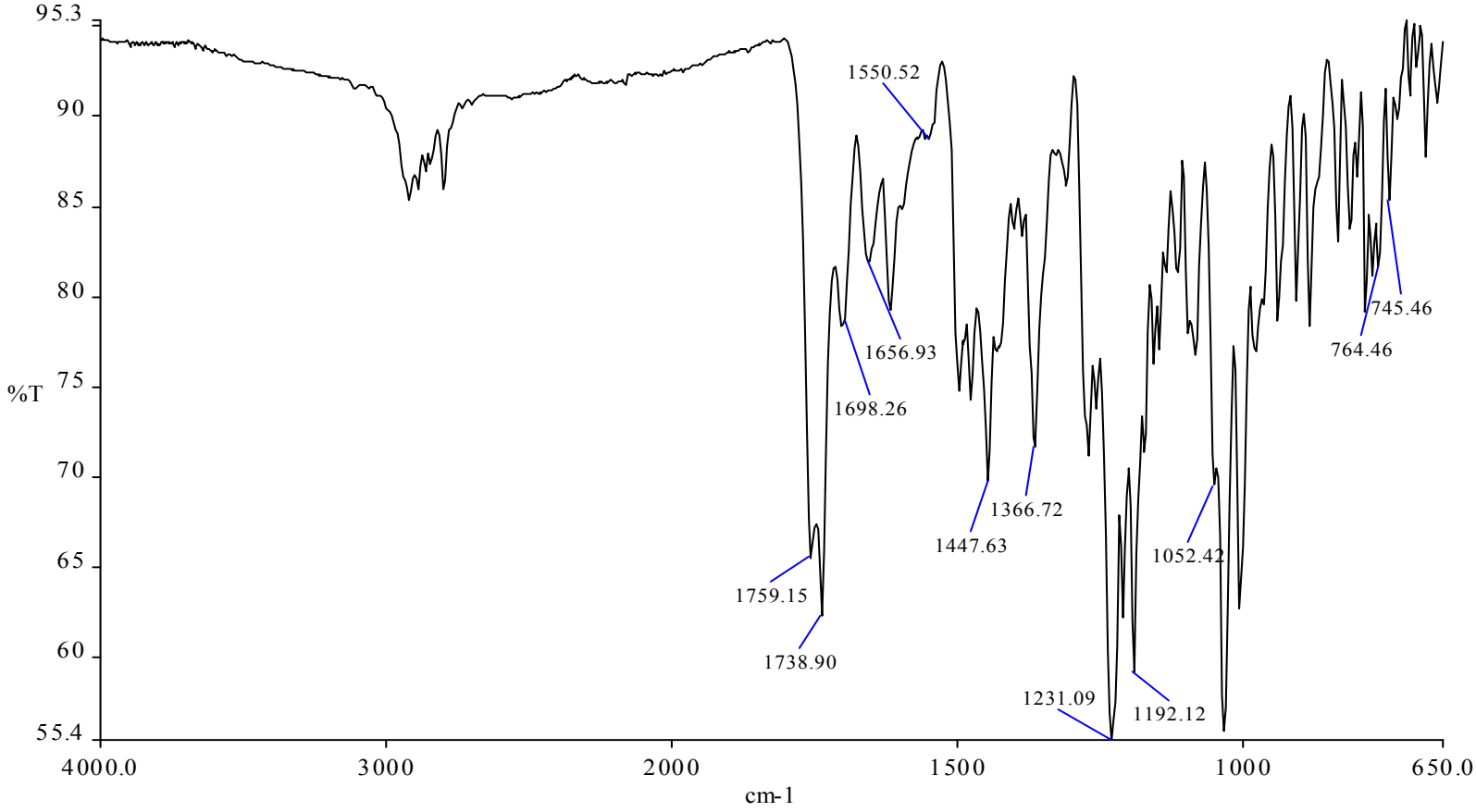


Figure B-23 IR-ATR Spectrum of Heroin containing Caffeine (P7)
(34.1% Heroin, 5.3 % Caffeine)

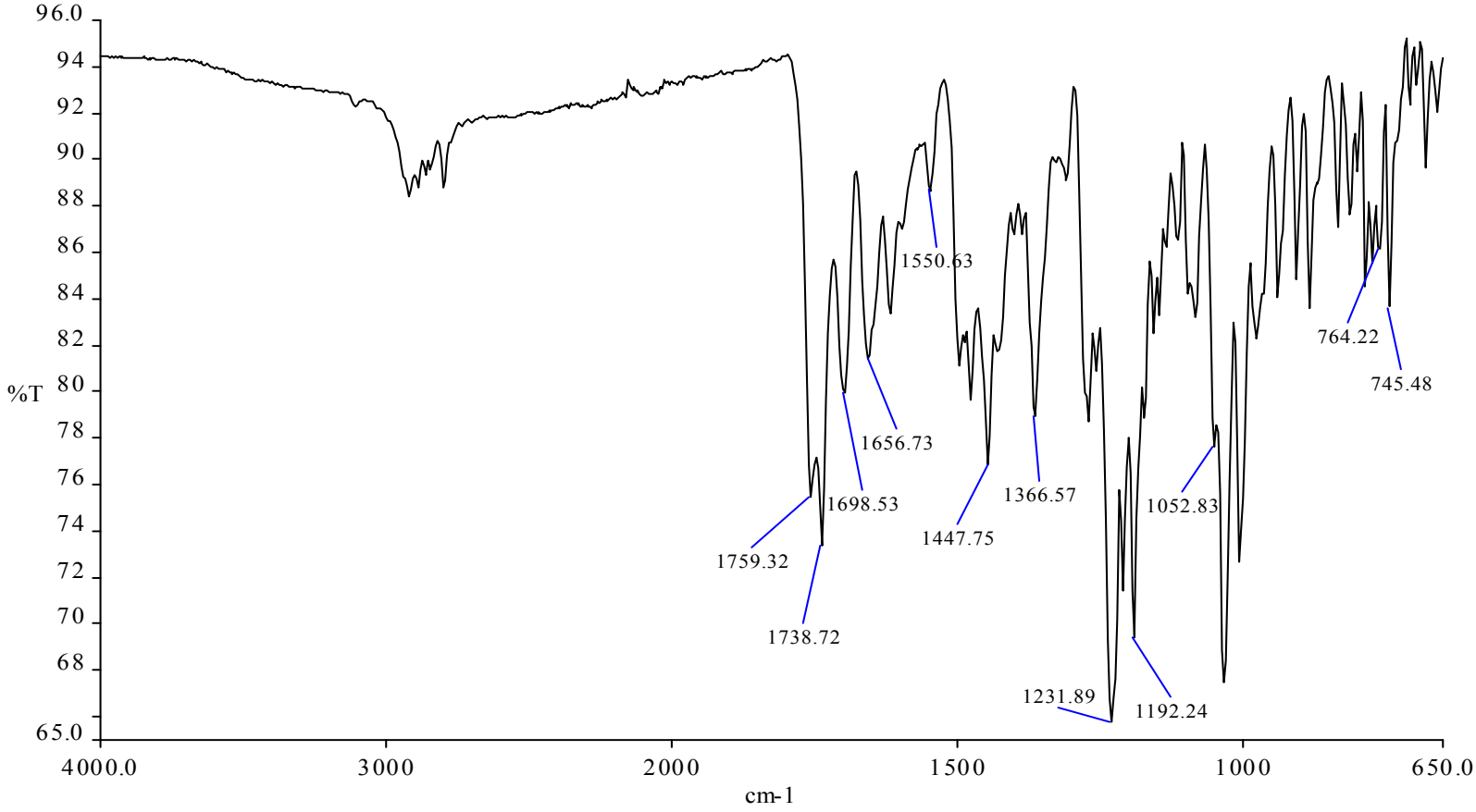


Figure B-24 IR-ATR Spectrum of Heroin containing Caffeine (P8)
(32.4 % Heroin, 10.0 Caffeine)

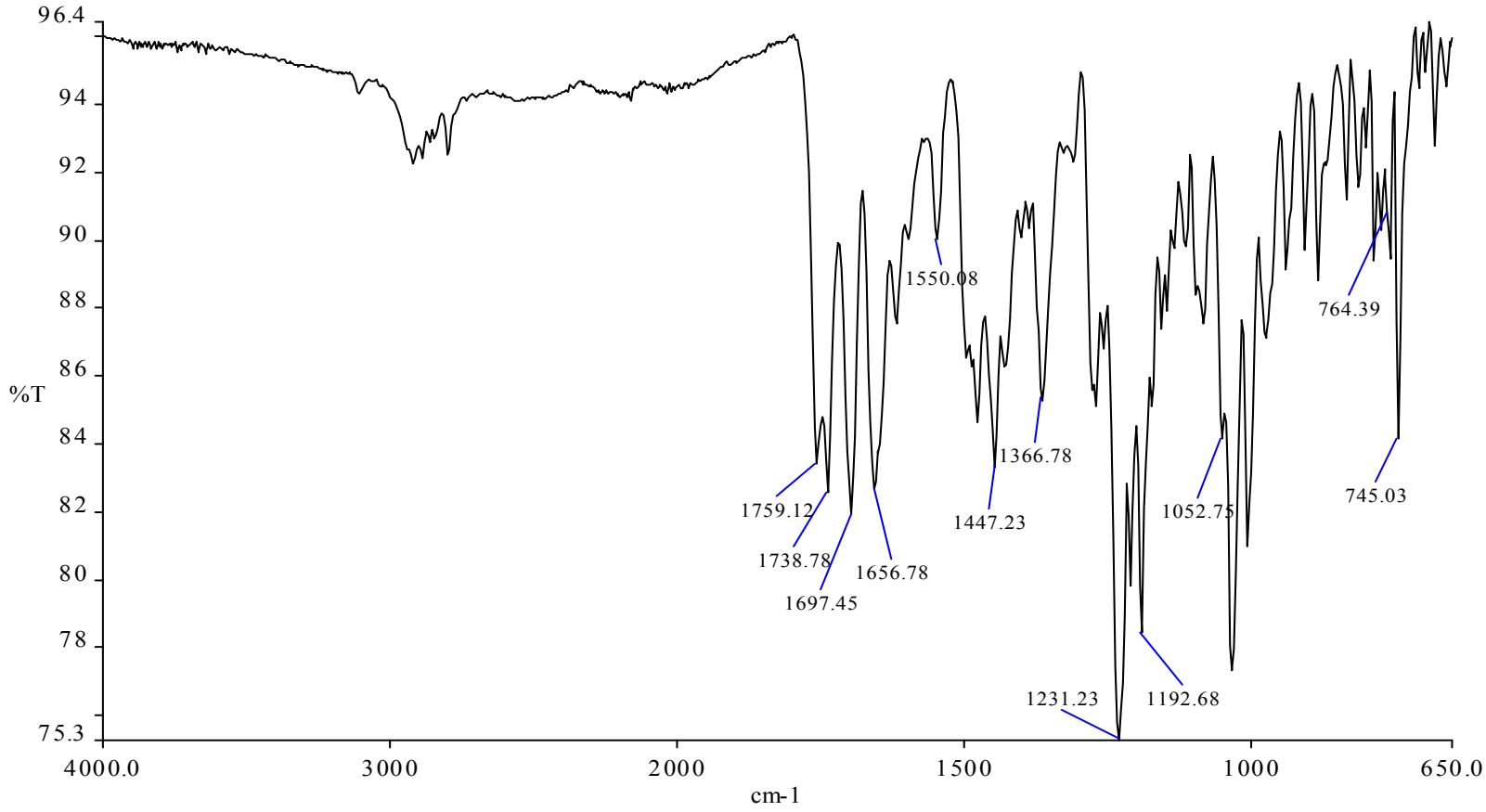


Figure B-25 IR-ATR Spectrum of Heroin containing Caffeine (P9)
(30.3 % Heroin, 15.8 % Caffeine)

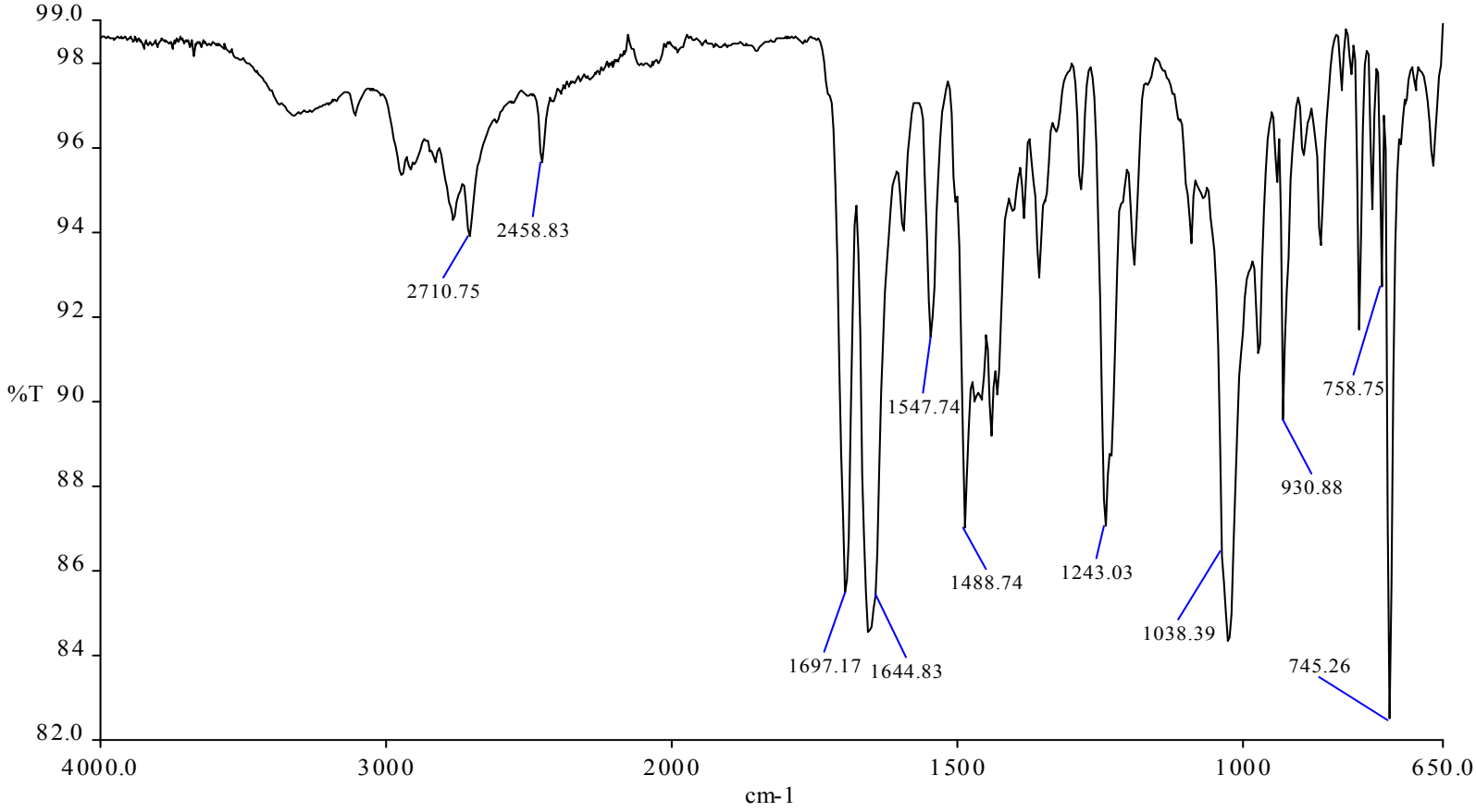


Figure B-26 IR-ATR Spectrum of MDMA containing Caffeine (P10)
(35.7 % MDMA, 36.2 % Caffeine)

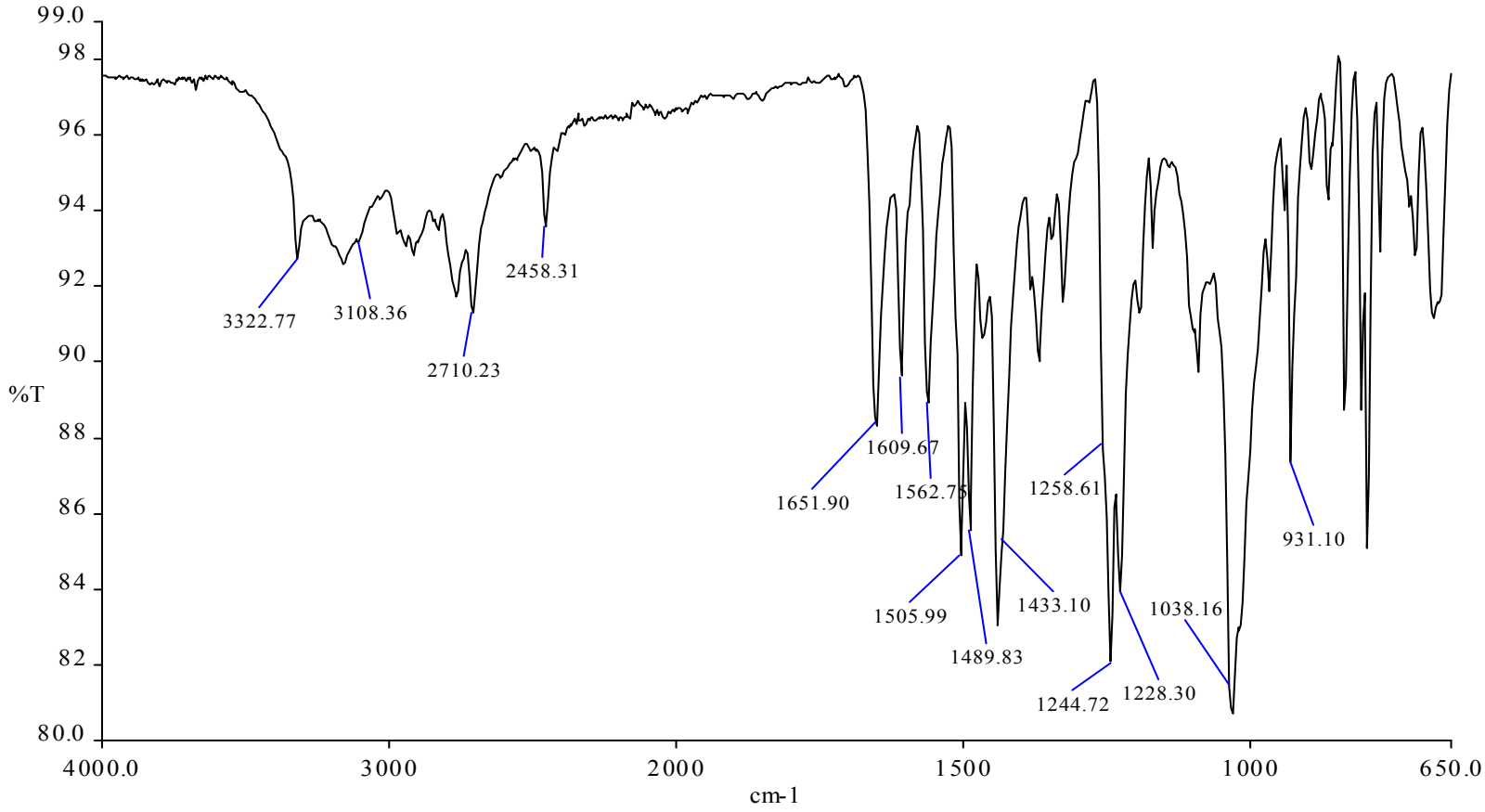


Figure B-27 IR-ATR Spectrum of MDMA containing Paracetamol (P11)
(37.2 % MDMA, 33.5 % Paracetamol)

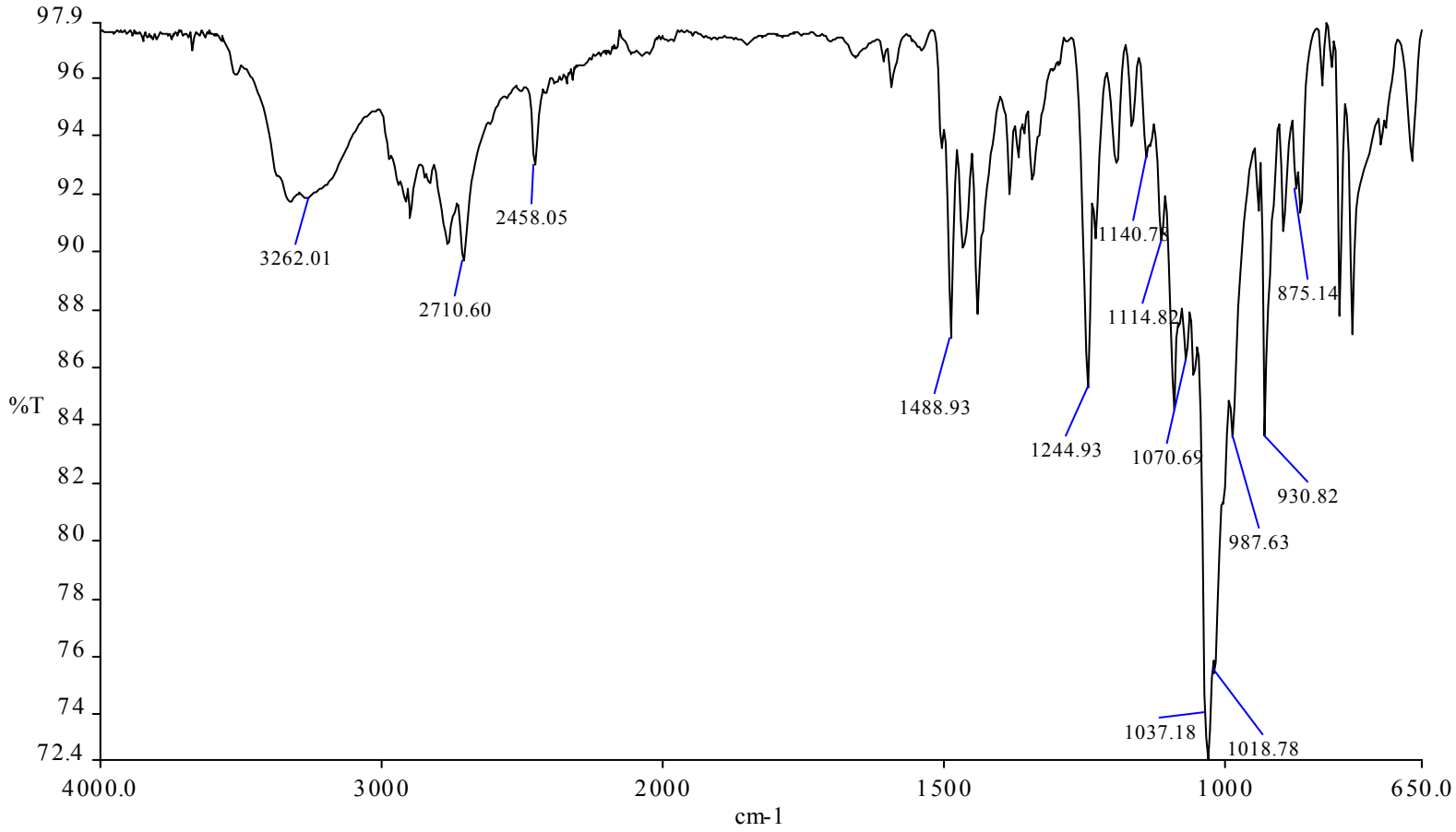


Figure B-28 IR-ATR Spectrum of MDMA containing Lactose (P12)
(34.2 % MDMA, 38.8 % Lactose)

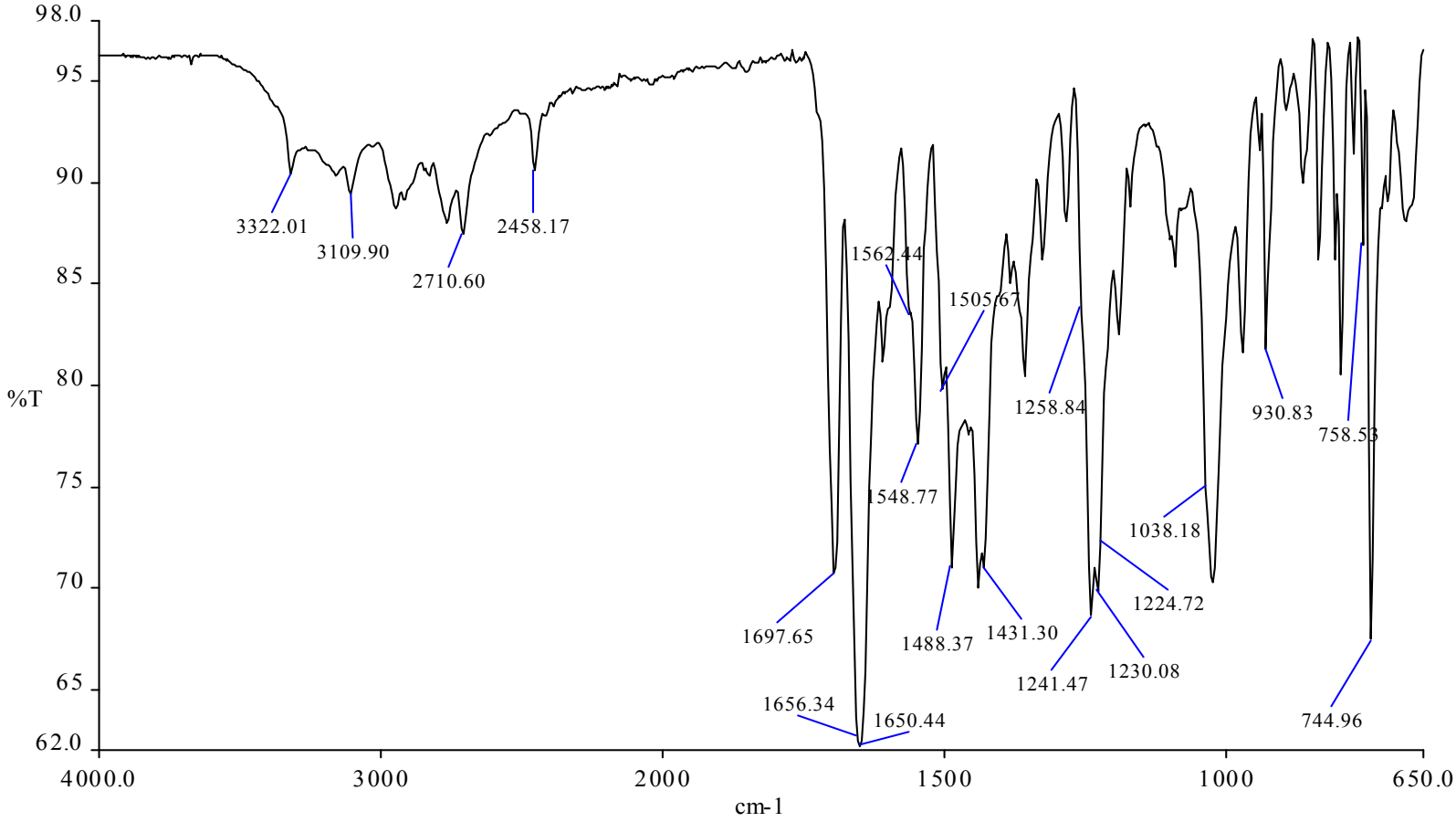


Figure B-29 IR-ATR Spectrum of MDMA containing Caffeine and Paracetamol (P13)
(33.4 % MDMA, 17.4 % Caffeine, 22.9 % Paracetamol)

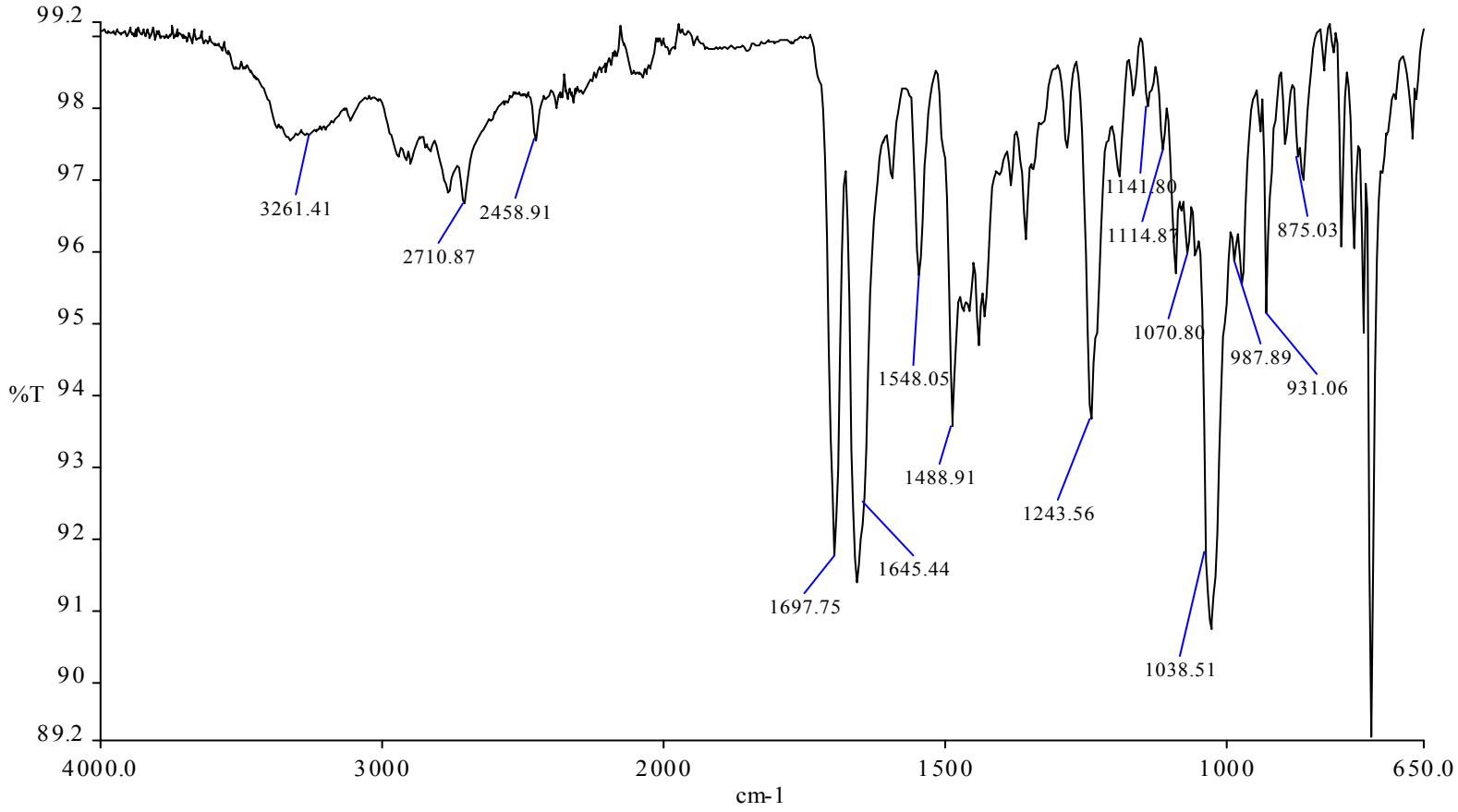


Figure B-30 IR-ATR Spectrum of MDMA containing Caffeine and Lactose (P14)
(35.9 % MDMA, 19.4 % Caffeine, 16.5 % Lactose)

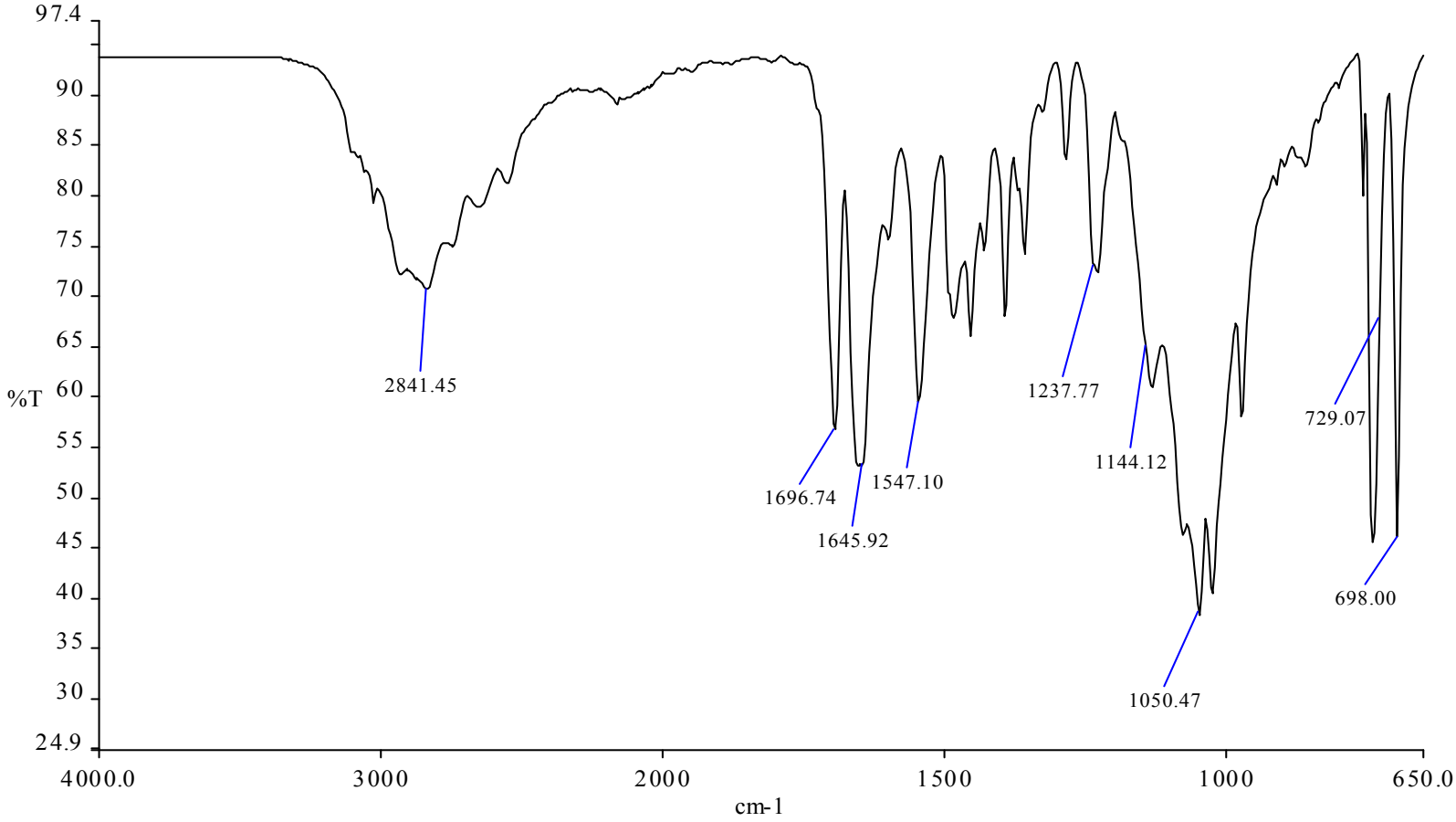


Figure B-31 IR-ATR Spectrum of Amphetamine containing Caffeine (P15)
(66.4 % Amphetamine, 33.5 % Caffeine)

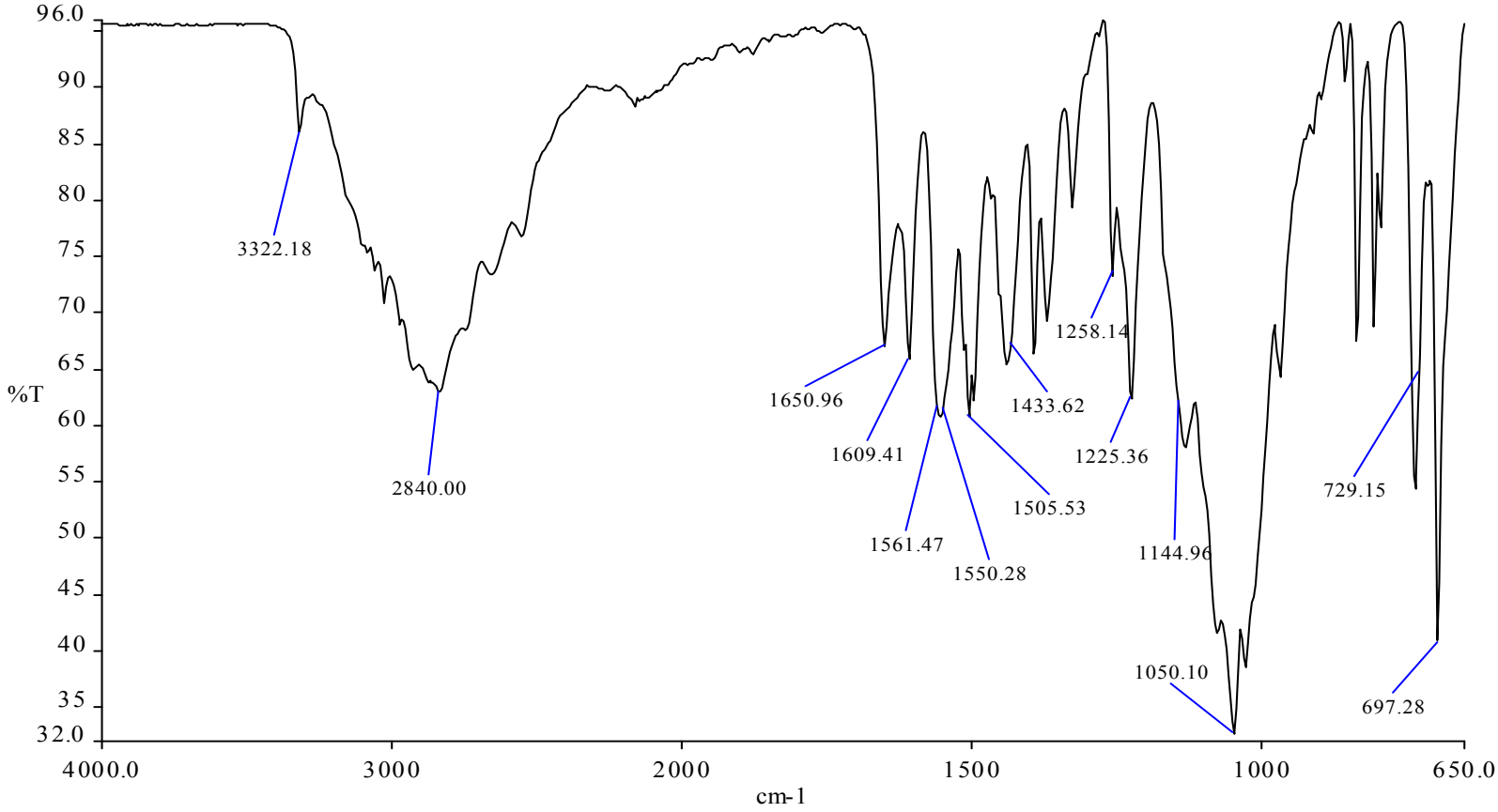


Figure B-32 IR-ATR Spectrum of Amphetamine containing Paracetamol (P16)
(66.8 % Amphetamine, 33.1 % Paracetamol)

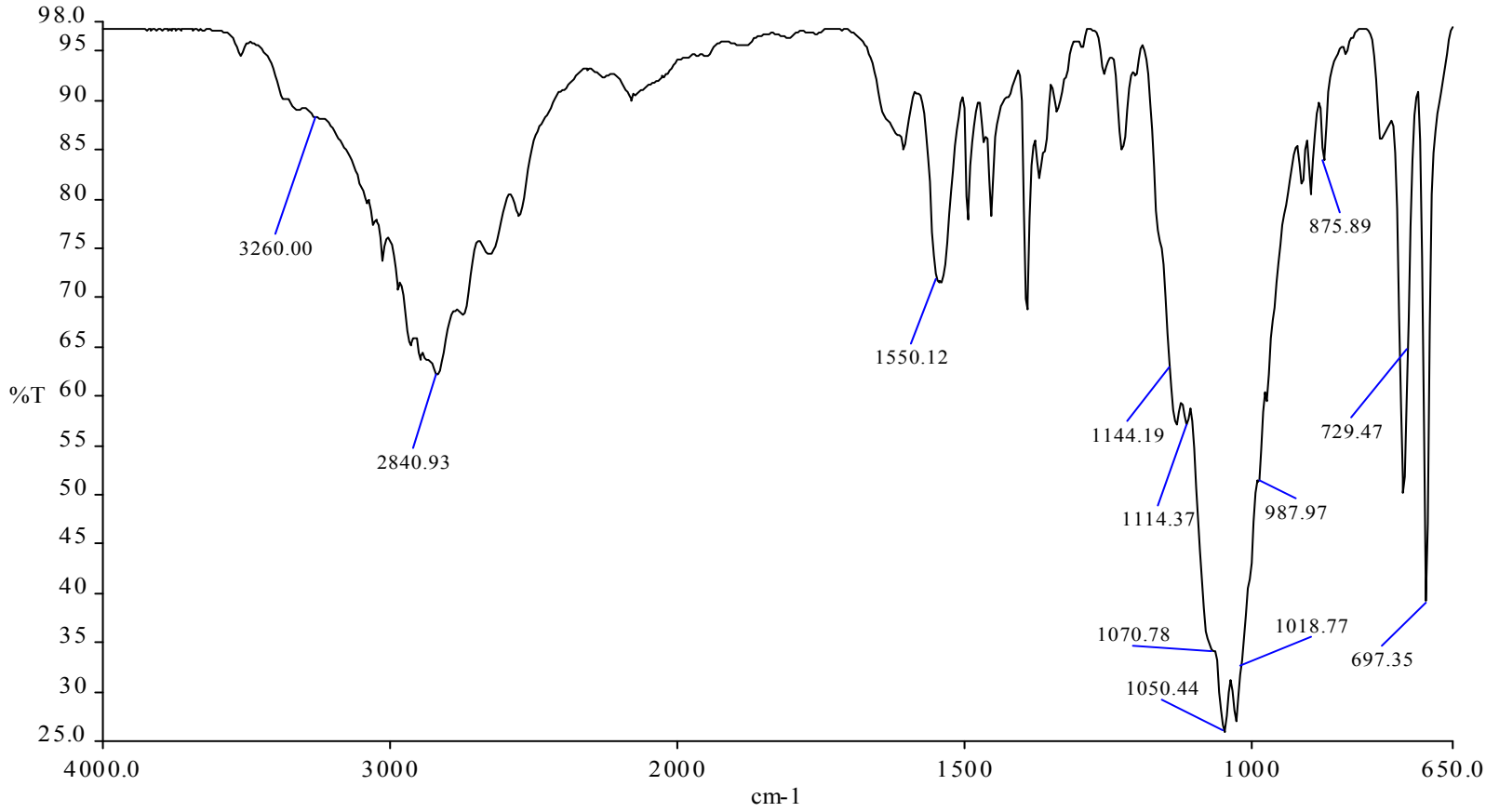


Figure B-33 IR-ATR Spectrum of Amphetamine containing Lactose (P17)
(71.4 % Amphetamine, 28.6 % Lactose)

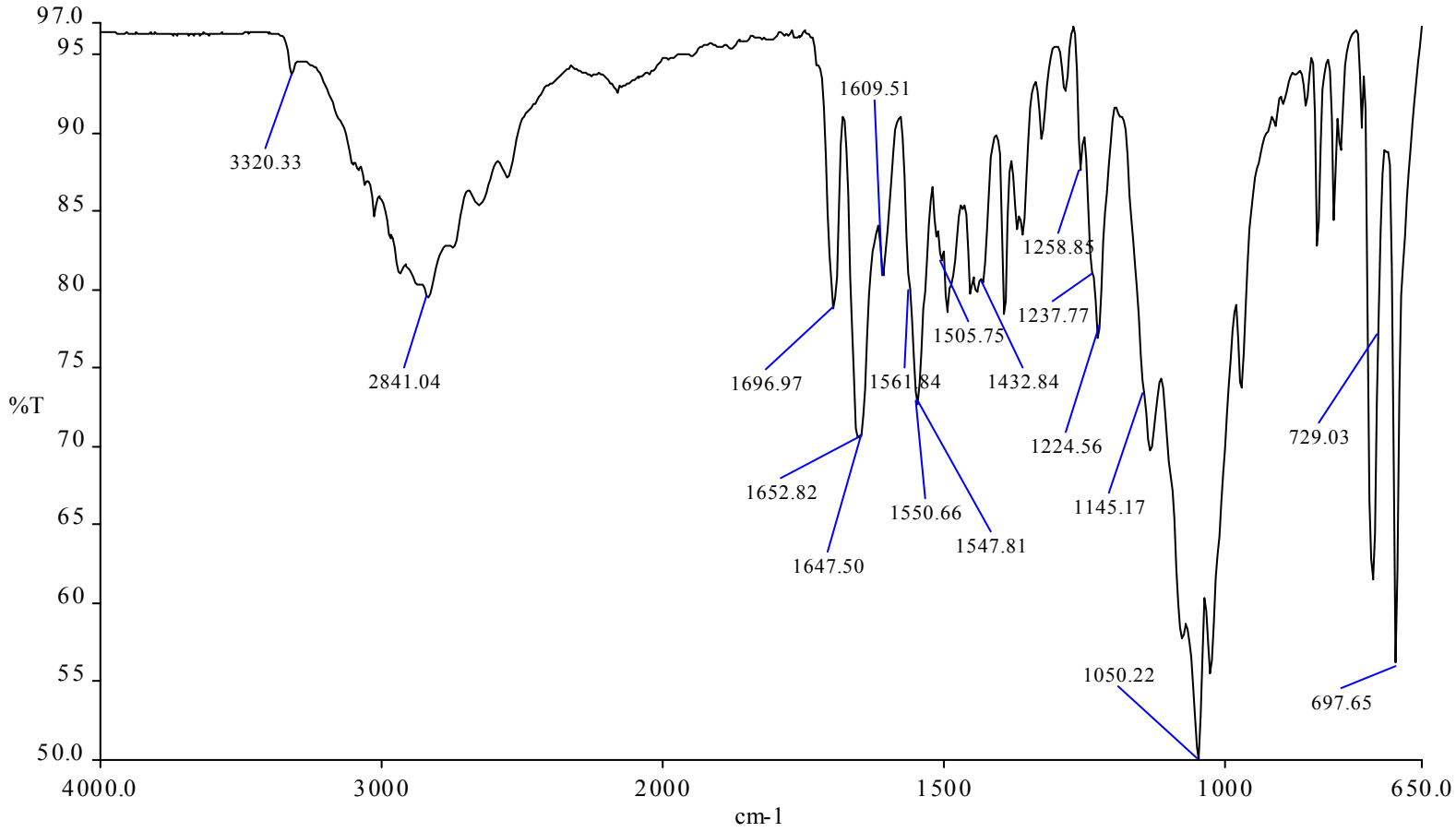


Figure B-34 IR-ATR Spectrum of Amphetamine containing Caffeine and Paracetamol (P18)
(62.2 % Amphetamine, 17.9 % Caffeine, 19.7 % Paracetamol)

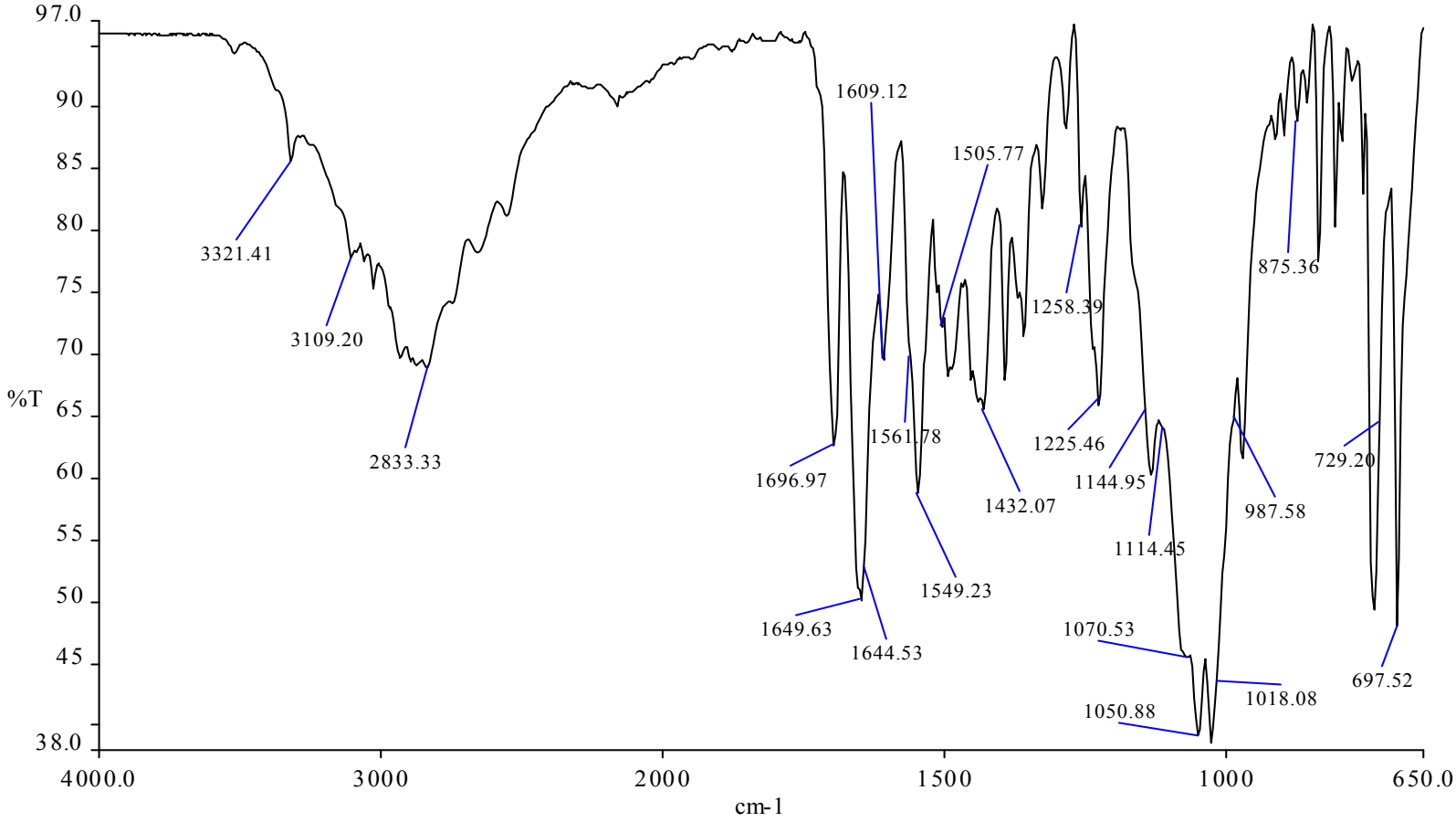


Figure B-35 IR-ATR Spectrum of Amphetamine containing Caffeine, Paracetamol and Lactose (P19)
(42.4 % Amphetamine, 18.8 % Caffeine, 16.4 % Paracetamol, 22.4 % Lactose)

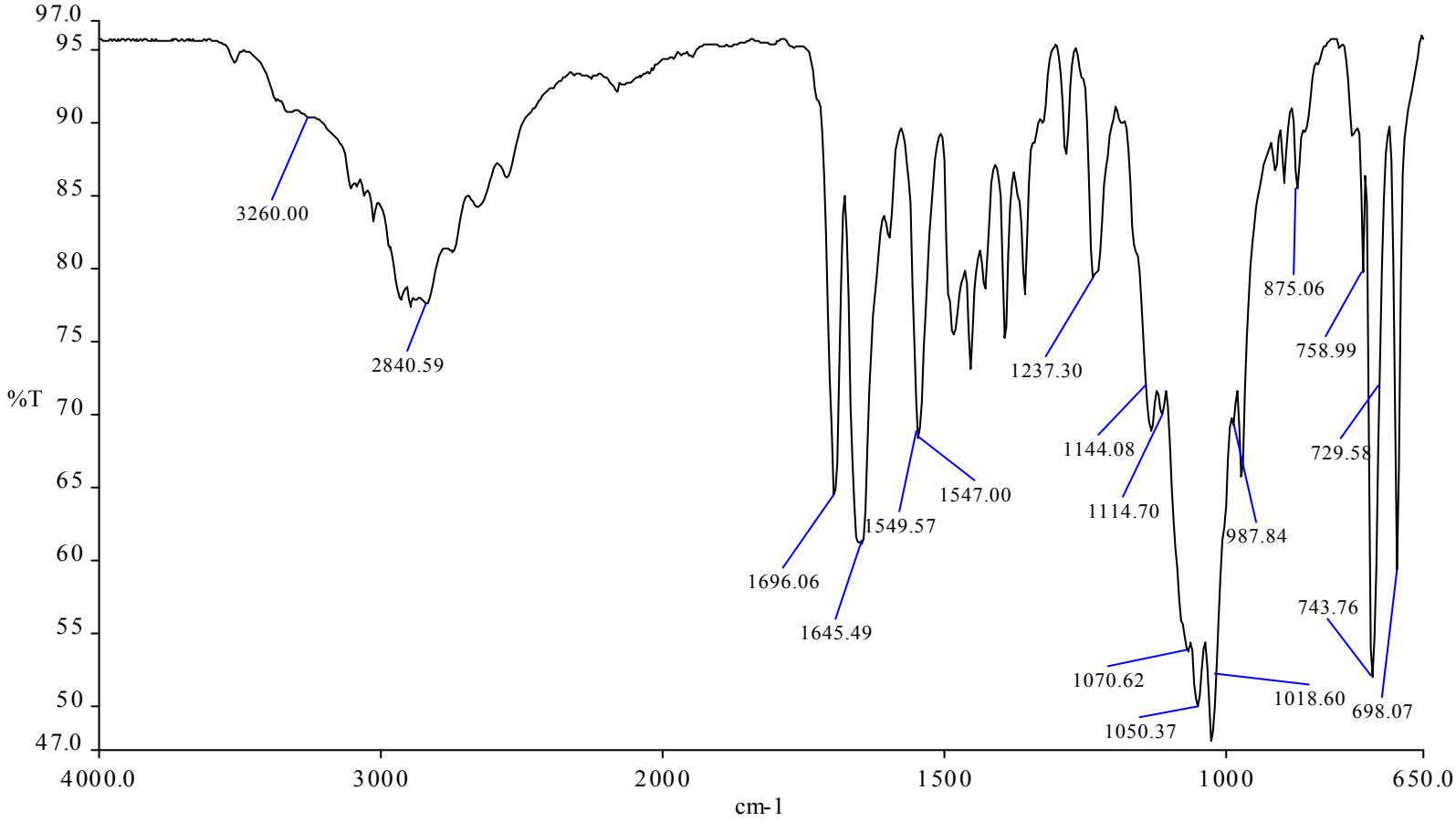


Figure B-36 IR-ATR Spectrum of Amphetamine containing Caffeine and Lactose (P20)
(46.6 % Amphetamine, 22.7 % Caffeine, 30.6 % Lactose)

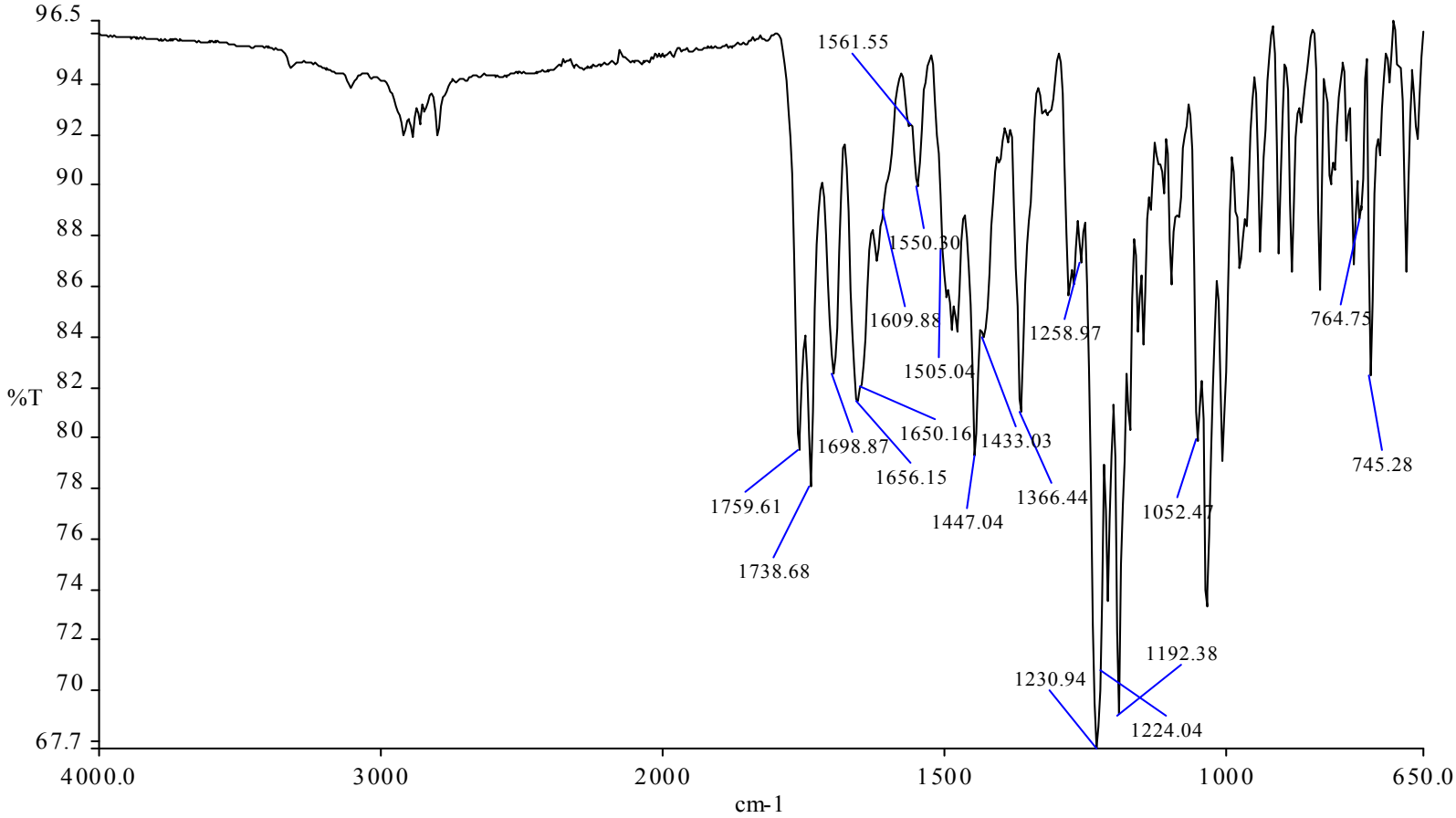


Figure B-37 IR-ATR Spectrum of Heroin containing Caffeine and Paracetamol (P21)
(43.5 % Heroin, 14.7 % Caffeine, 15.0 % Paracetamol)

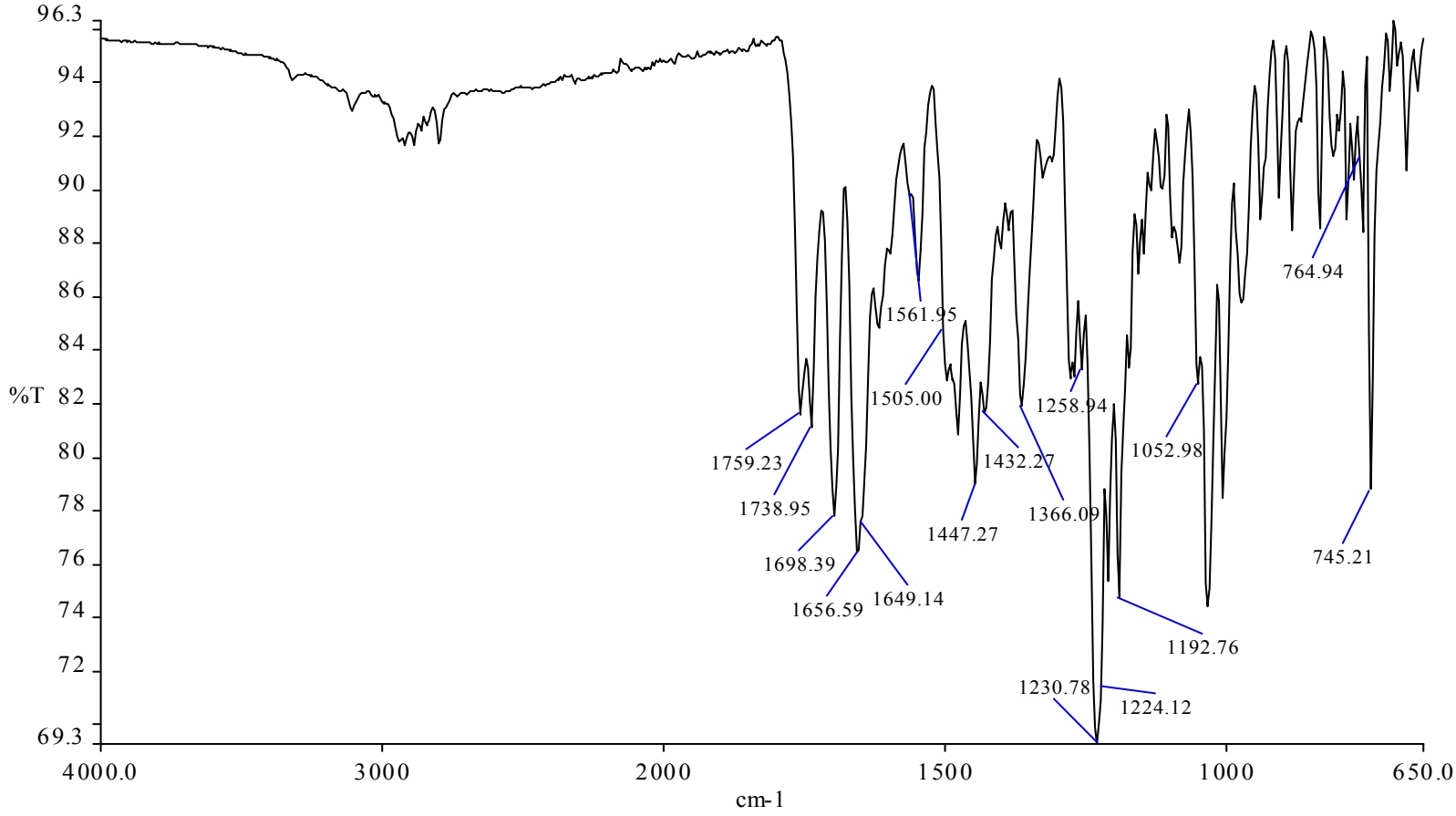


Figure B-38 IR-ATR Spectrum of Heroin containing Caffeine and Paracetamol (P22)
(24.7 % Heroin, 18.2 % Caffeine, 13.1 % Paracetamol)

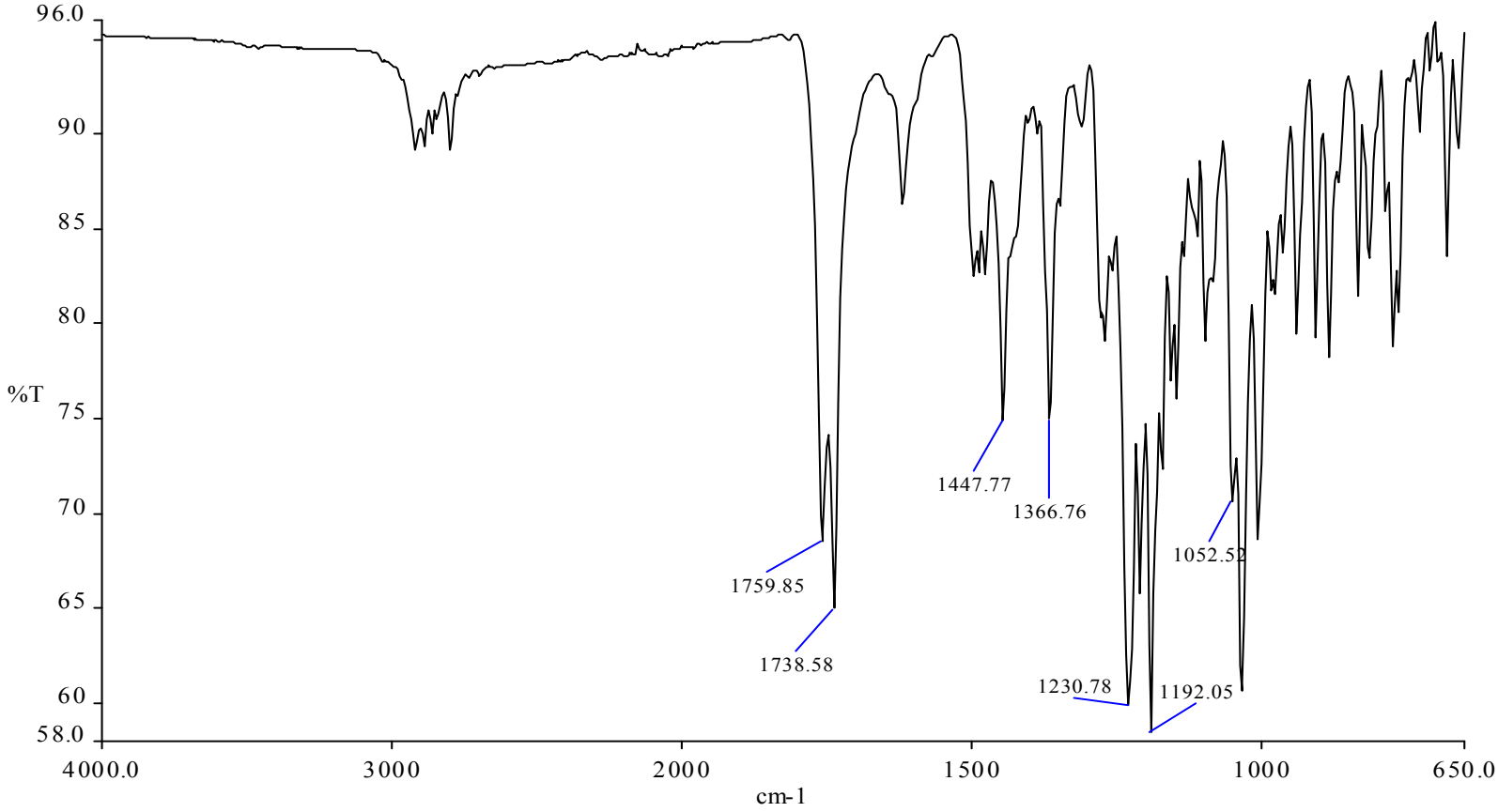


Figure B-39 IR-ATR Spectrum of Heroin Base (P23)
(62.6 % Heroin, 1.9 % Monoacetylmorphine, 5.1 % Acetyl Codeine, 2.3 % Papaverine, 20.6 % Narcotine)

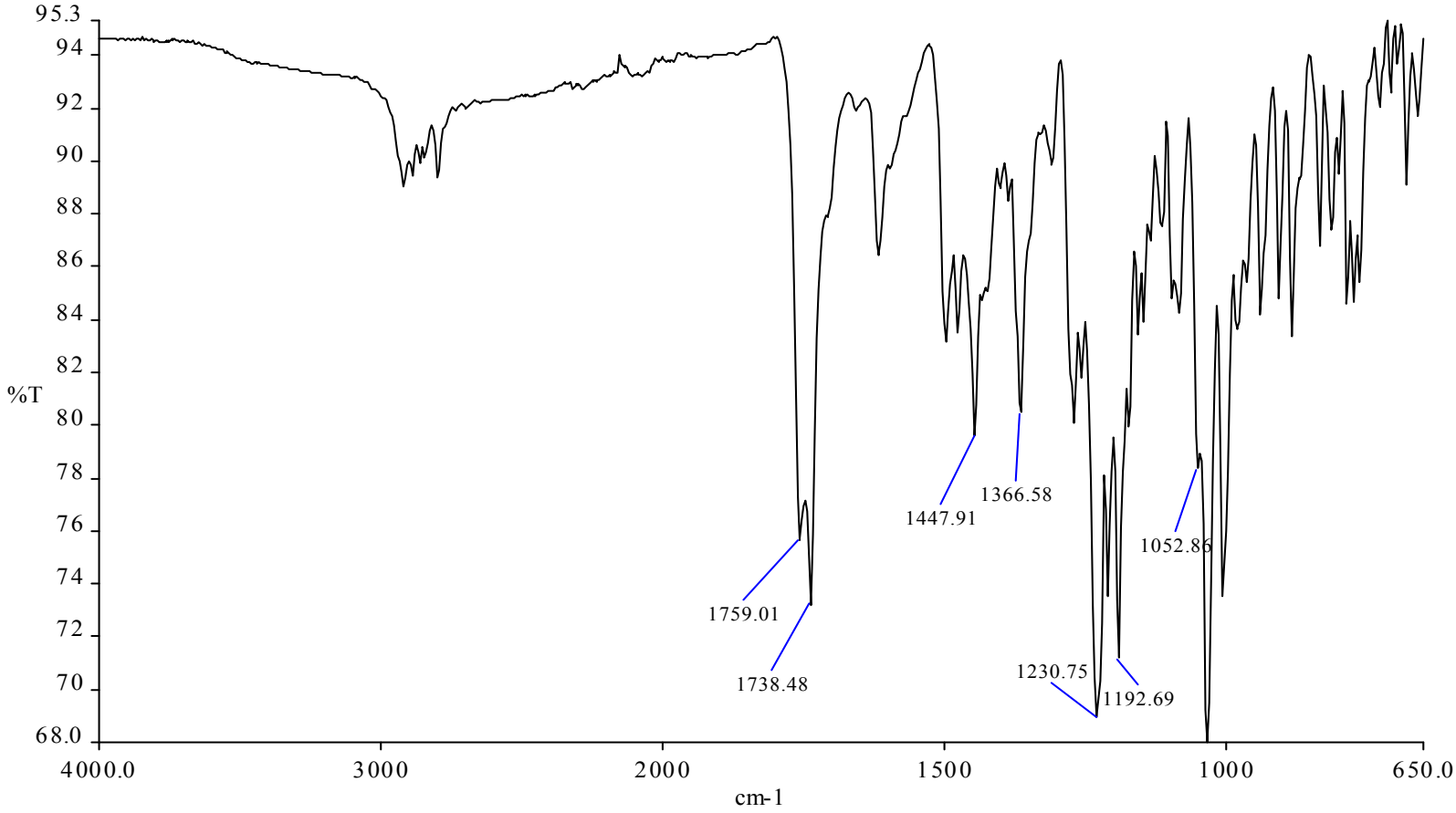


Figure B-40 IR-ATR Spectrum of Heroin Base (P24)
(36.5 % Heroin, 9.2 % Monoacetylmorphine, 3.1 % Acetyl Codeine, 1.9 % Papaverine, 30.6 % Narcotine)

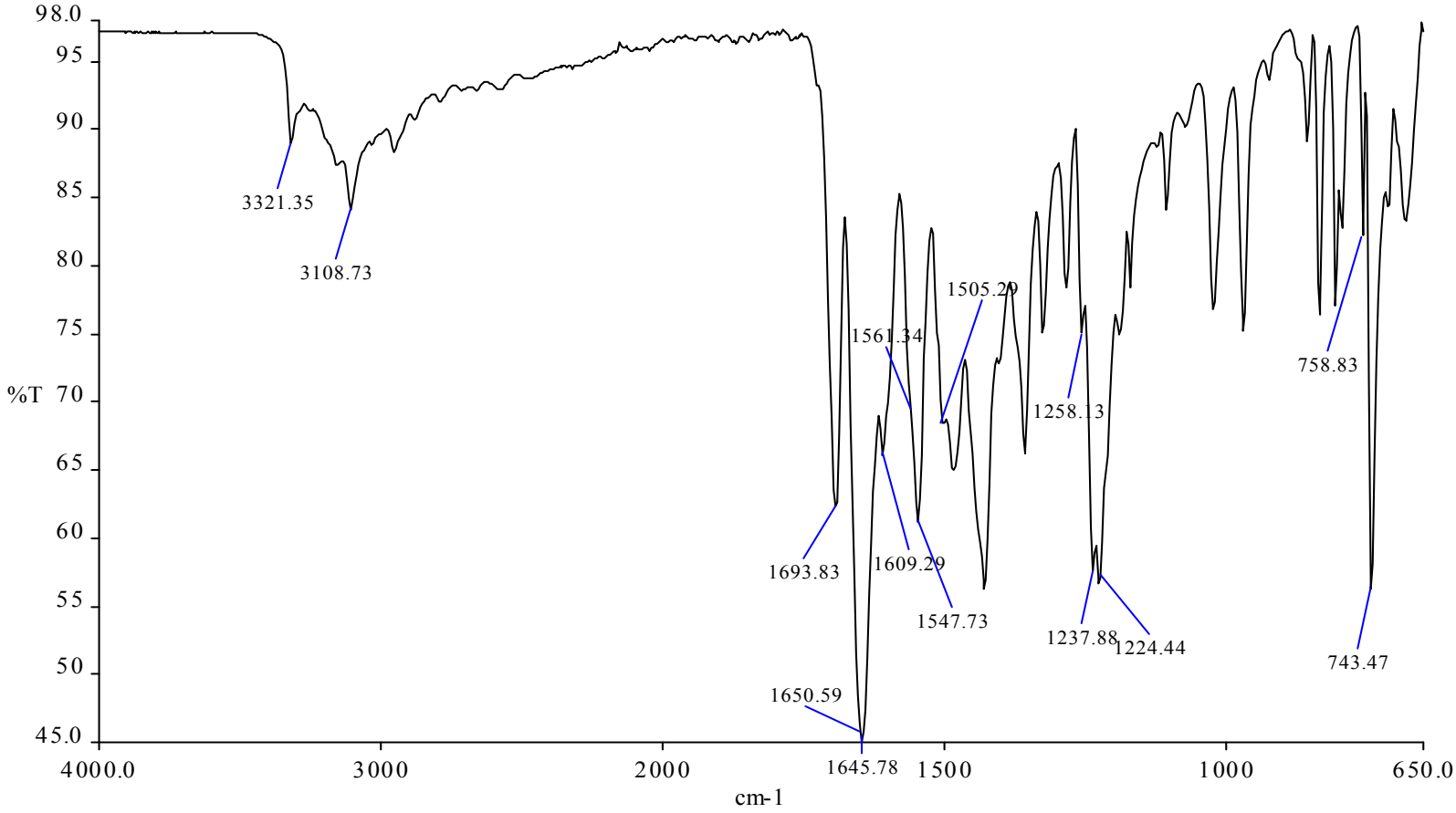


Figure B-41 IR-ATR Spectrum of Caffeine with Paracetamol (P25)
(41.4 % Caffeine, 47.6 % Paracetamol)

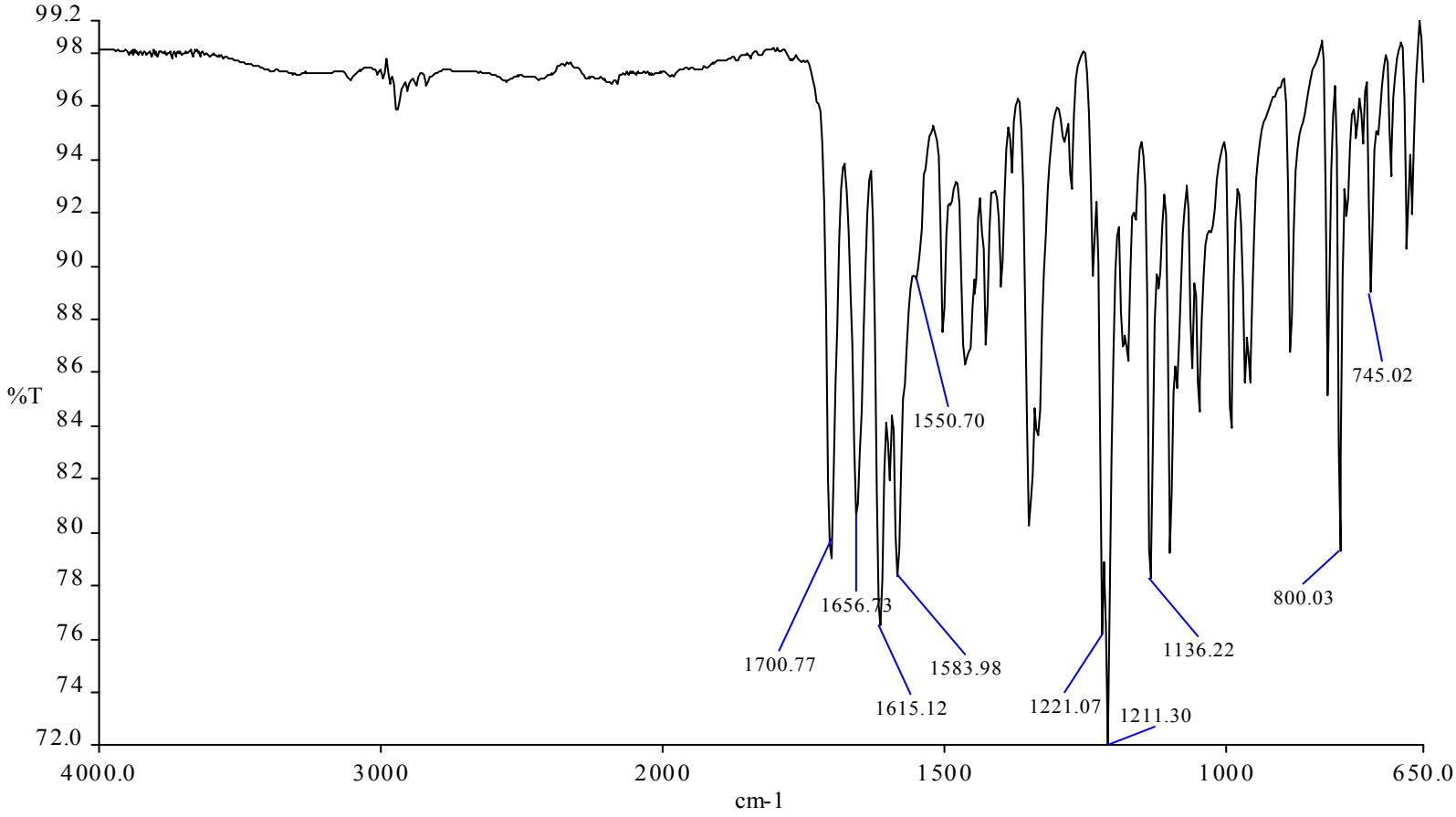


Figure B-42 IR-ATR Spectrum of Caffeine with Griseofulvin (P26)
(12.9 % Caffeine and Griseofulvin)

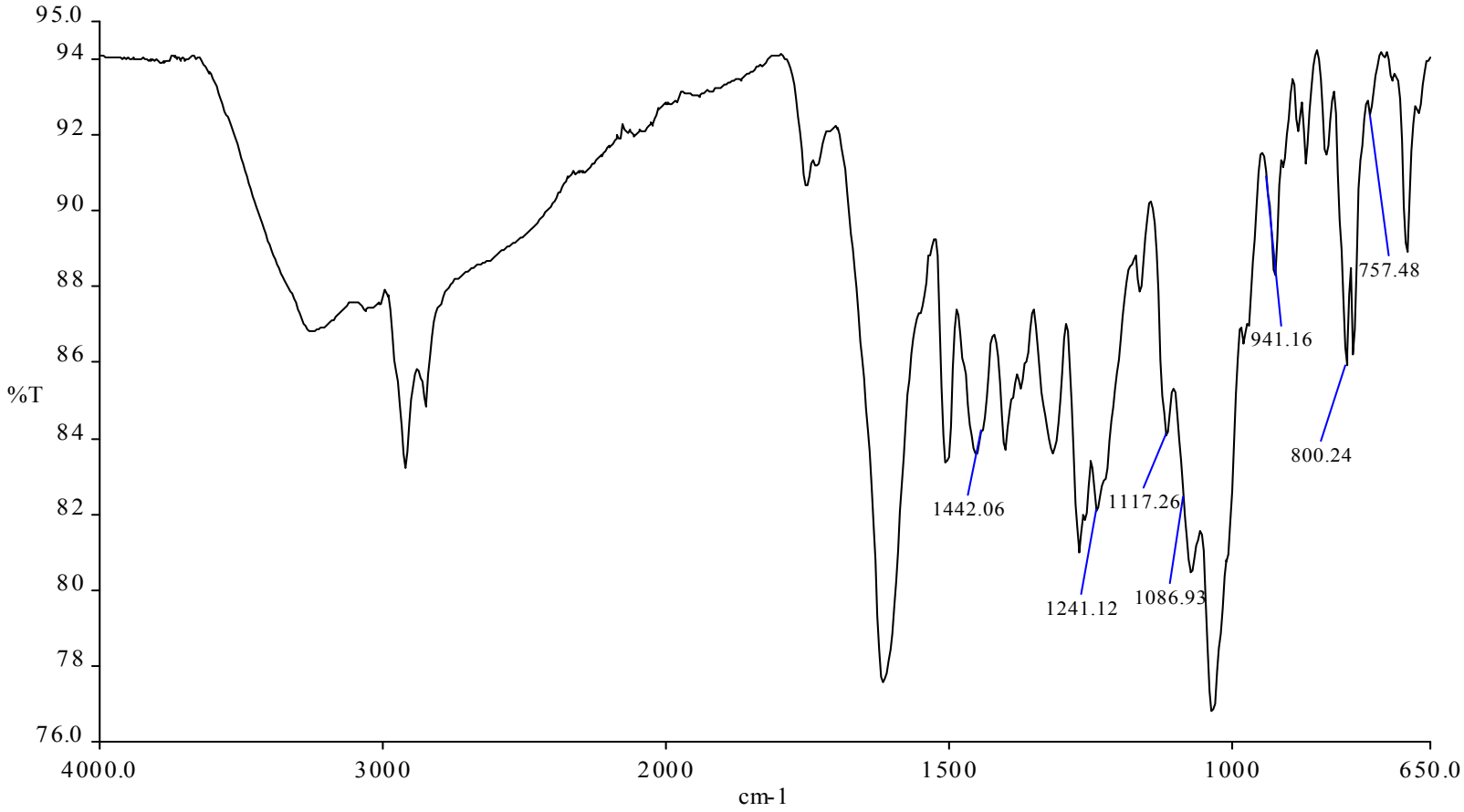


Figure B-43 IR-ATR Spectrum of Morphine (P27)
(10.8 % Morphine, 3.5 % Codeine, 1.6 % Papaverine, 7.6 % Narcotine)

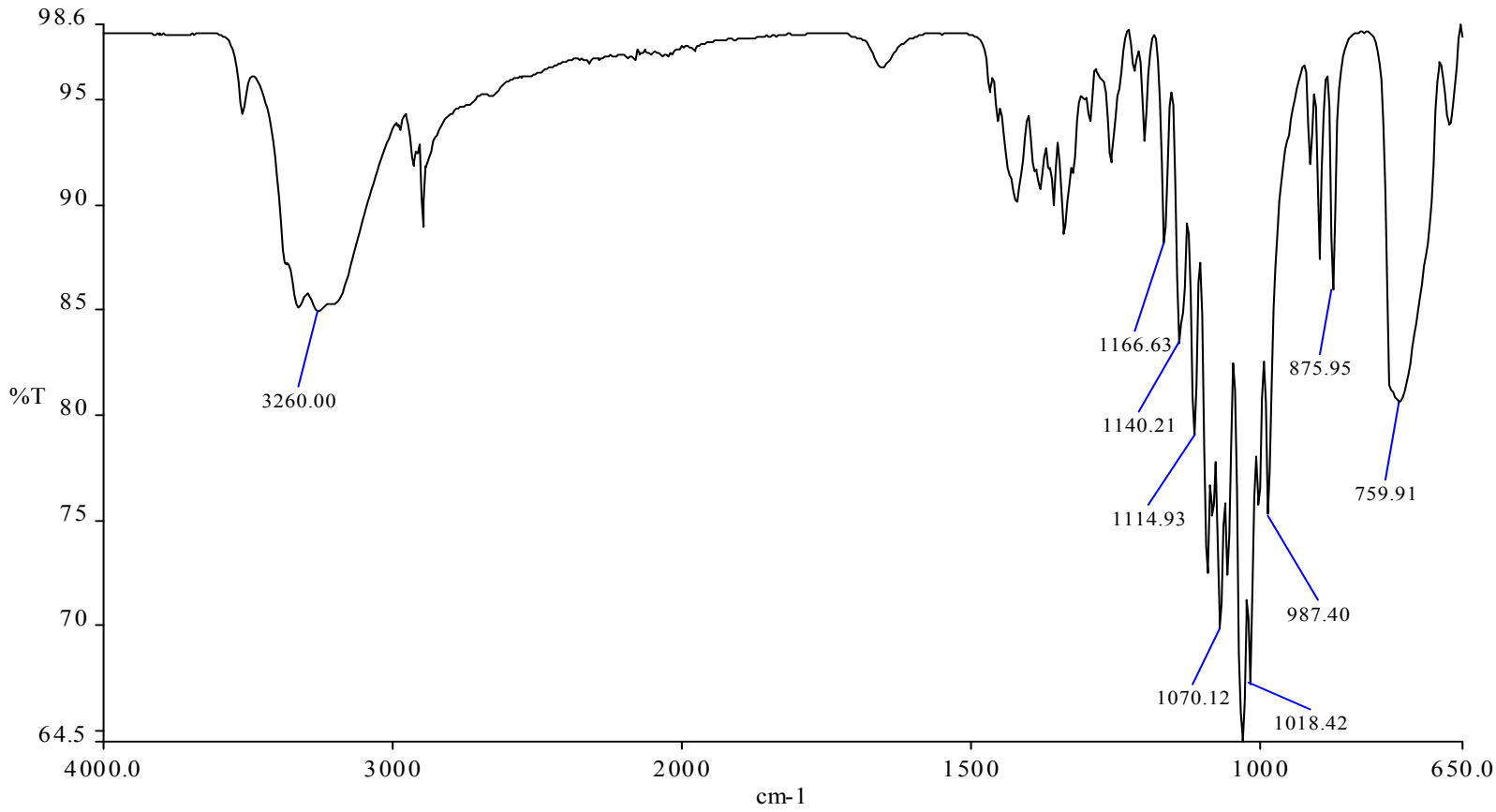


Figure B-44 IR-ATR Spectrum of Lactose Standard

APPENDIX C

IR-ATR SPECTRA OF ILLICIT SAMPLES

(S: Sample)

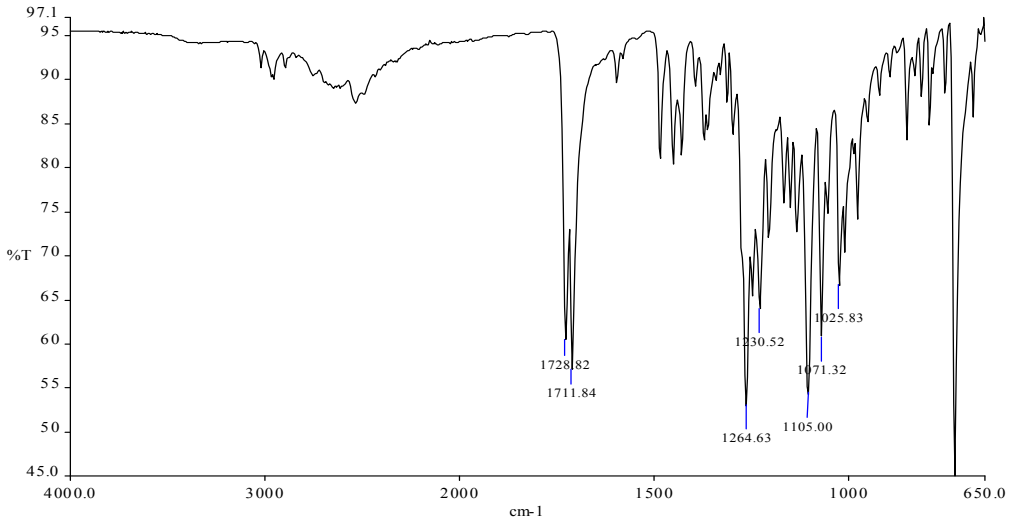


Figure C-1 IR-ATR Spectrum of S1
(89.3 % Cocaine)

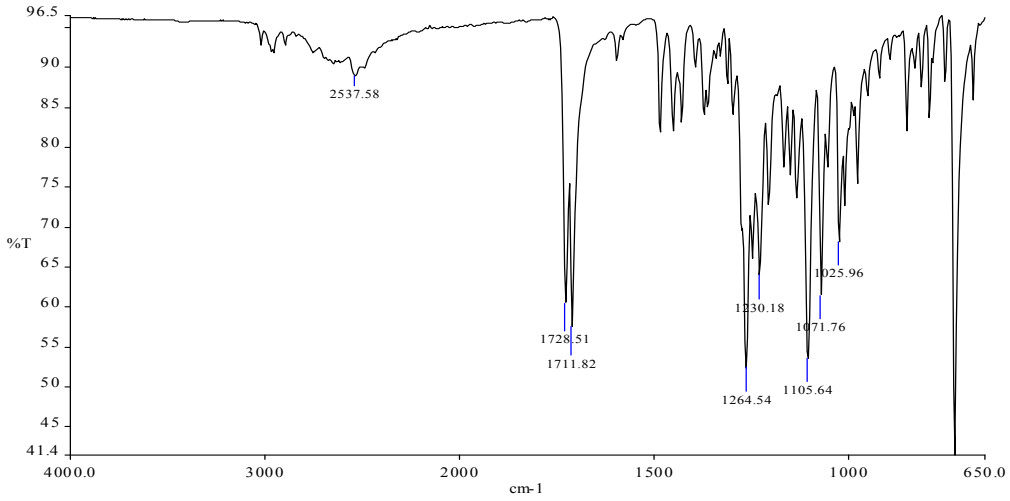


Figure C-2 IR-ATR Spectrum of S2
(90.4 % Cocaine)

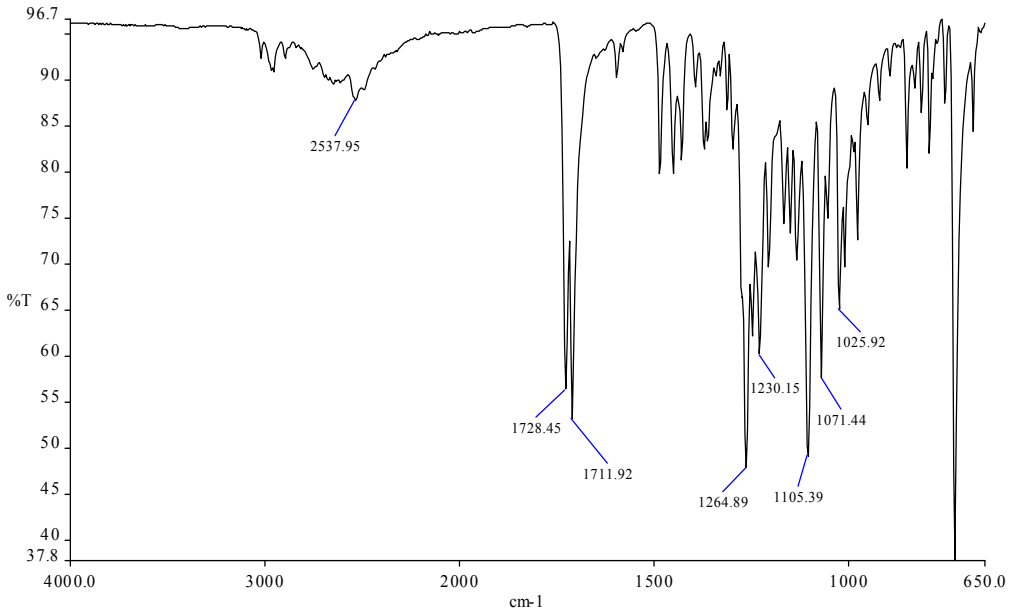


Figure C-3 IR-ATR Spectrum of S3
(58.1 % Cocaine)

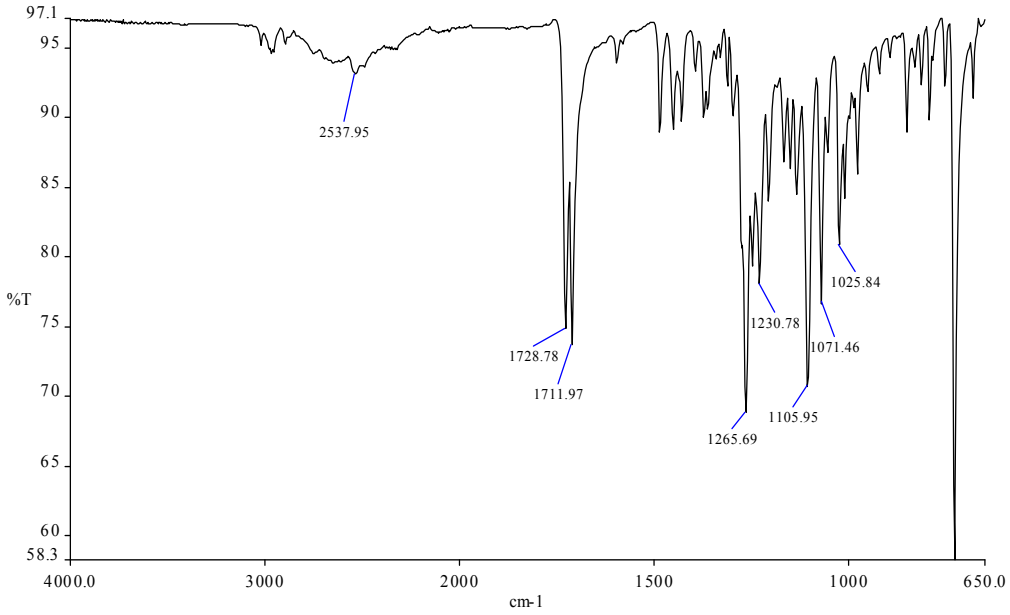


Figure C-4 IR-ATR Spectrum of S4
(63.6 % Cocaine)

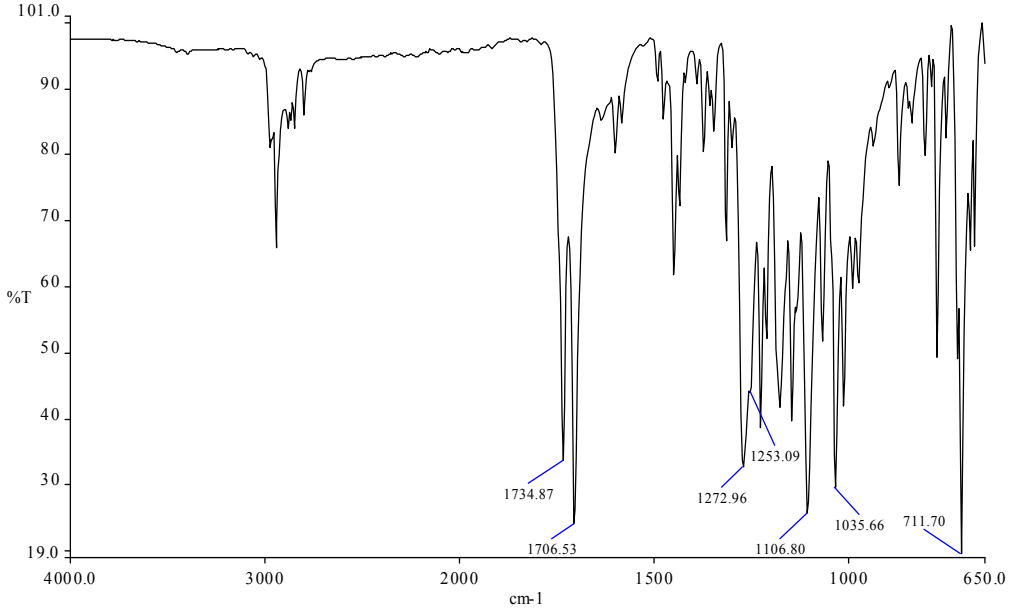


Figure C-5 IR-ATR Spectrum of S5
(80.1 % Cocaine)

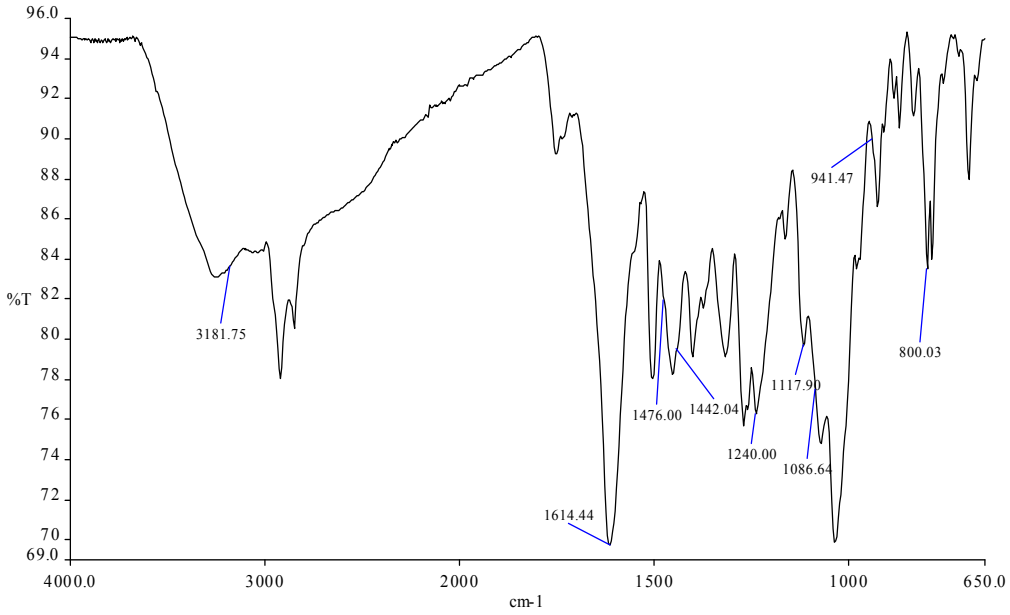


Figure C-6 IR-ATR Spectrum of S6
(11.6 % Morphine)

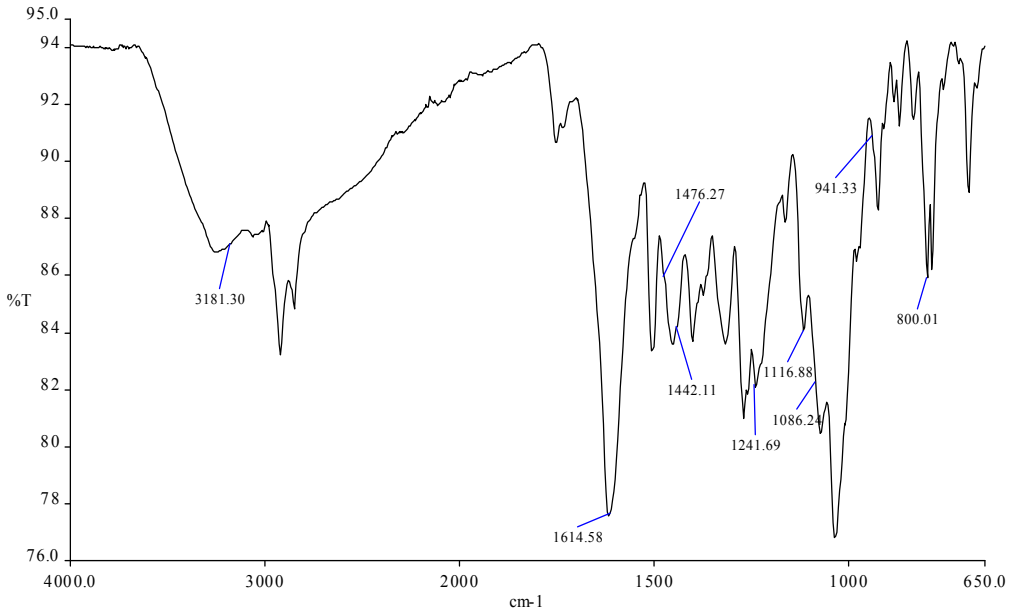


Figure C-7 IR-ATR Spectrum of S7
(10.8 %Morphine)

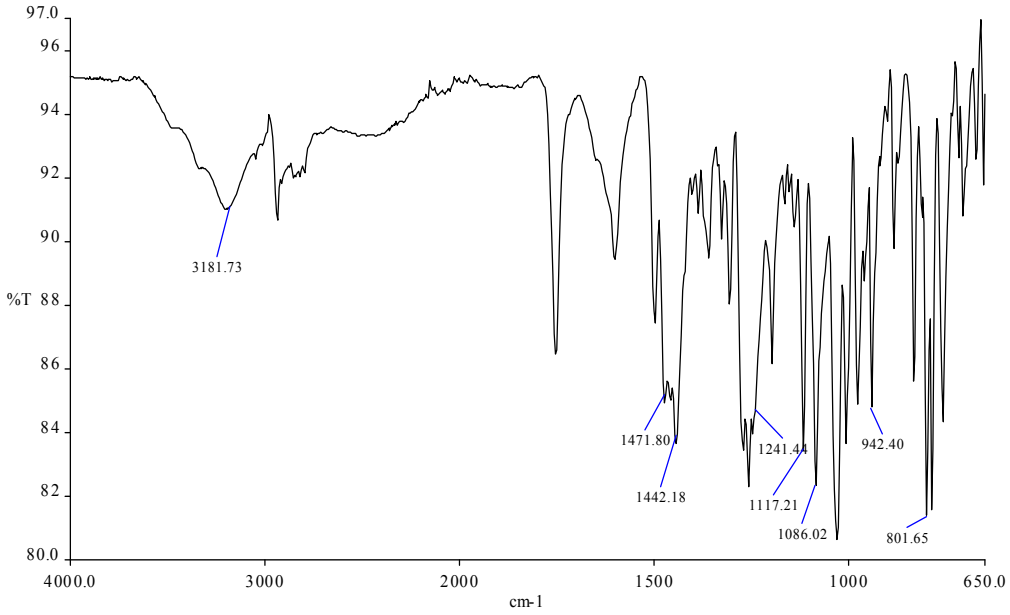


Figure C-8 IR-ATR Spectrum of S8
(73.3 % Morphine)

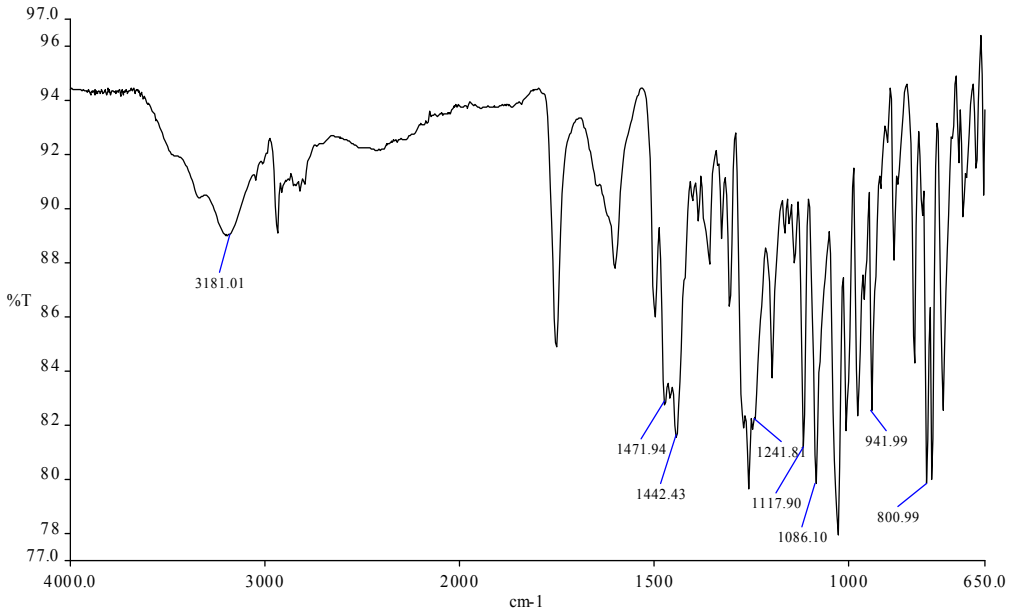


Figure C-9 IR-ATR Spectrum of S9
(27.2 % Morphine)

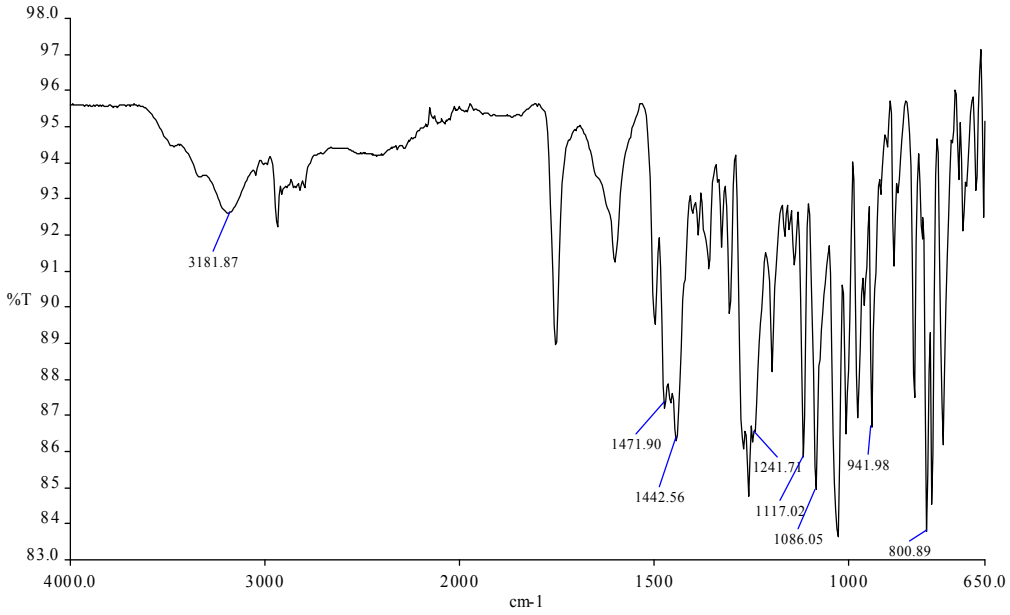


Figure C-10 IR-ATR Spectrum of S10
(42.7 % Morphine)

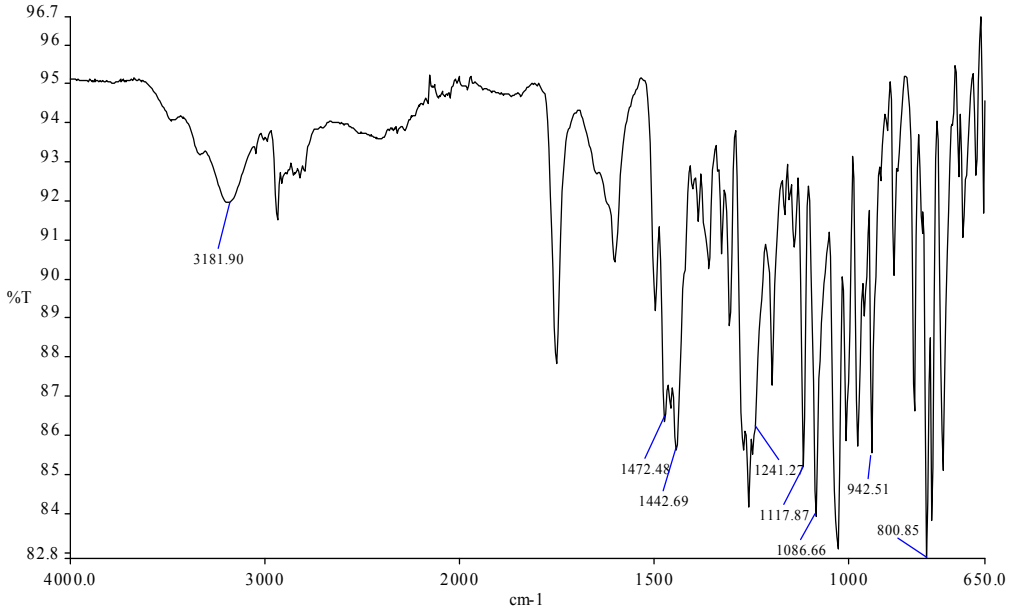


Figure C-11 IR-ATR Spectrum of S11
(51.2 % Morphine)

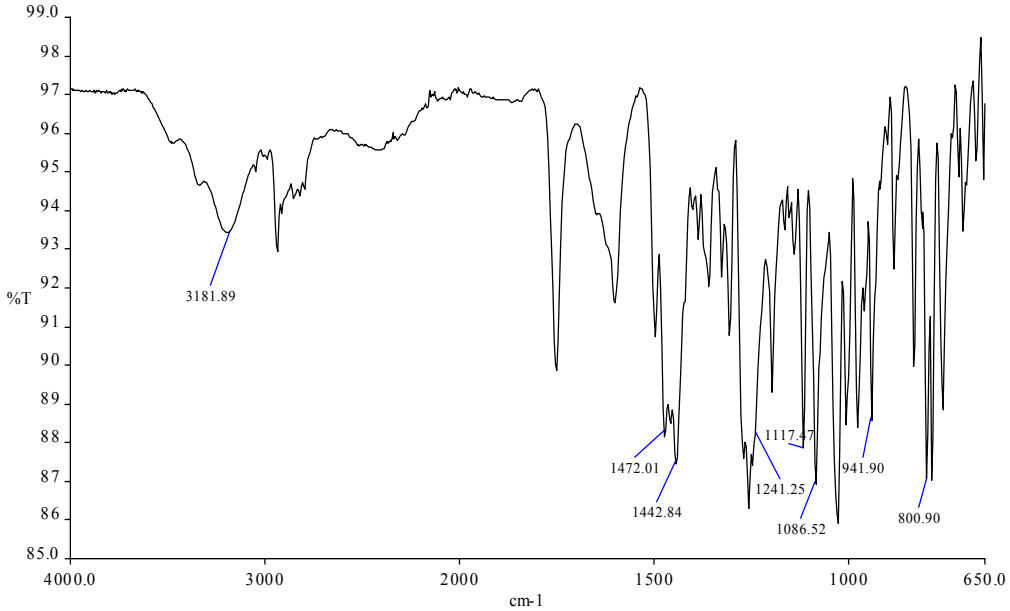


Figure C-12 IR-ATR Spectrum of S12
(54.3 % Morphine)

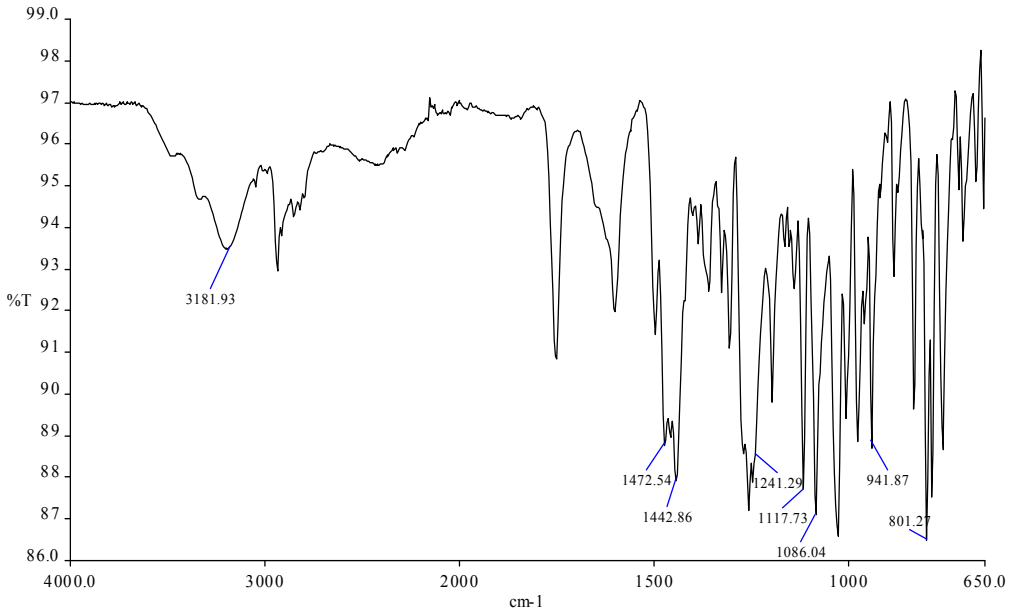


Figure C-13 IR-ATR Spectrum of S13
(50.6 % Morphine)

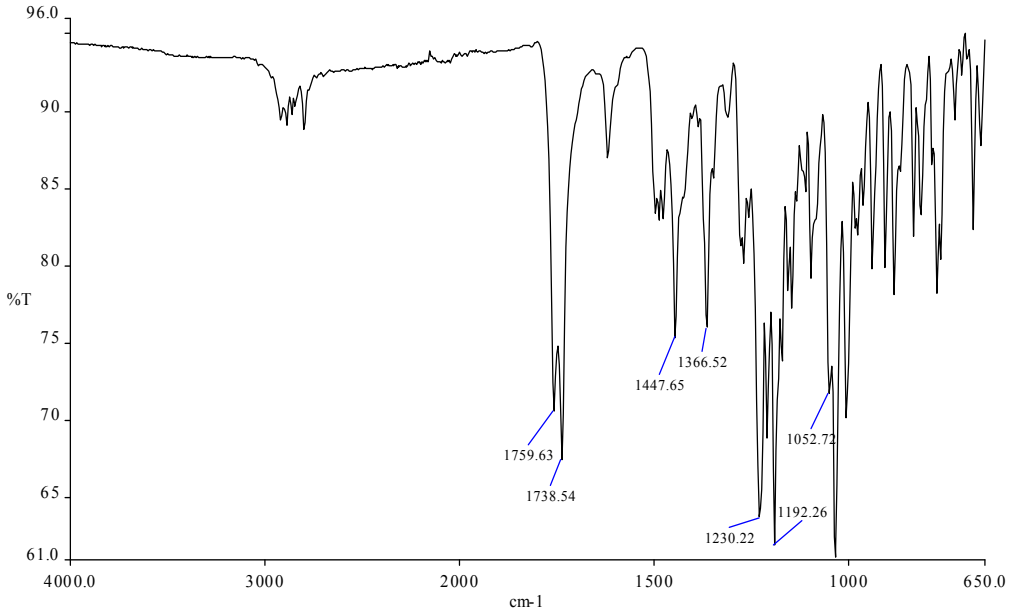


Figure C-14 IR-ATR Spectrum of S14
(63.7 % Heroin, 26.7 % Narcotine)

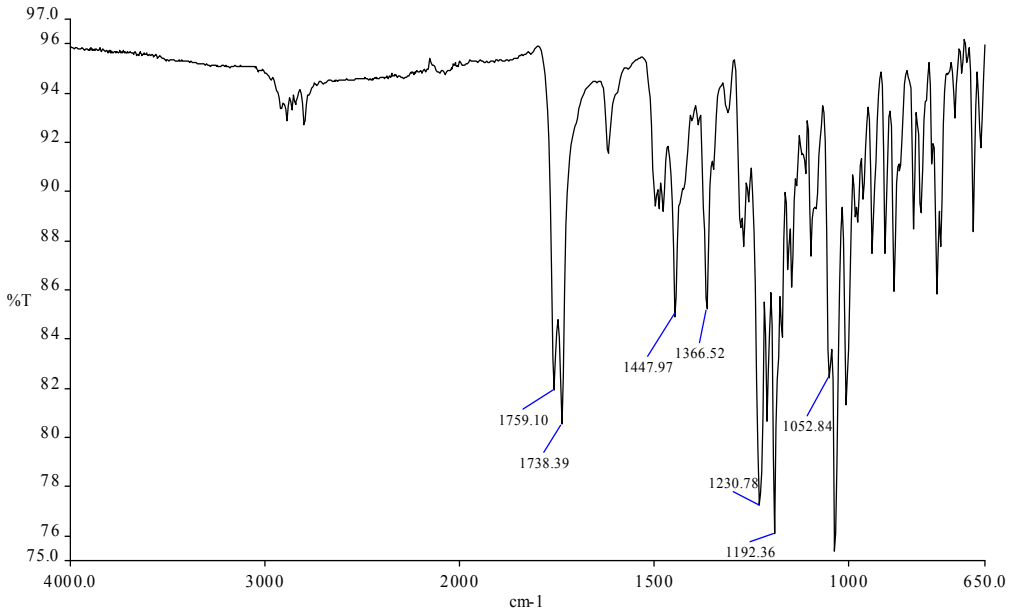


Figure C-15 IR-ATR Spectrum of S15
(63.7 % Heroin, 27.4 % Narcotine)

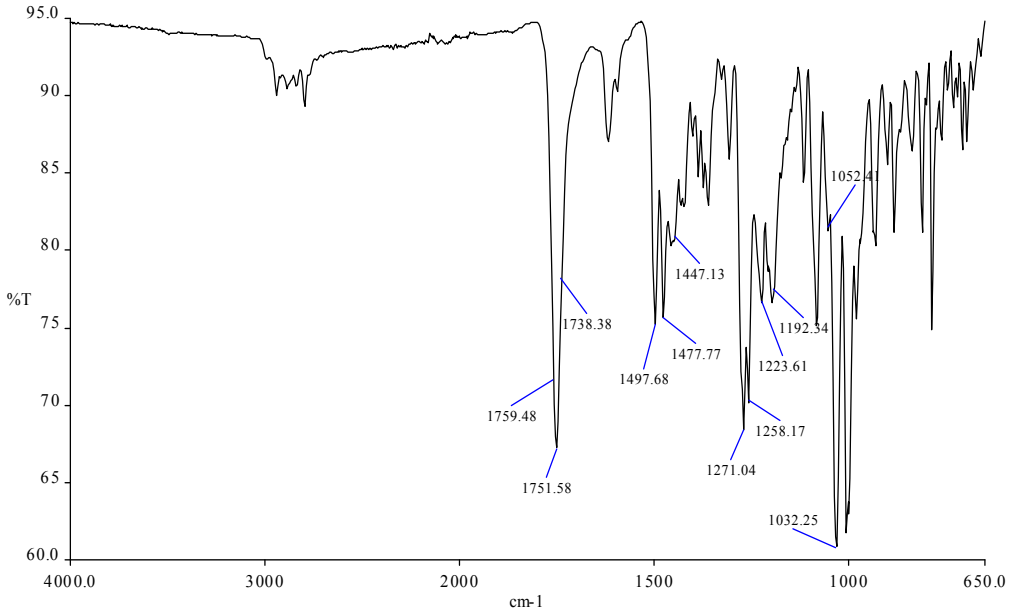


Figure C-16 IR-ATR Spectrum of S16
(19.9 % Heroin, 49,6 % Narcotine)

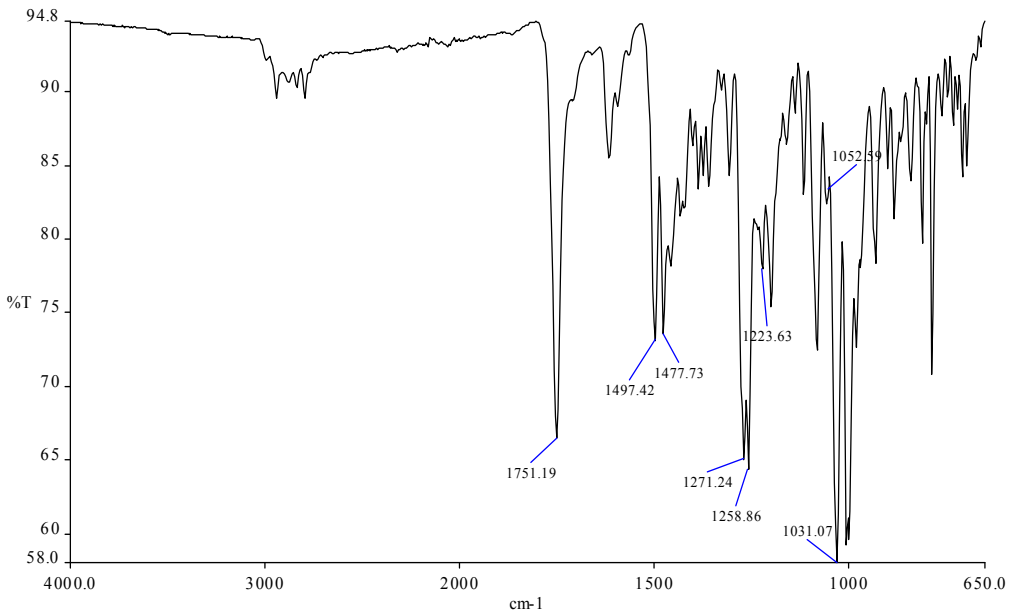


Figure C-17 IR-ATR Spectrum of S17
(0.4 % Heroin, 58.4 % Narcotine)

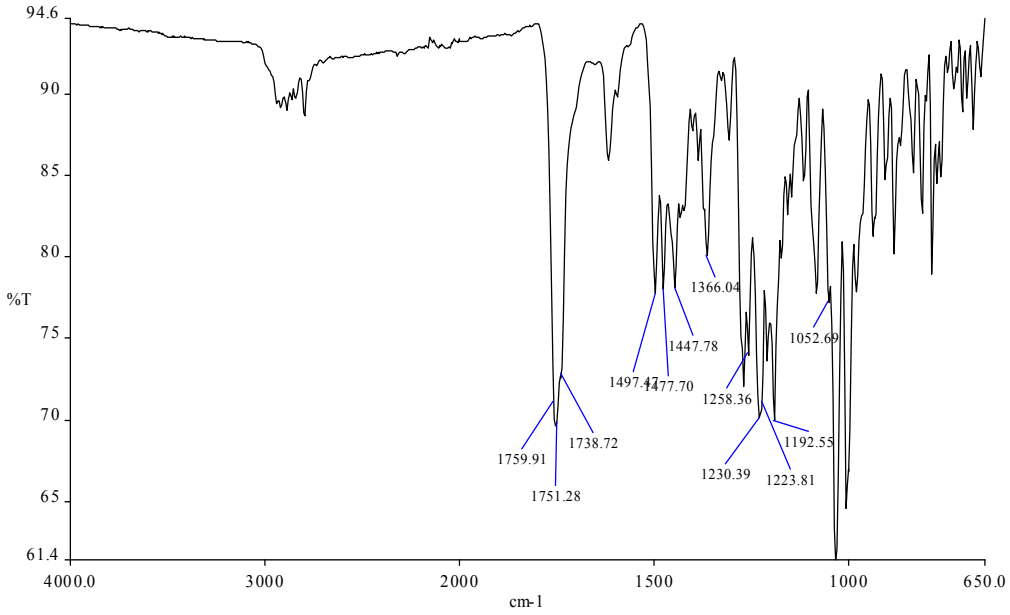


Figure C-18 IR-ATR Spectrum of S18
(17.5 % Heroin, 49.6 % Narcotine)

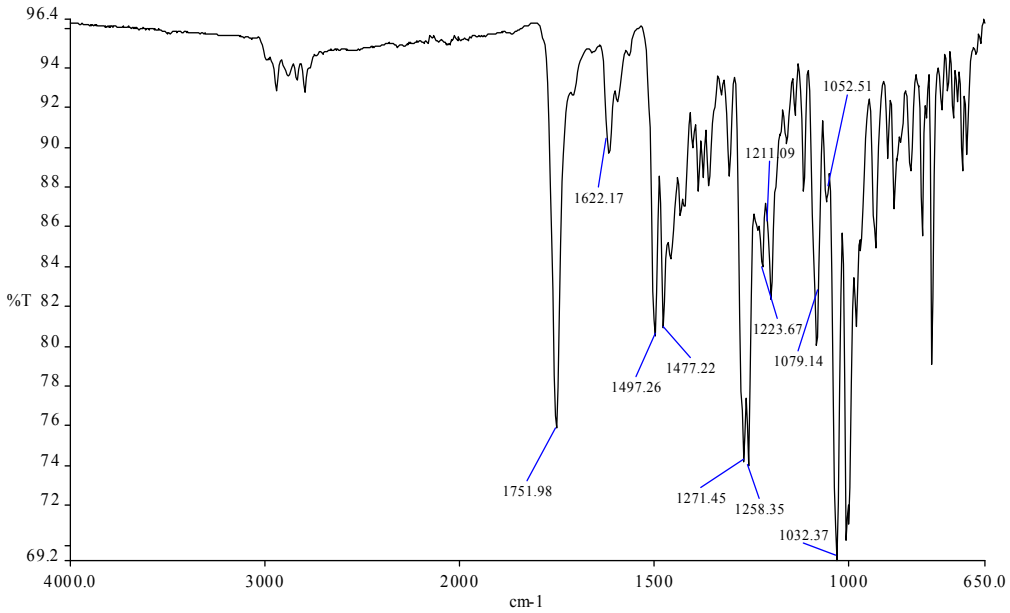


Figure C-19 IR-ATR Spectrum of S19
(0.2 % Heroin, 55.5 % Narcotine)

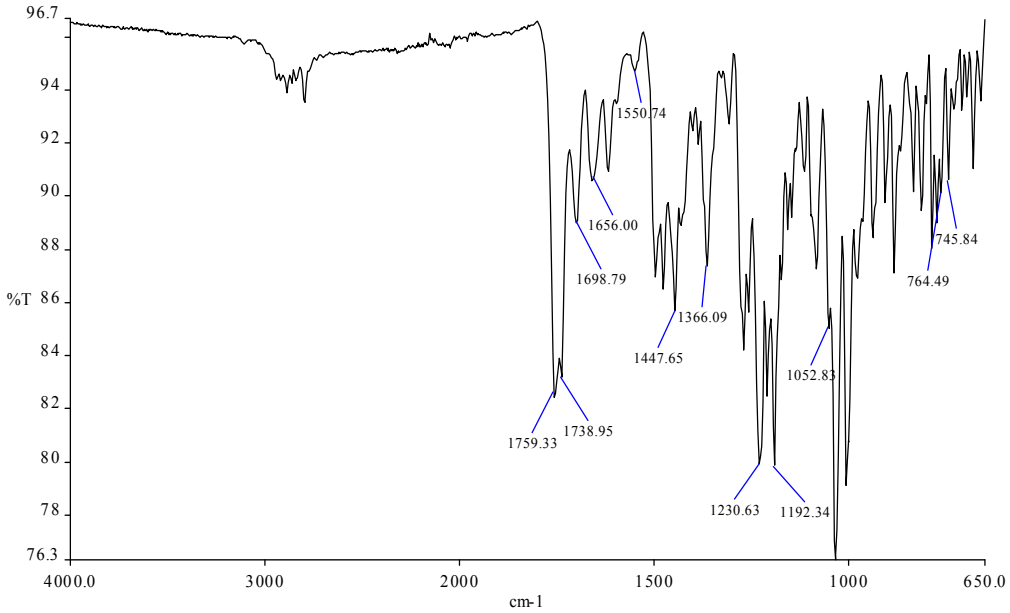


Figure C-20 IR-ATR Spectrum of S20
(27.8 % Heroin, 13.7 % Caffeine, 35.4 % Narcotine)

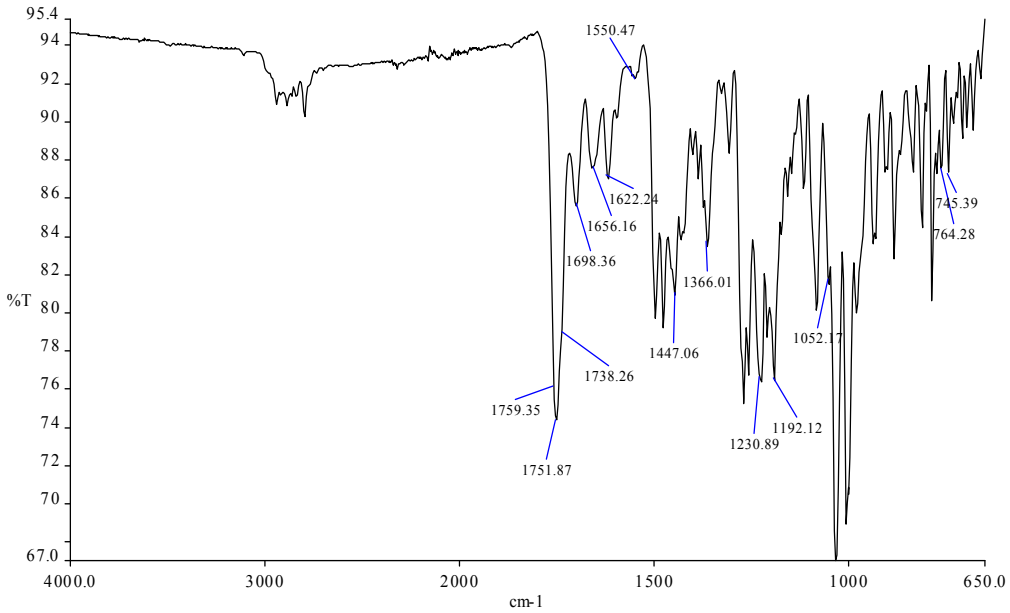


Figure C-21 IR-ATR Spectrum of S21
(29.6 % Heroin, 13.7 % Caffeine, 34.8 % Narcotine)

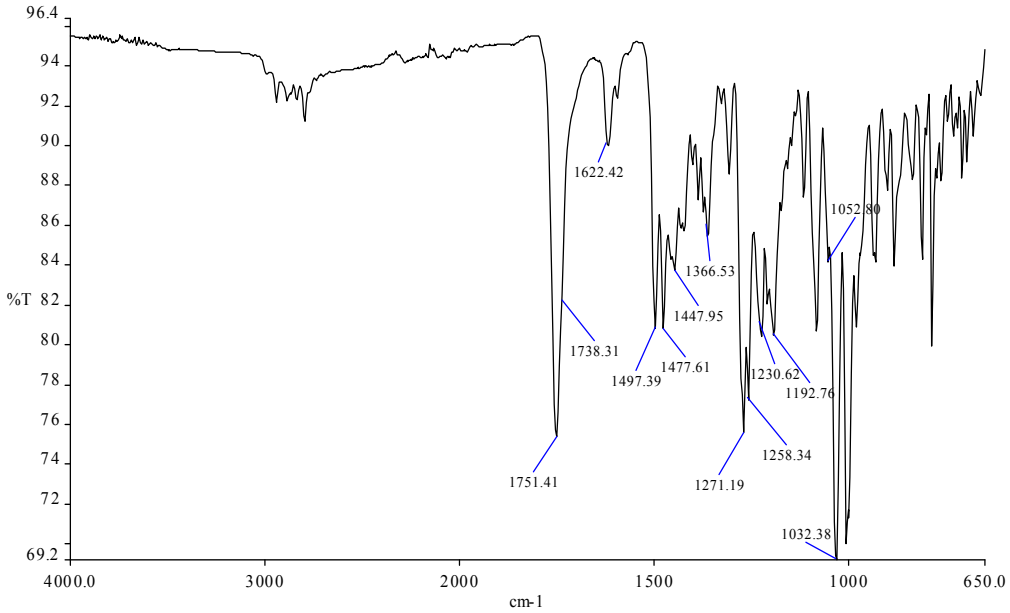


Figure C-22 IR-ATR Spectrum of S22
(30.6 % Heroin, 45.8 % Narcotine)

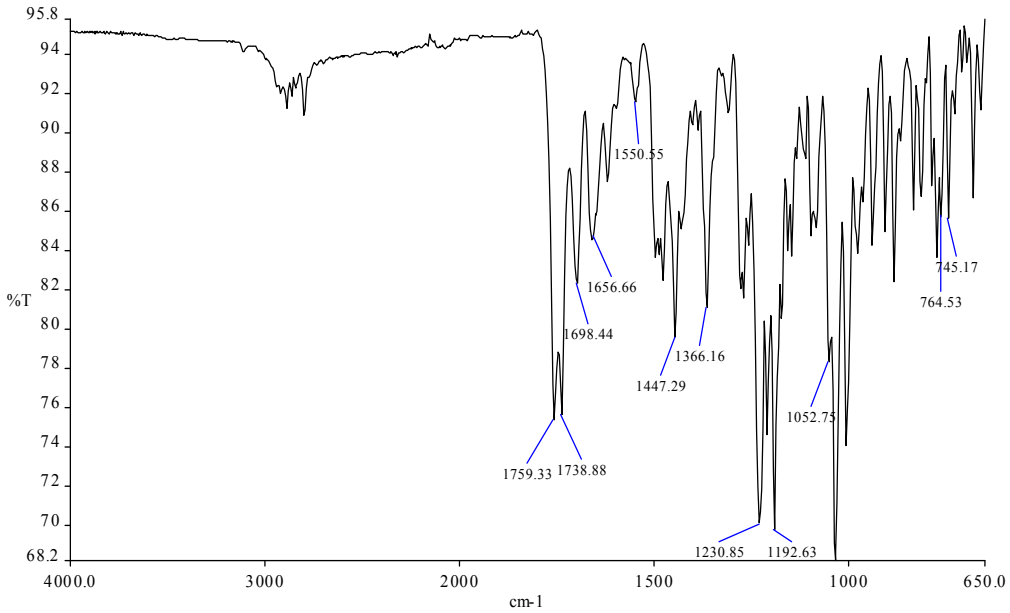


Figure C-23 IR-ATR Spectrum of S23
(43.5 % Heroin, 8.2 % Caffeine, 26.9 % Narcotine)

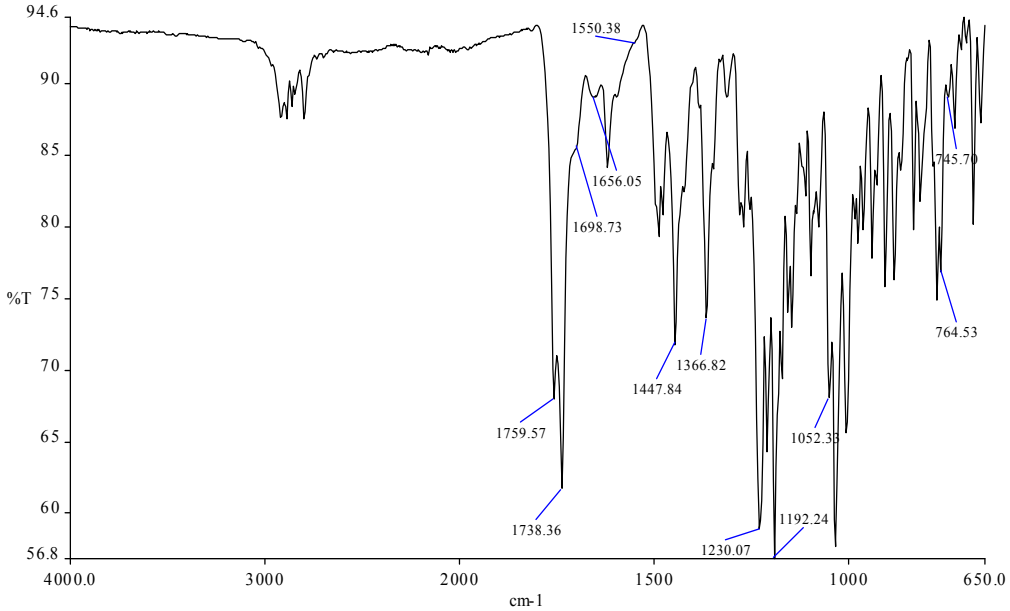


Figure C-24 IR-ATR Spectrum of S24
(58.8 % Heroin, 3.3 % Caffeine, 20.1 % Narcotine)

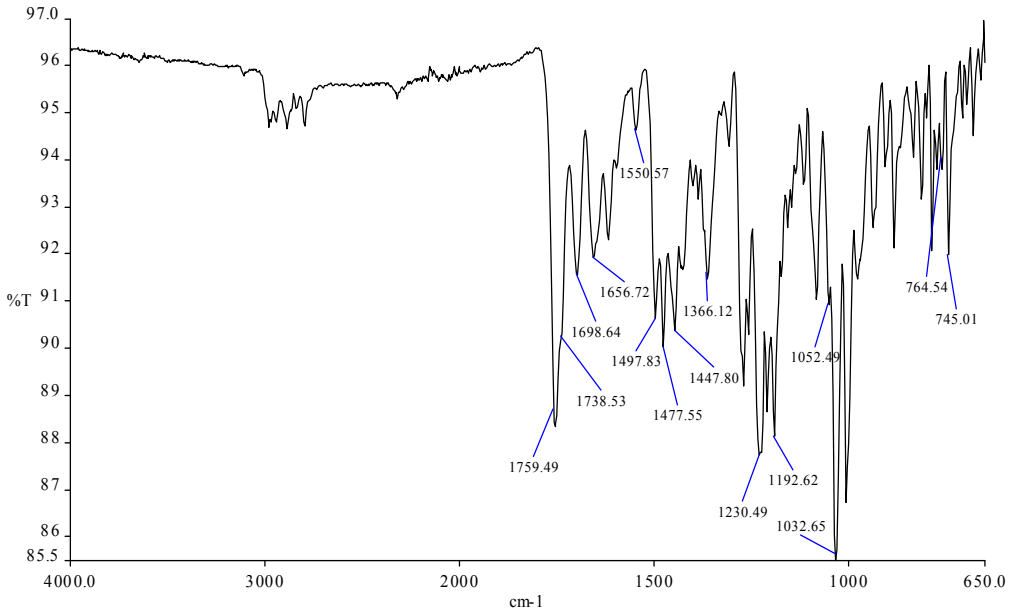


Figure C-25 IR-ATR Spectrum of S25
(27 % Heroin, 13 % Caffeine, 33.3 % Narcotine)

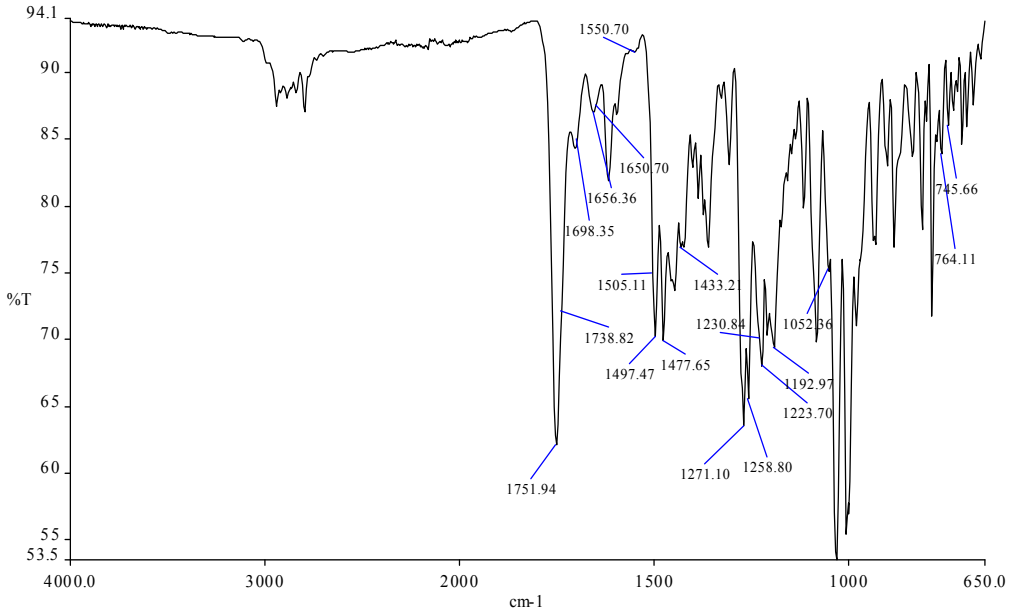


Figure C-26 IR-ATR Spectrum of S26
(26.7 % Heroin, 0.4 % Caffeine, 1.4 % Paracetamol, 40.9 % Narcotine)

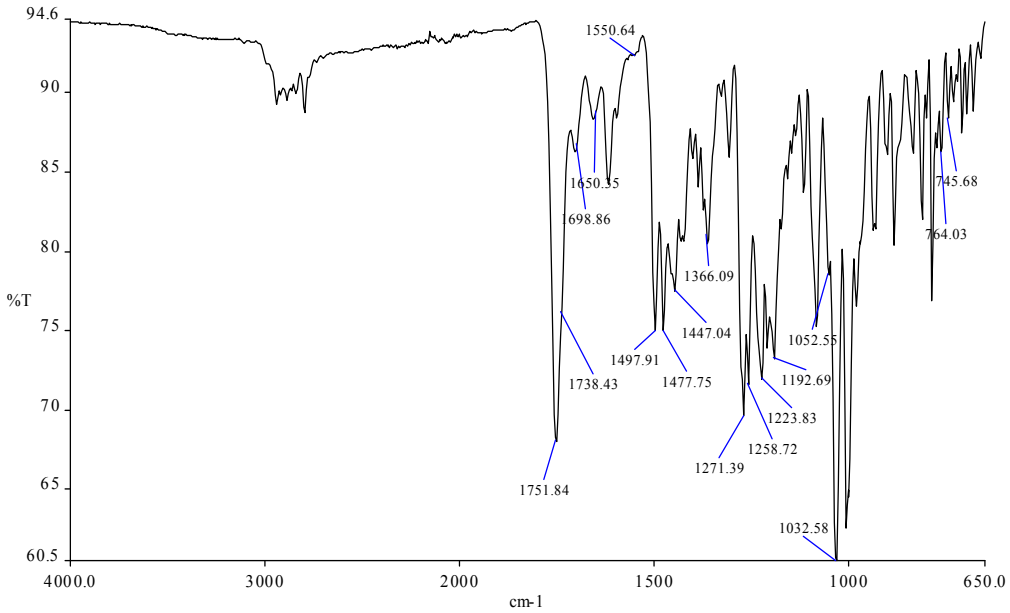


Figure C-27 IR-ATR Spectrum of S27
(25.1 % Heroin, 4.6% Caffeine, 0.9 % Paracetamol, 42.8 % Narcotine)

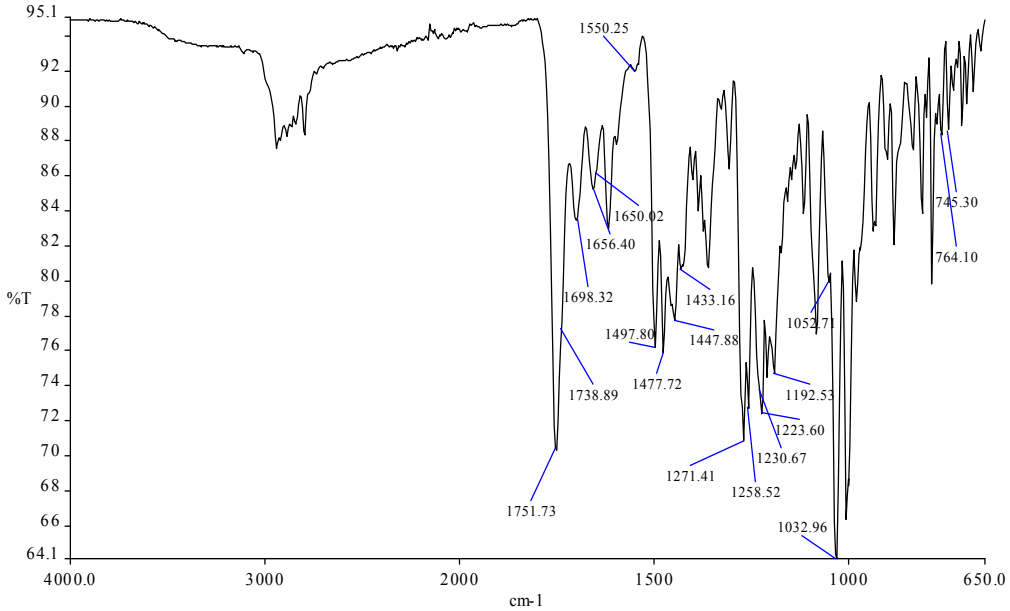


Figure C-28 IR-ATR Spectrum of S28
(27 % Heroin, 5.3 % Caffeine, 1.0 % Paracetamol, 40.7 % Narcotine)

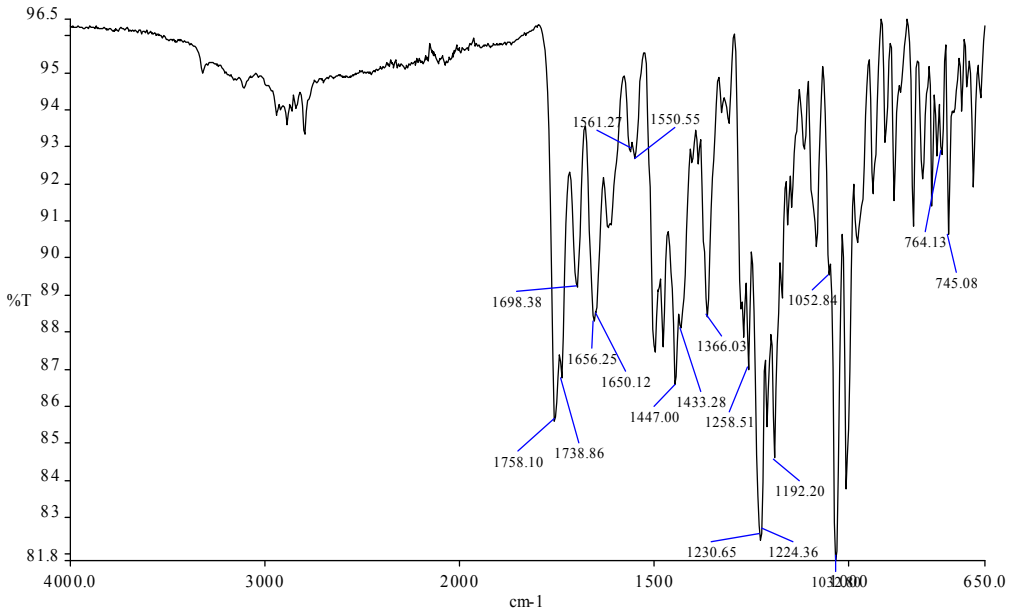


Figure C-29 IR-ATR Spectrum of S29
(35.5 % Heroin, 13.9 % Caffeine, 12.8 % Paracetamol, 24.3 % Narcotine)

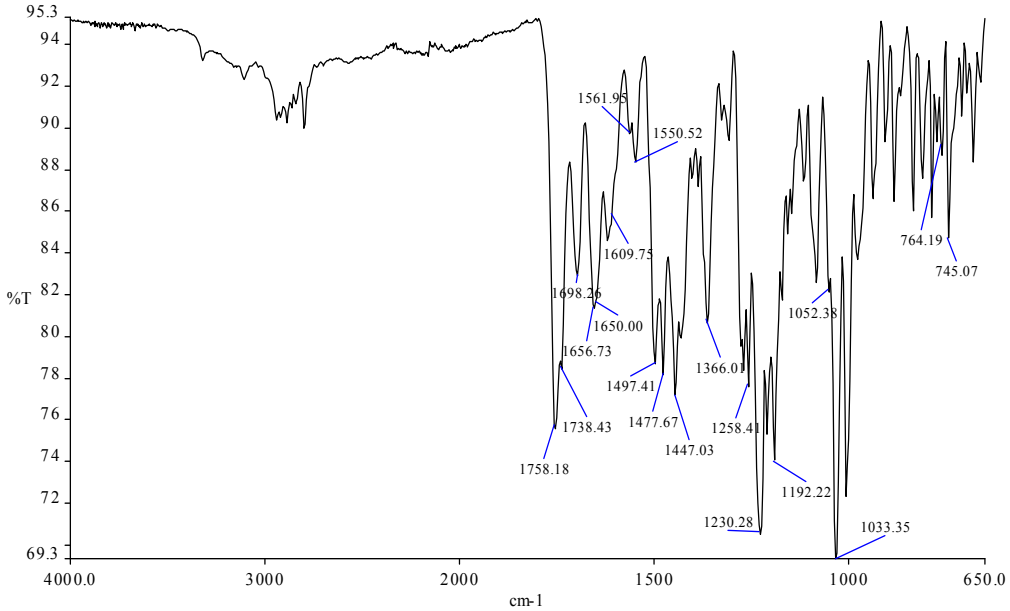


Figure C-30 IR-ATR Spectrum of S30
(35.9 % Heroin, 14.4 % Caffeine, 14.4 % Paracetamol, 23.1 % Narcotine)

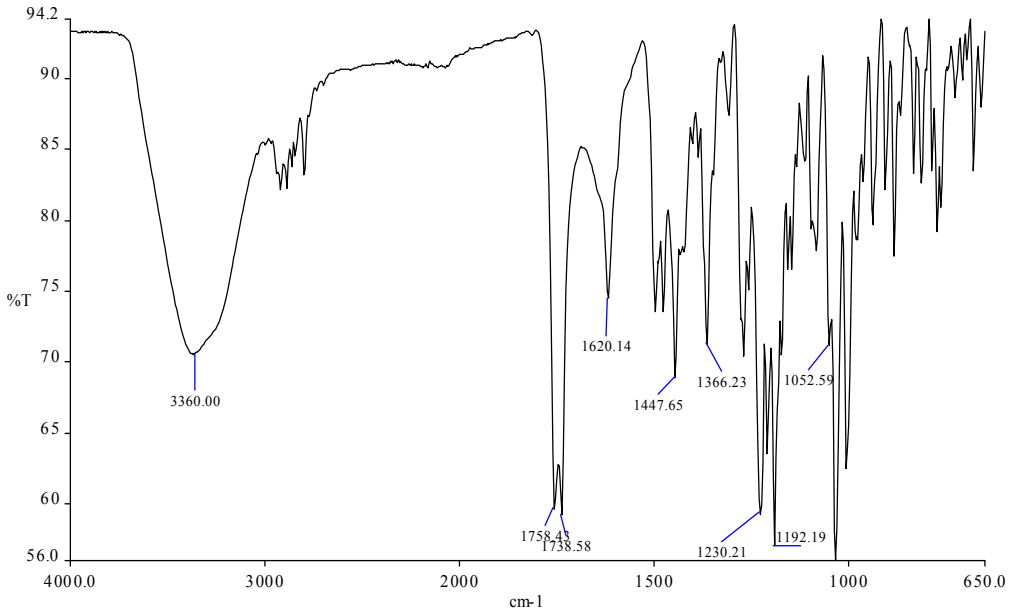


Figure C-31 IR-ATR Spectrum of S31
(51.3 % Heroin, 26.2 % Narcotine)

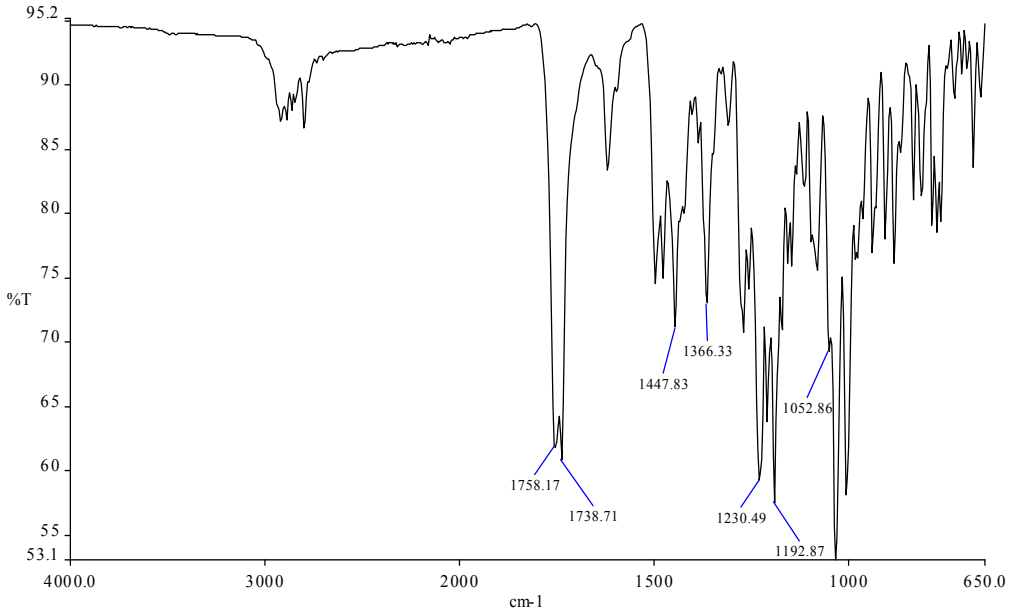


Figure C-32 IR-ATR Spectrum of S32
(55.2 % Heroin, 25.3 % Narcotine)

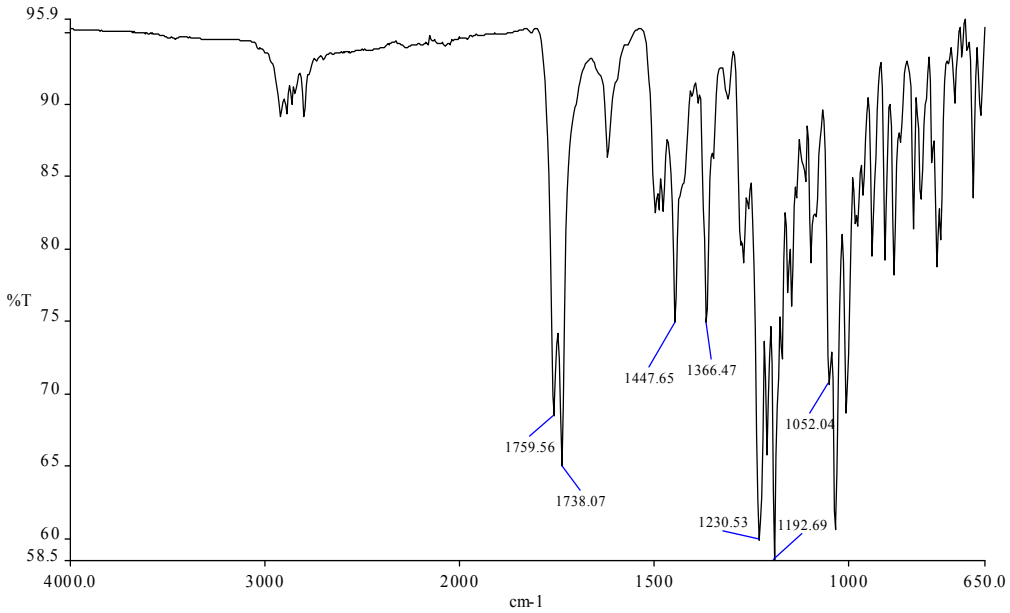


Figure C-33 IR-ATR Spectrum of S33
(62.6 % Heroin, 20.6 % Narcotine)

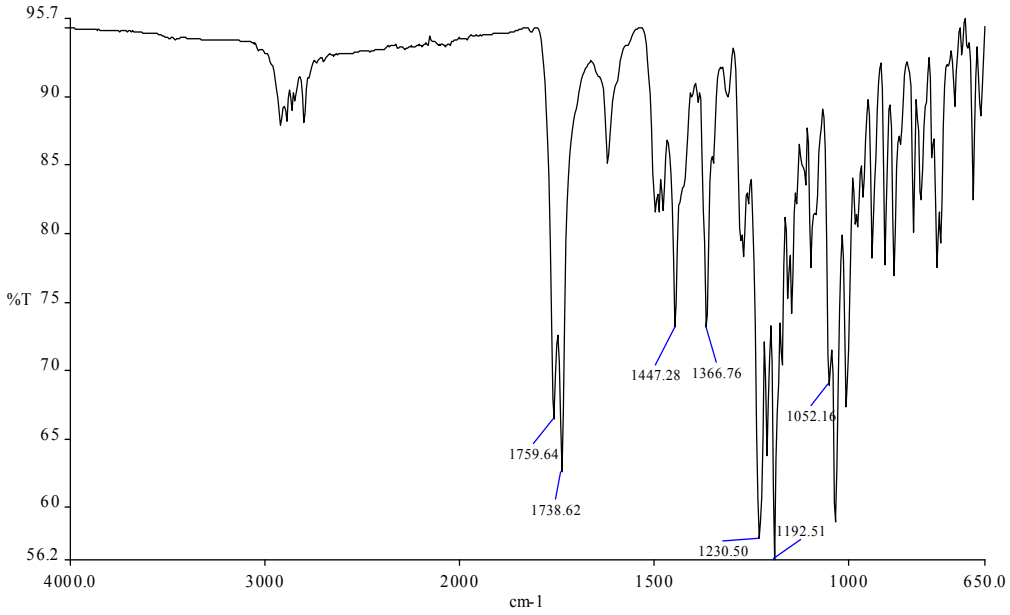


Figure C-34 IR-ATR Spectrum of S34
(62.3 % Heroin, 22.2 % Narcotine)

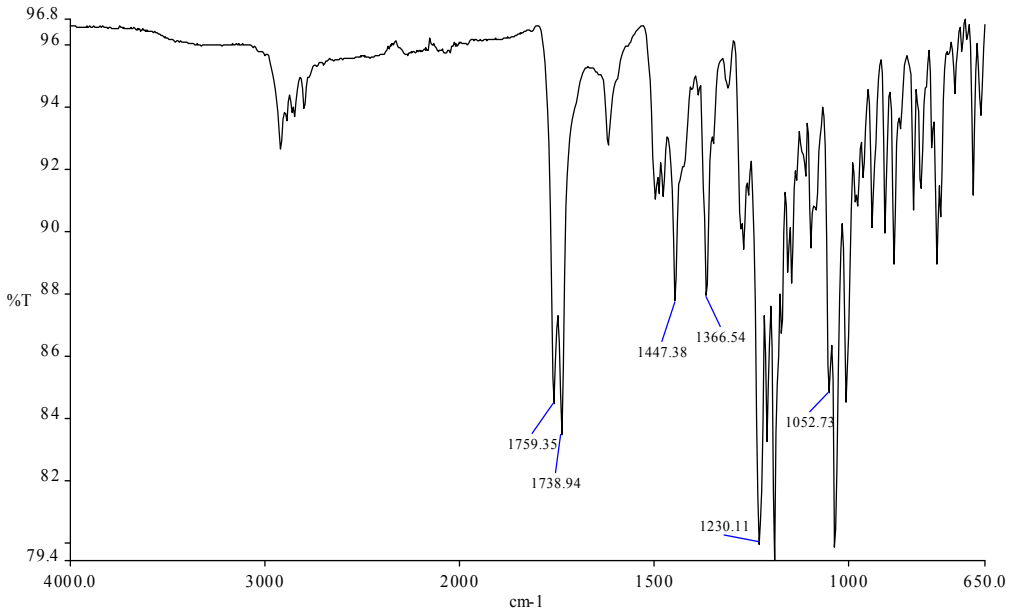


Figure C-35 IR-ATR Spectrum of S35
(61.2 % Heroin, 20.3 % Narcotine)

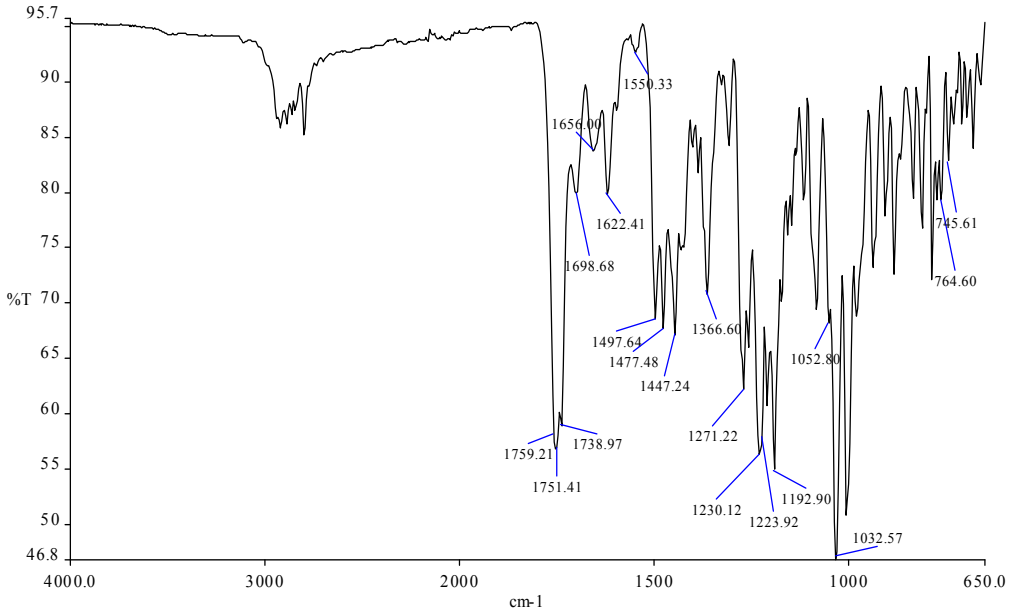


Figure C-36 IR-ATR Spectrum of S36
(32.2 % Heroin, 5.1 % Caffeine, 43.4 % Narcotine)

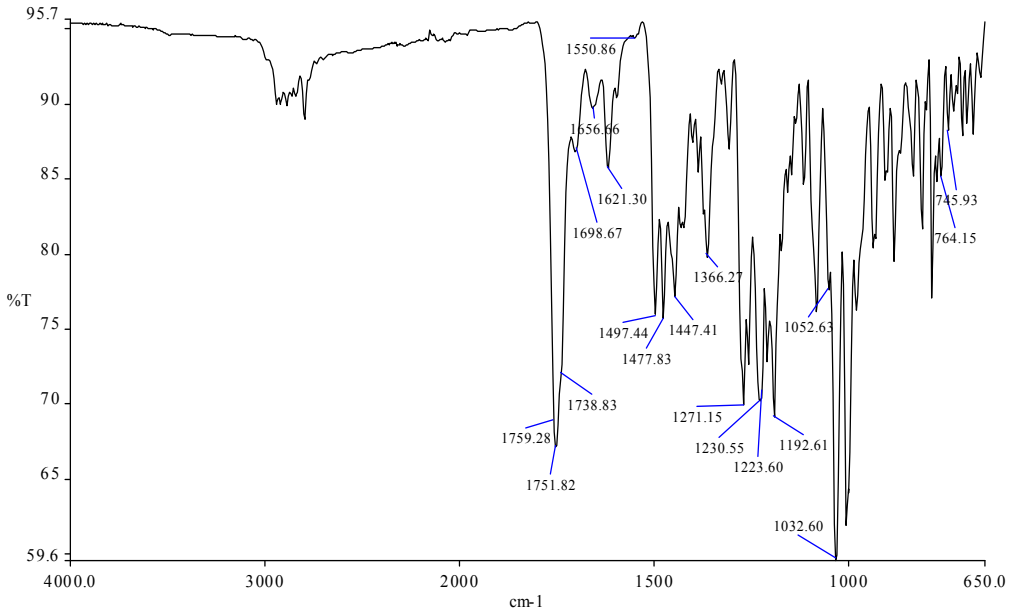


Figure C-37 IR-ATR Spectrum of S37
(35.9 % Heroin, 3.9 % Caffeine, 44.2 % Narcotine)

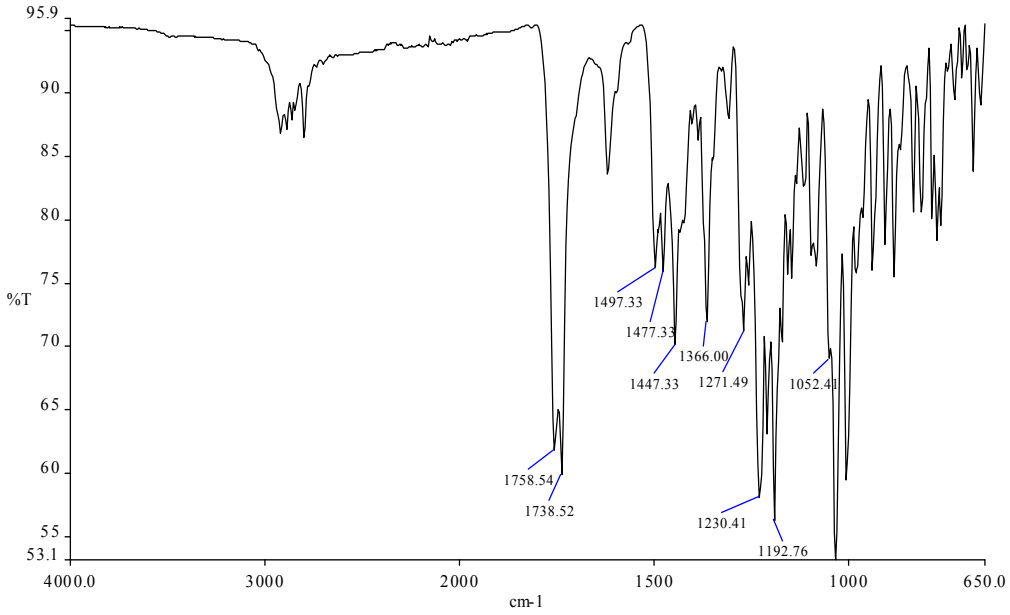


Figure C-38 IR-ATR Spectrum of S38
(55.2 % Heroin, 30.8 % Narcotine)

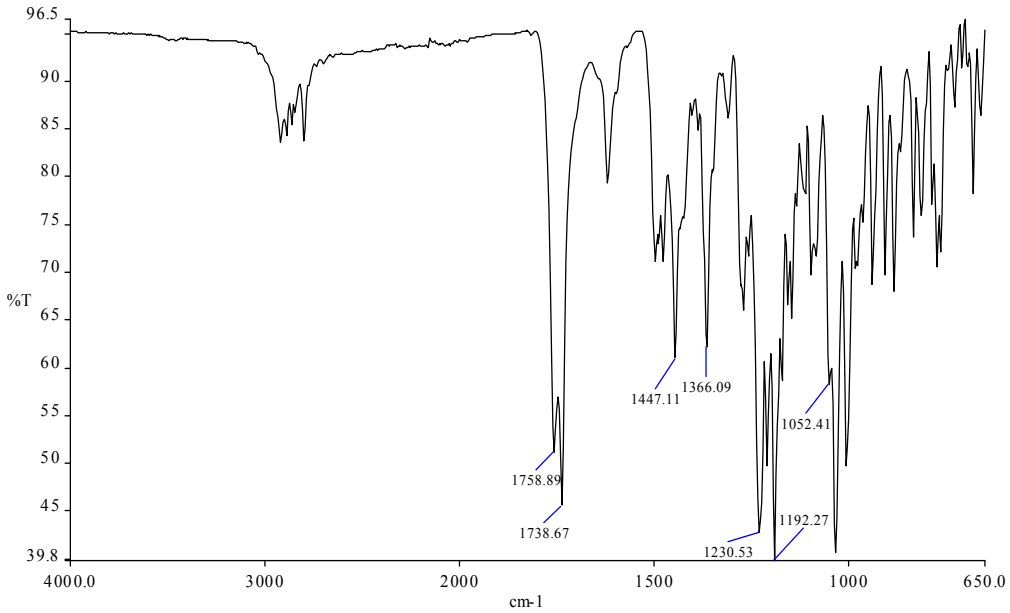


Figure C-39 IR-ATR Spectrum of S39
(54.8 % Heroin, 29.9 % Narcotine)

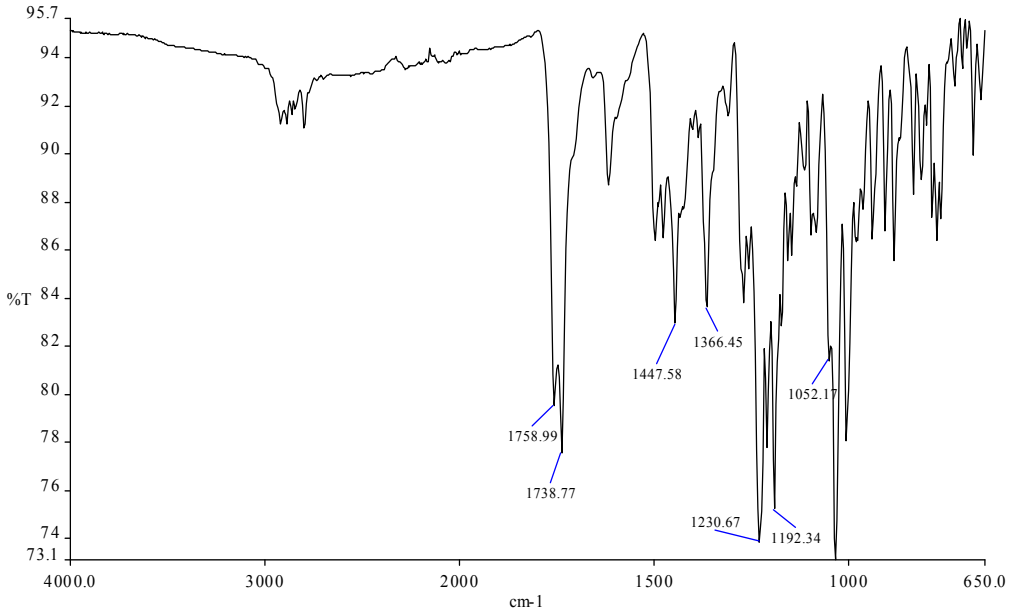


Figure C-40 IR-ATR Spectrum of S40
(43.6 % Heroin, 26.6 % Narcotine)

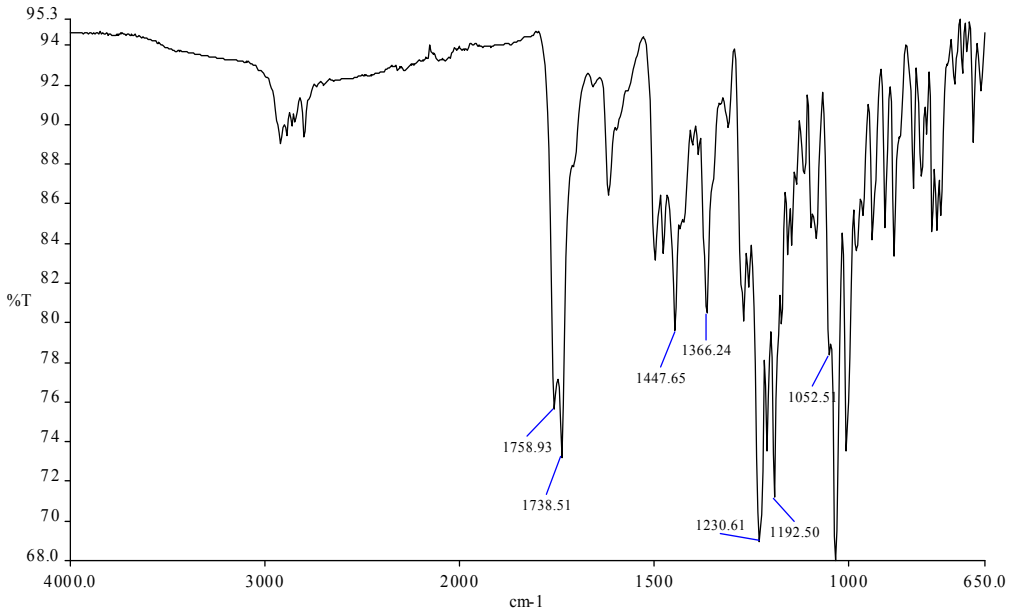


Figure C-41 IR-ATR Spectrum of S41
(36.5 % Heroin, 30.6 % Narcotine)

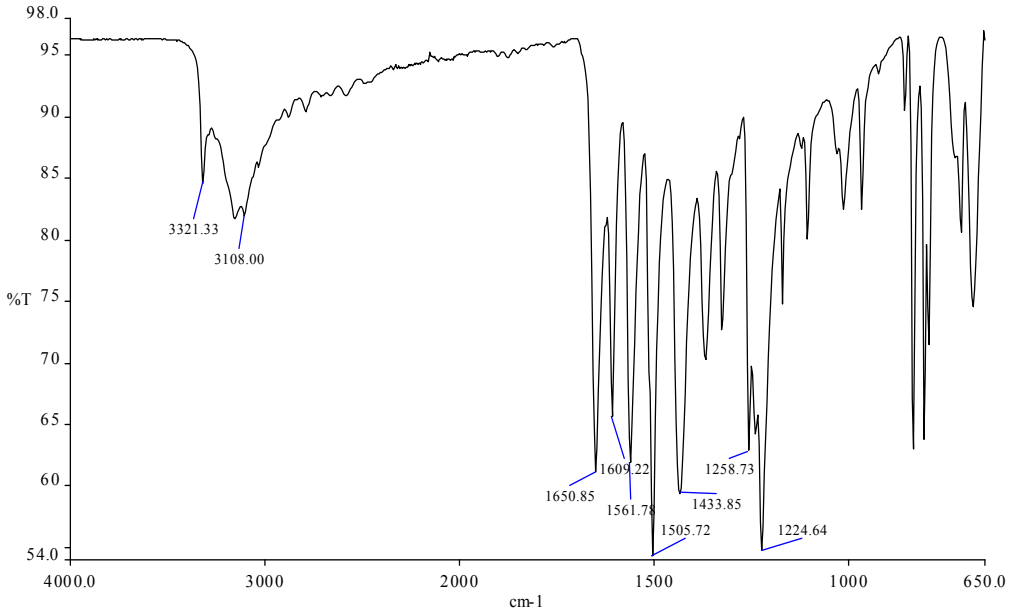


Figure C-42 IR-ATR Spectrum of S42
(90.5 % Paracetamol)

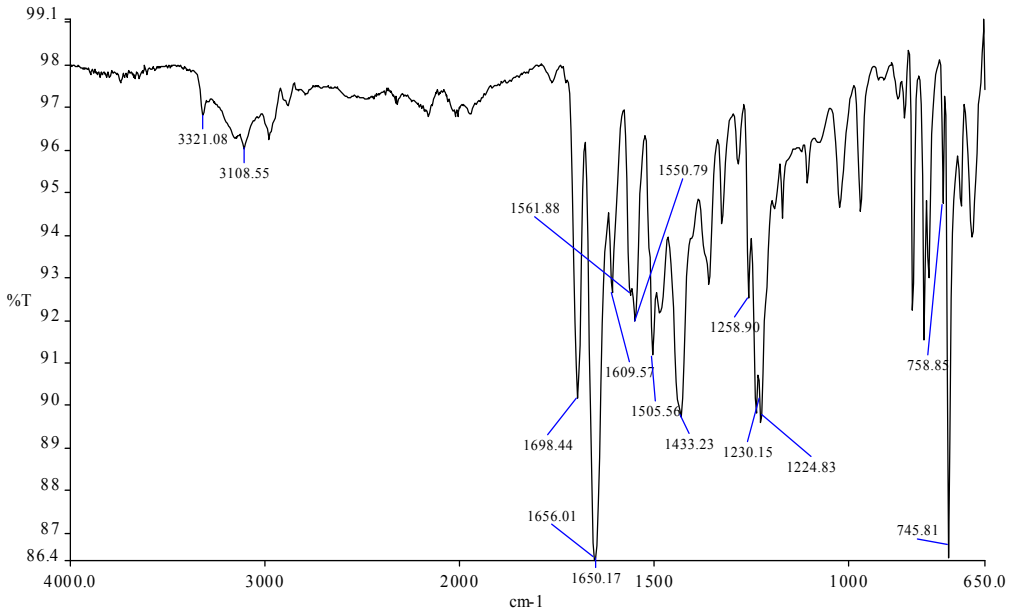


Figure C-43 IR-ATR Spectrum of S43
(41.4 % Caffeine, 47.6 % Paracetamol)

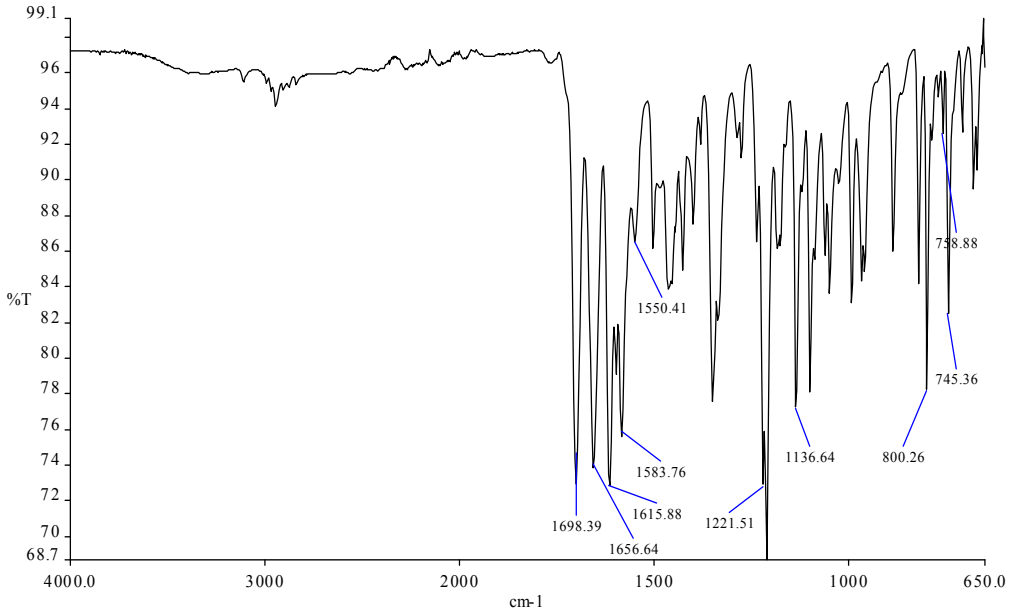


Figure C-44 IR-ATR Spectrum of S44
(16.9 % Caffeine, Griseofulvin)

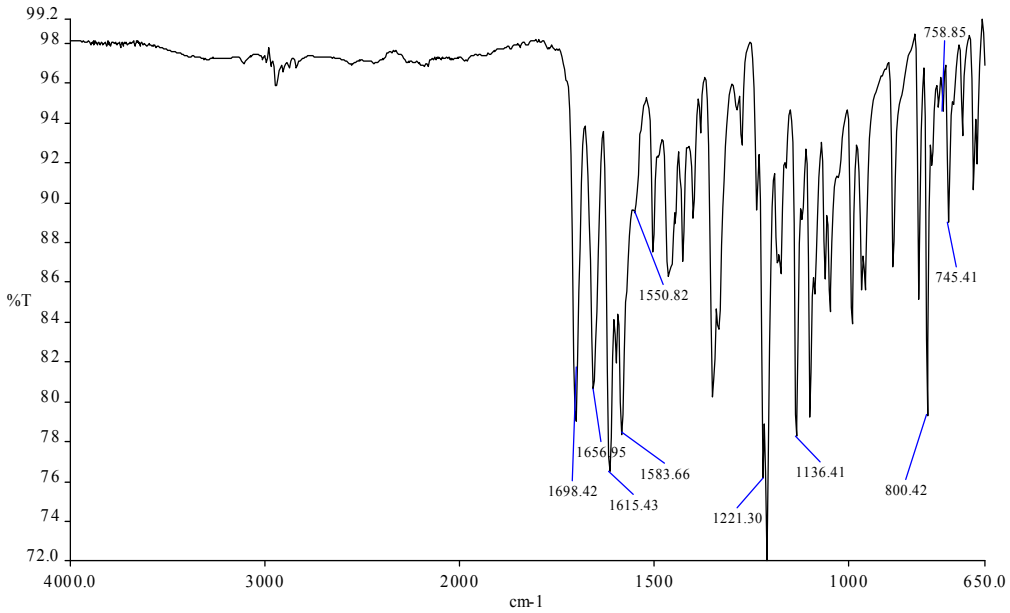


Figure C-45 IR-ATR Spectrum of S45
(12.9 % Caffeine, Griseofulvin)

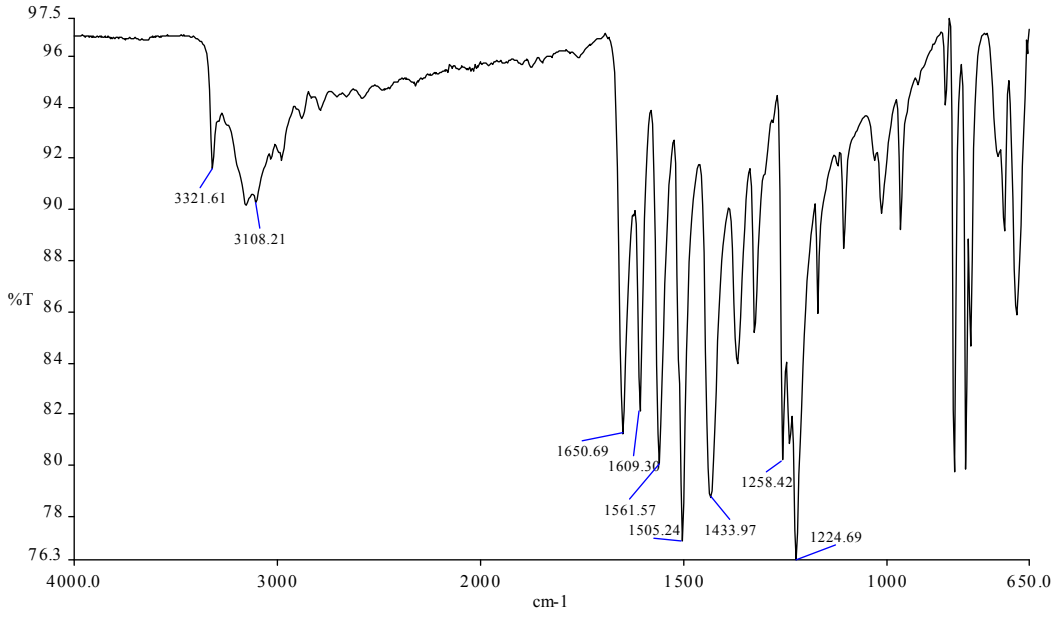


Figure C-46 IR-ATR Spectrum of S46
(88.3 % Paracetamol)

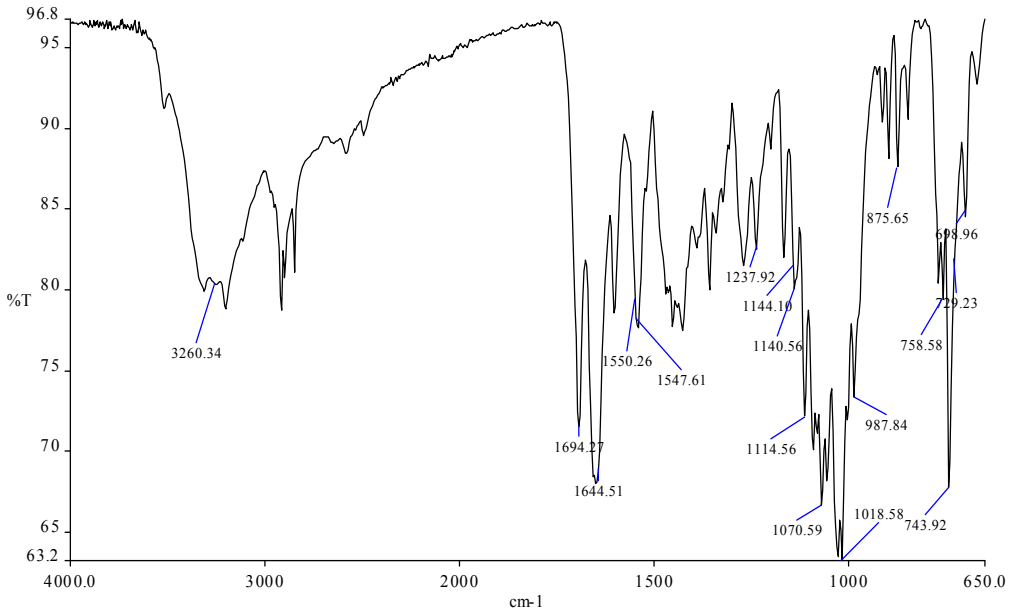


Figure C-47 IR-ATR Spectrum of S47
(3.5 % Amphetamine, 14.2 % Caffeine, Lactose)

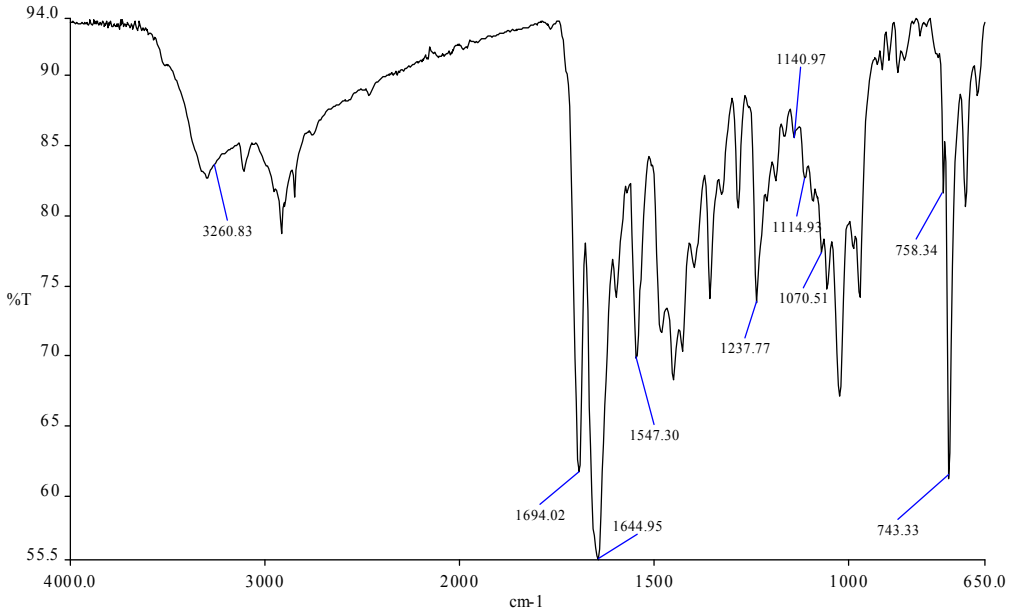


Figure C-48 IR-ATR Spectrum of S48
(1.6 % Amphetamine, 19.5 % Caffeine, Lactose)

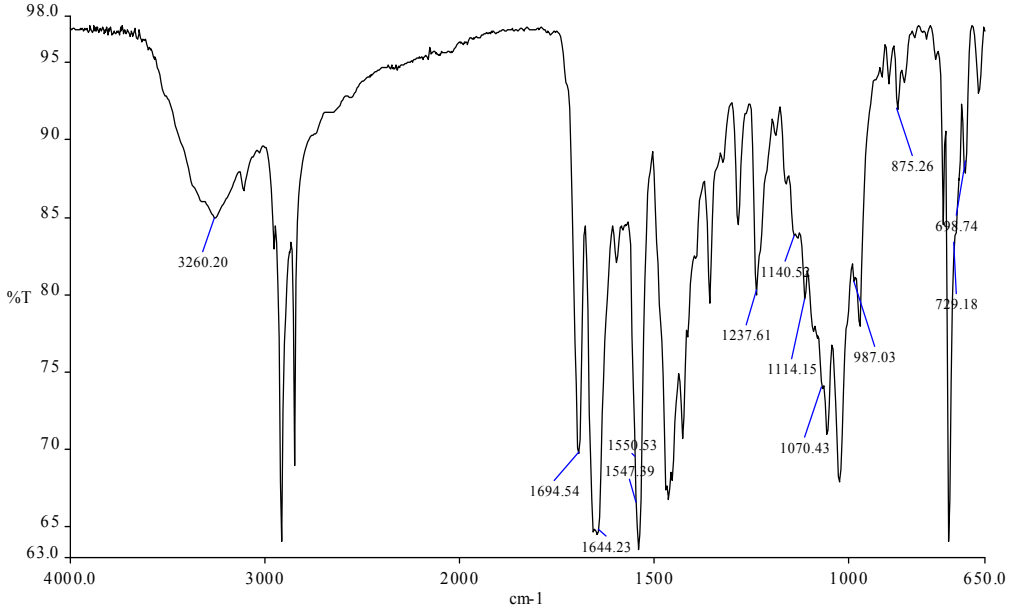


Figure C-49 IR-ATR Spectrum of S49
(8.6 % Amphetamine, 20.2 Caffeine, Lactose)

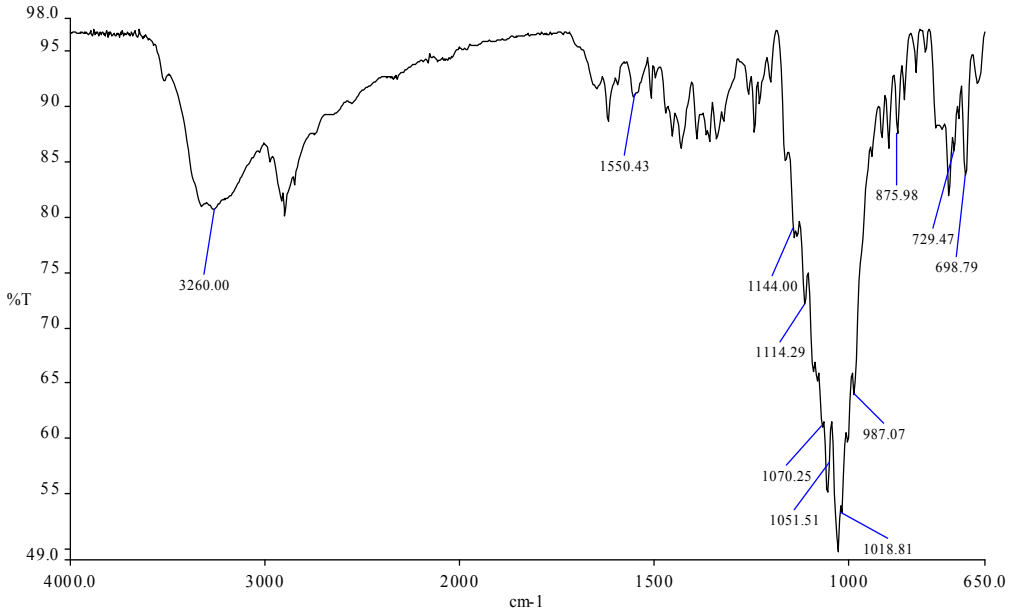


Figure C-50 IR-ATR Spectrum of S50
(14.3 % Amphetamine, 0.9 % Caffeine, Lactose)

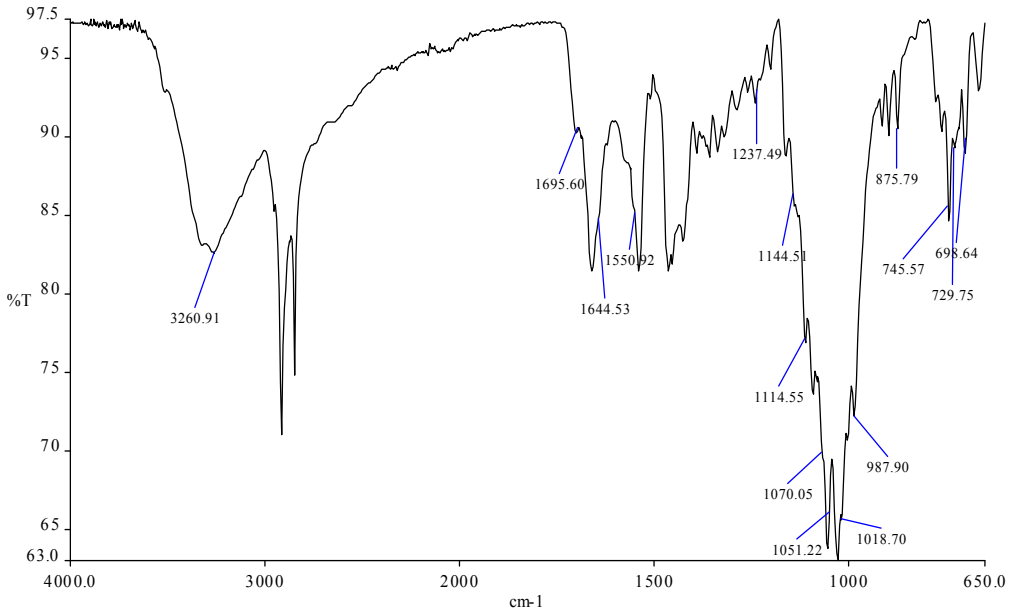


Figure C-51 IR-ATR Spectrum of S51
(11.2 % Amphetamine, 2.2 % Caffeine, Lactose)

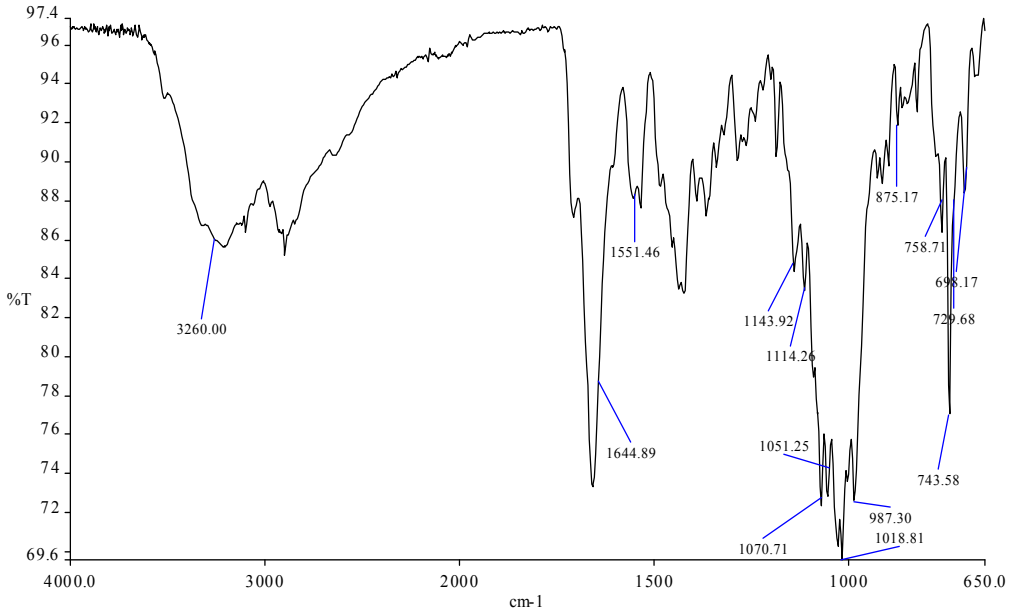


Figure C-52 IR-ATR Spectrum of S52
(19.9 % Amphetamine, 3.8 % Caffeine, Lactose)

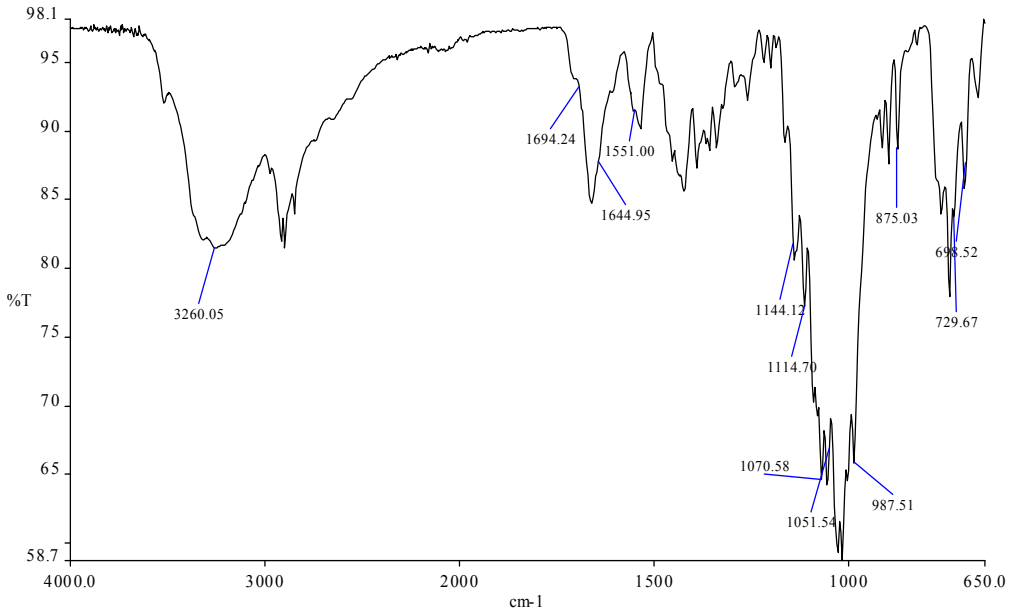


Figure C-53 IR-ATR Spectrum of S53
(15.1 % Amphetamine, 0.4 % Caffeine, Lactose)

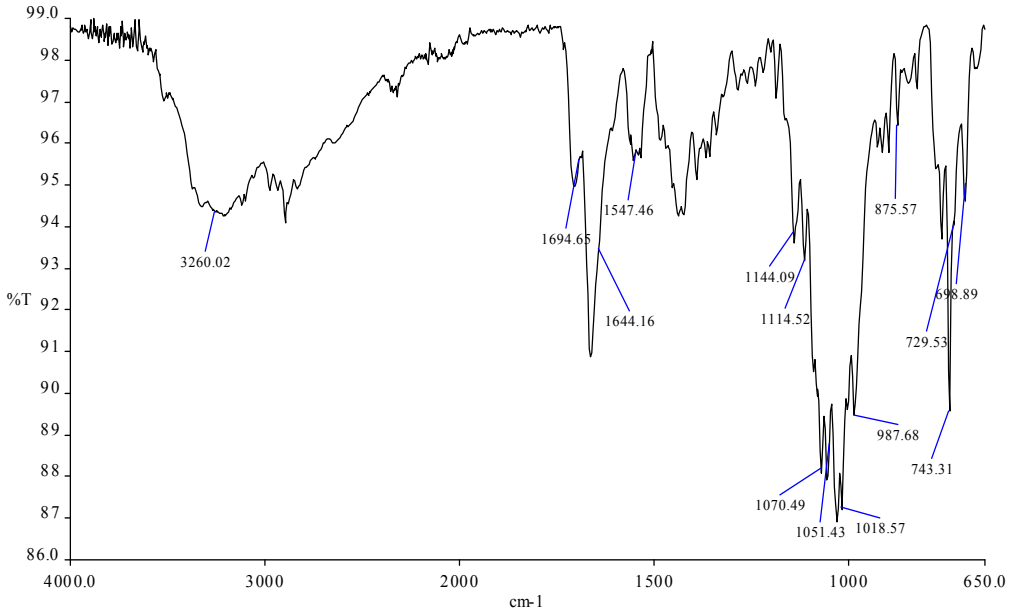


Figure C-54 IR-ATR Spectrum of S54
(18.6 % Amphetamine, 5.6 % Caffeine, Lactose)

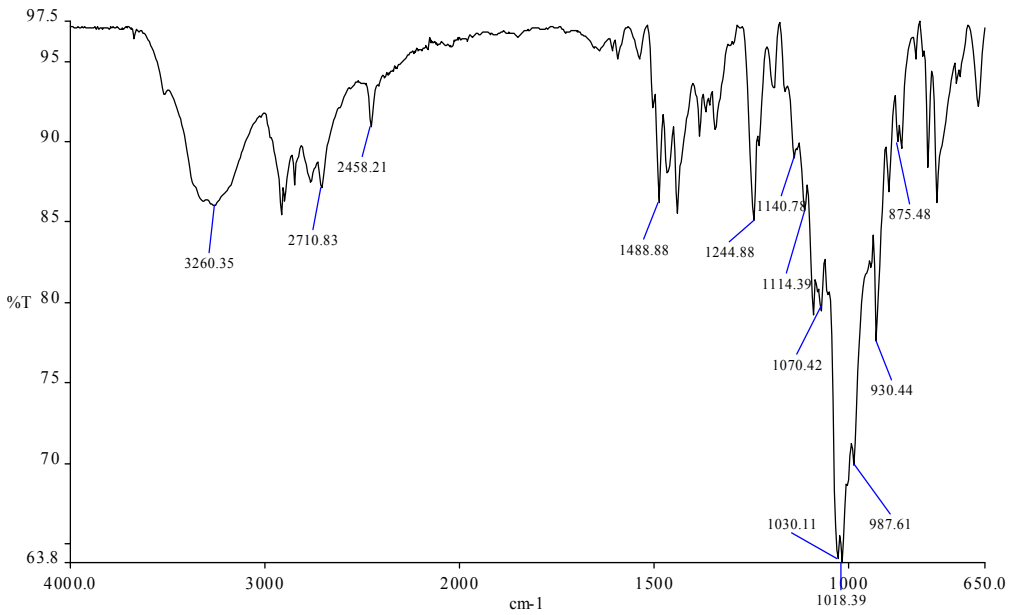


Figure C-55 IR-ATR Spectrum of S55
(15.0 % MDMA, Lactose)

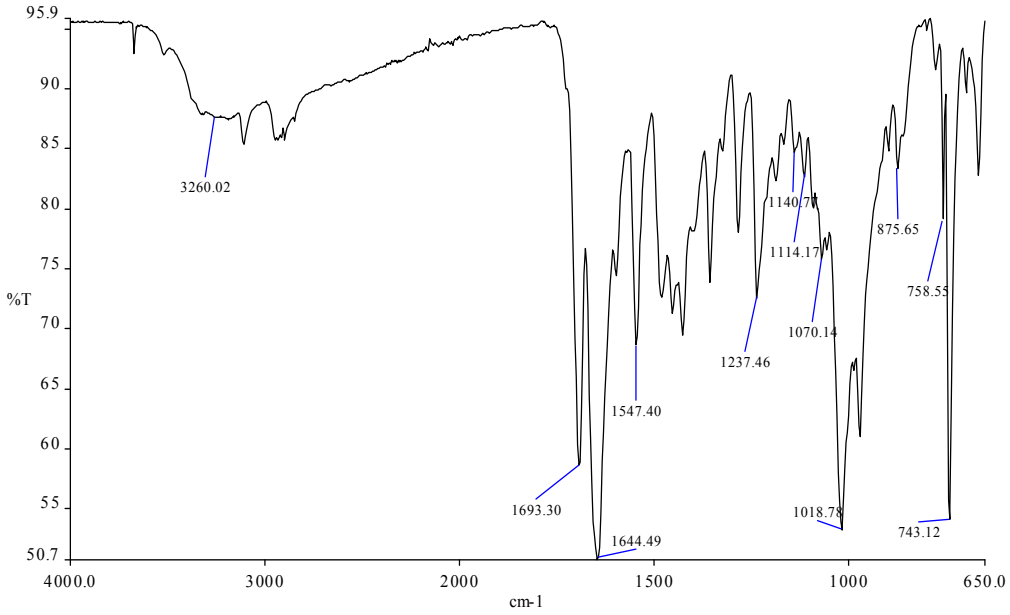


Figure C-56 IR-ATR Spectrum of S56
(5.5 % Amphetamine, 33.4 % Caffeine, Lactose)

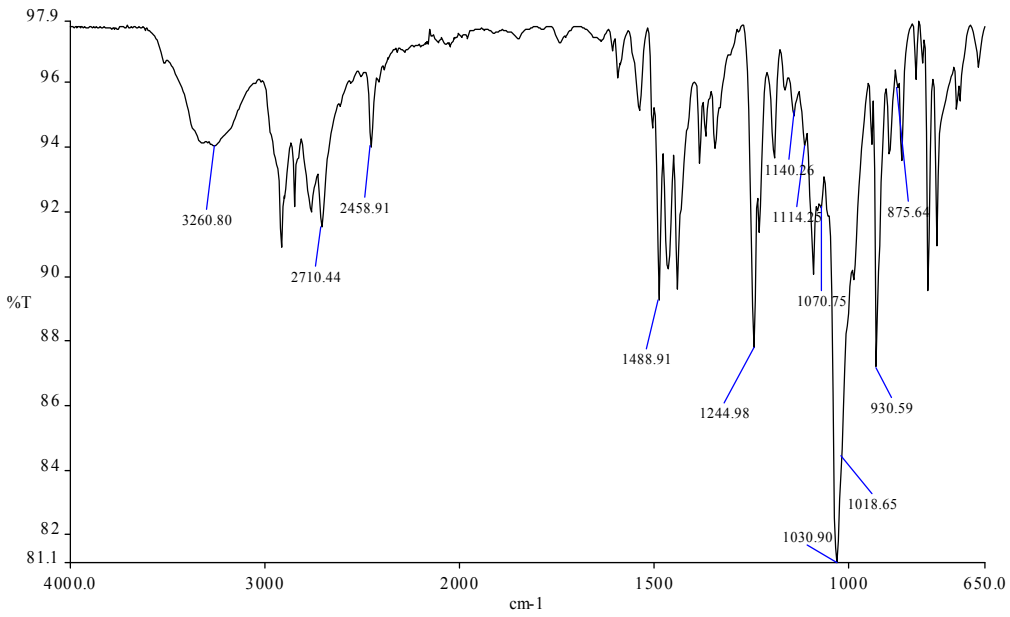


Figure C-57 IR-ATR Spectrum of S57
(33.0 % MDMA, Lactose)

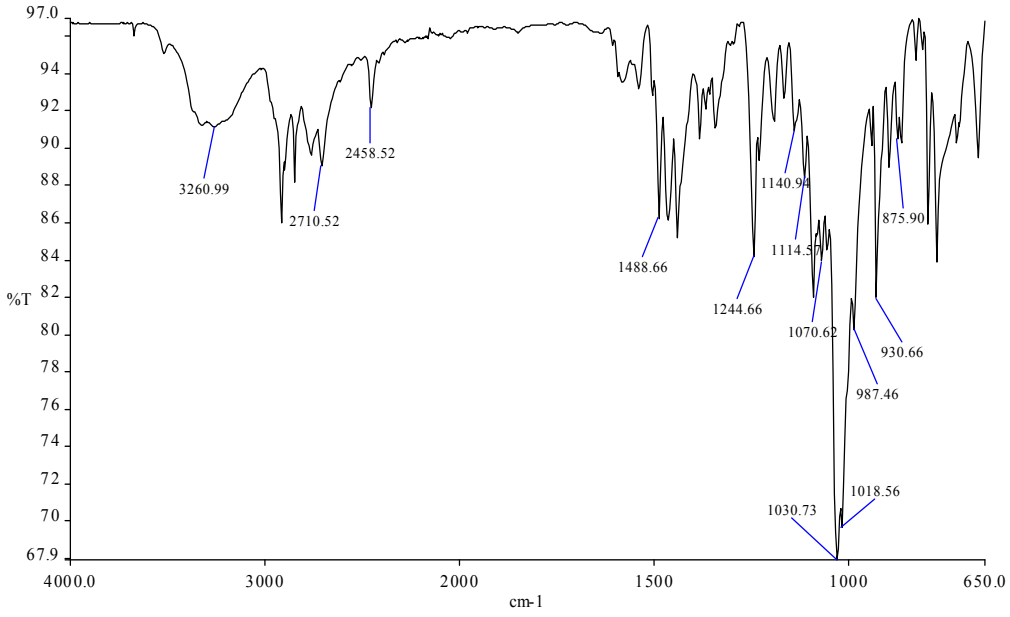


Figure C-58 IR-ATR Spectrum of S58
(35.1 % MDMA, LActose)

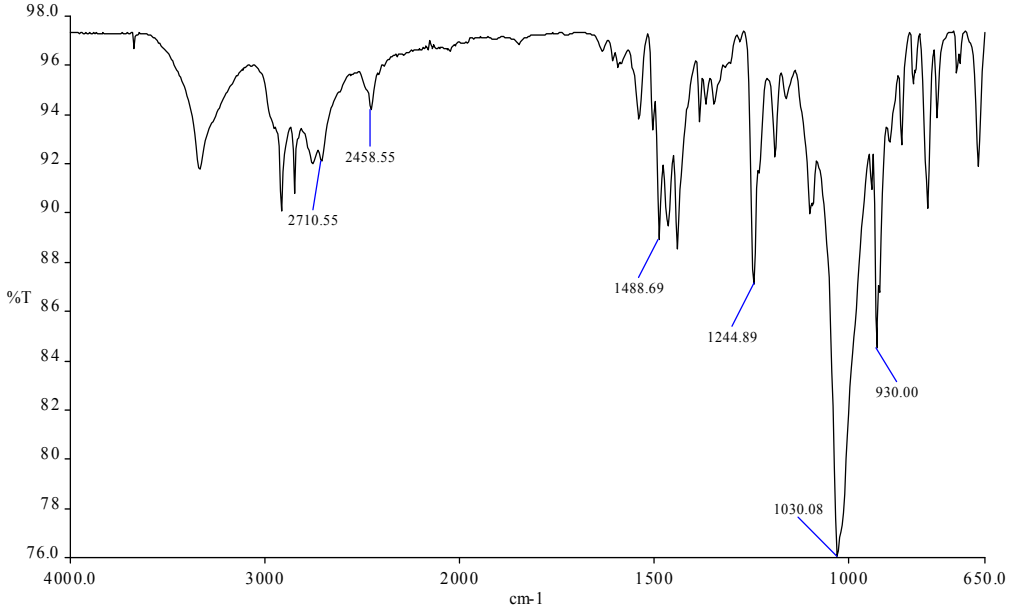


Figure C-59 IR-ATR Spectrum of S59
(22.6 % MDMA)

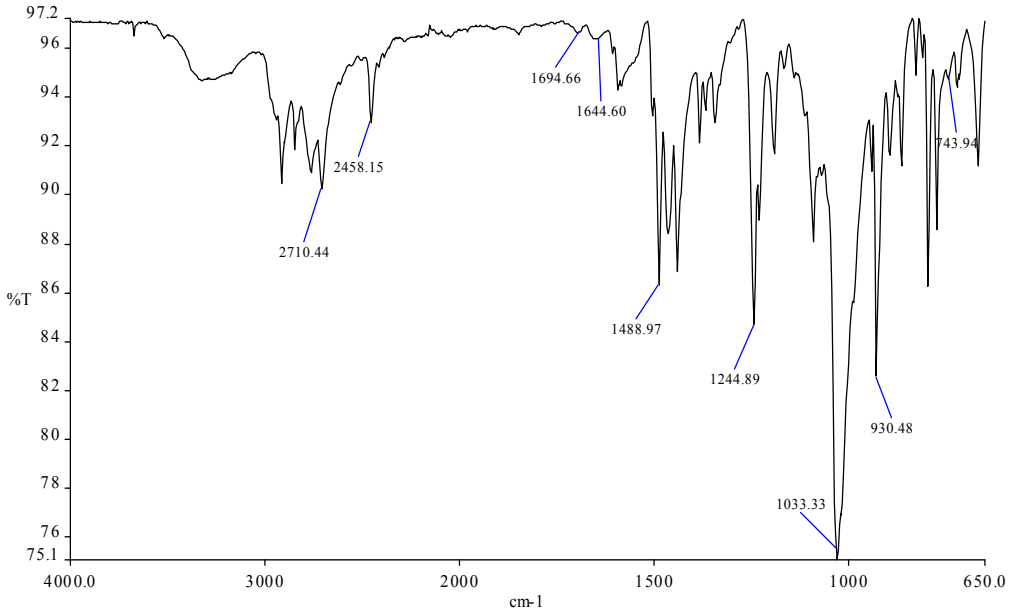


Figure C-60 IR-ATR Spectrum of S60
(38.9 % MDMA, 2.1 % Caffeine)

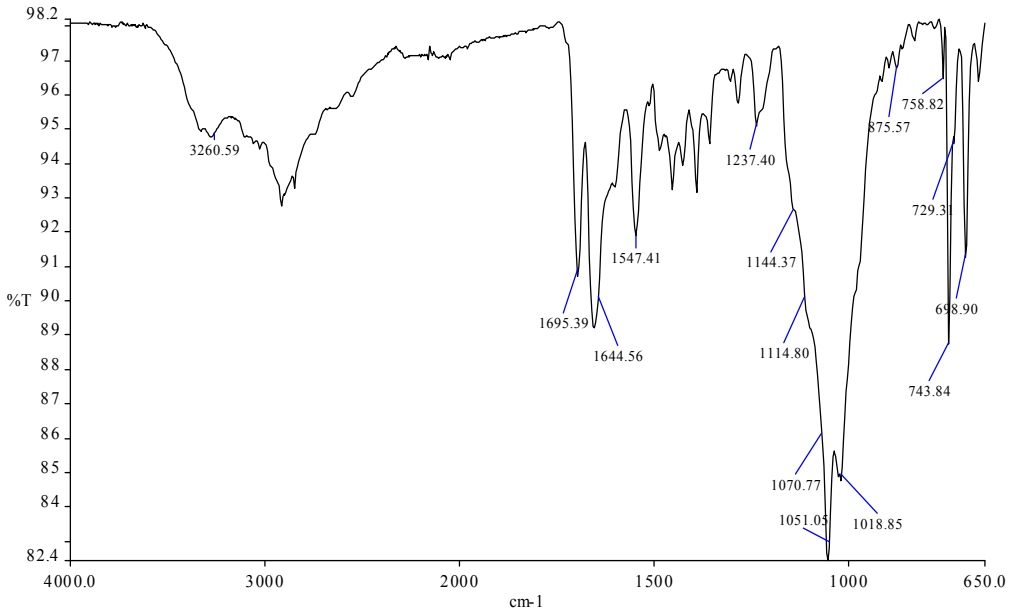


Figure C-61 IR-ATR Spectrum of S61
(17.1 % Amphetamine, 15.8 % Caffeine, Lactose)

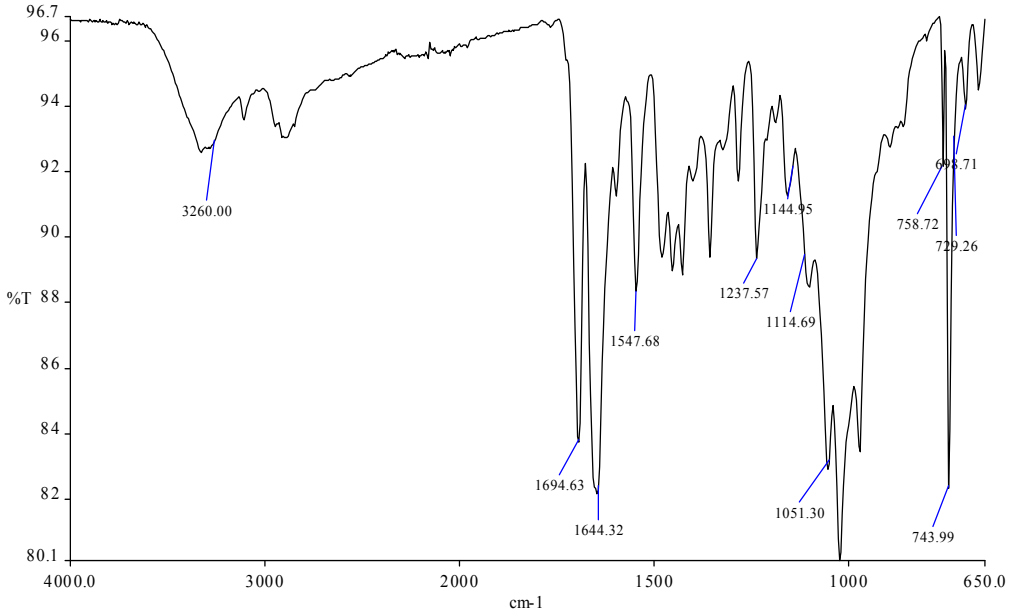


Figure C-62 IR-ATR Spectrum of S62
(2.4 % Amphetamine, 18.2 % Caffeine, Lactose)

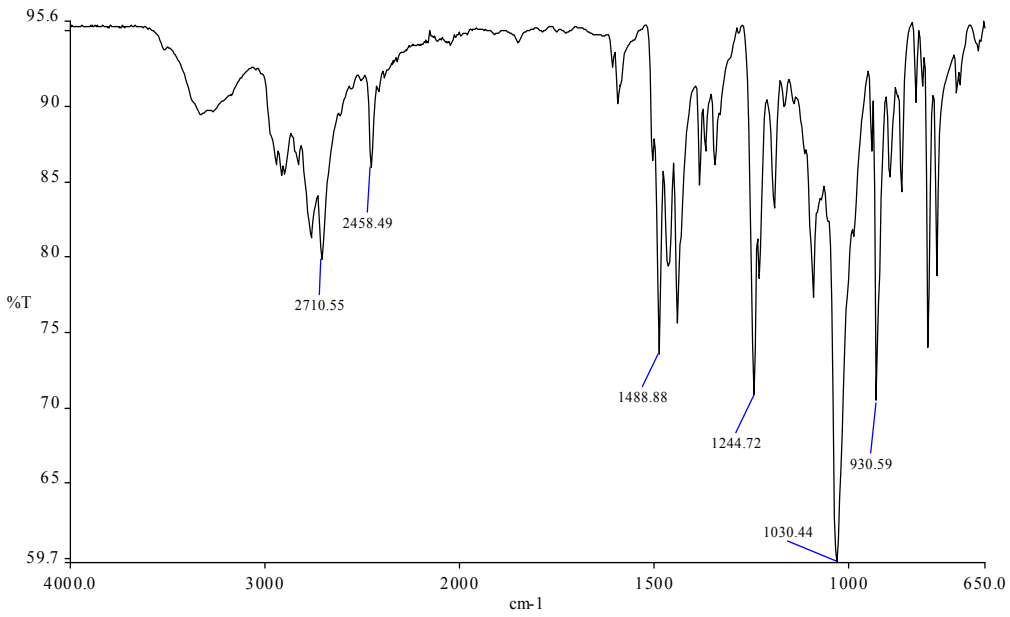


Figure C-63 IR-ATR Spectrum of S63
(31.5 % MDMA)

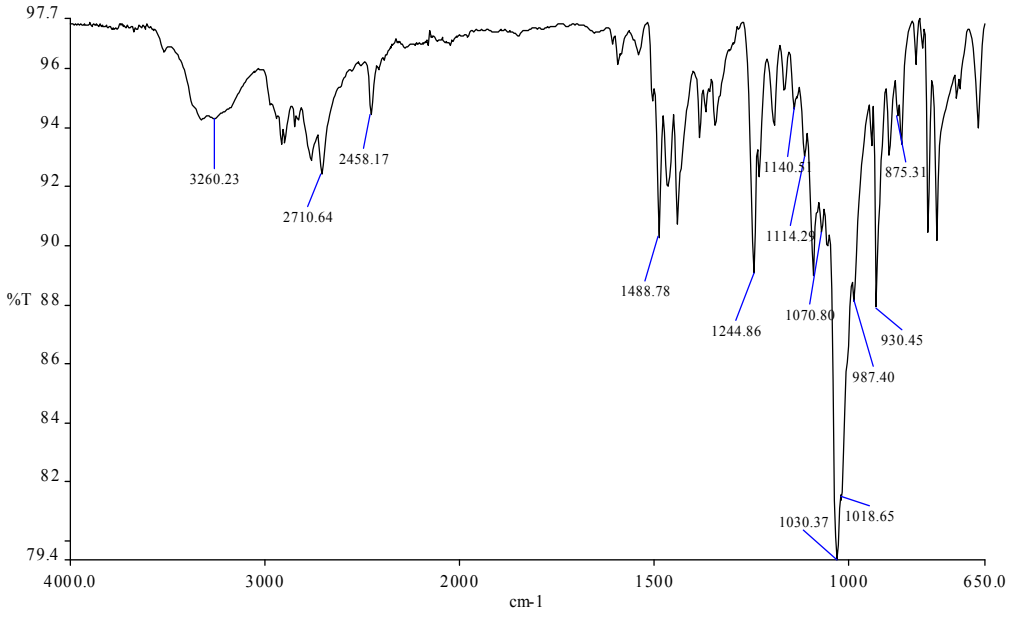


Figure C-64 IR-ATR Spectrum of S64
(34.5 MDMA, Lactose)

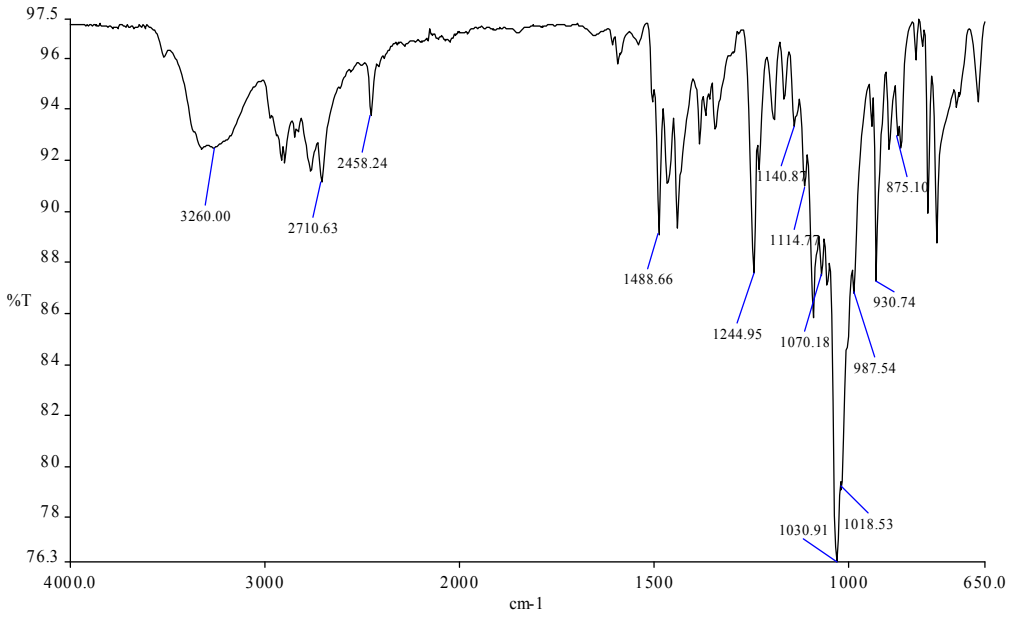


Figure C-65 IR-ATR Spectrum of S65
(29.2 % MDMA, Lactose)

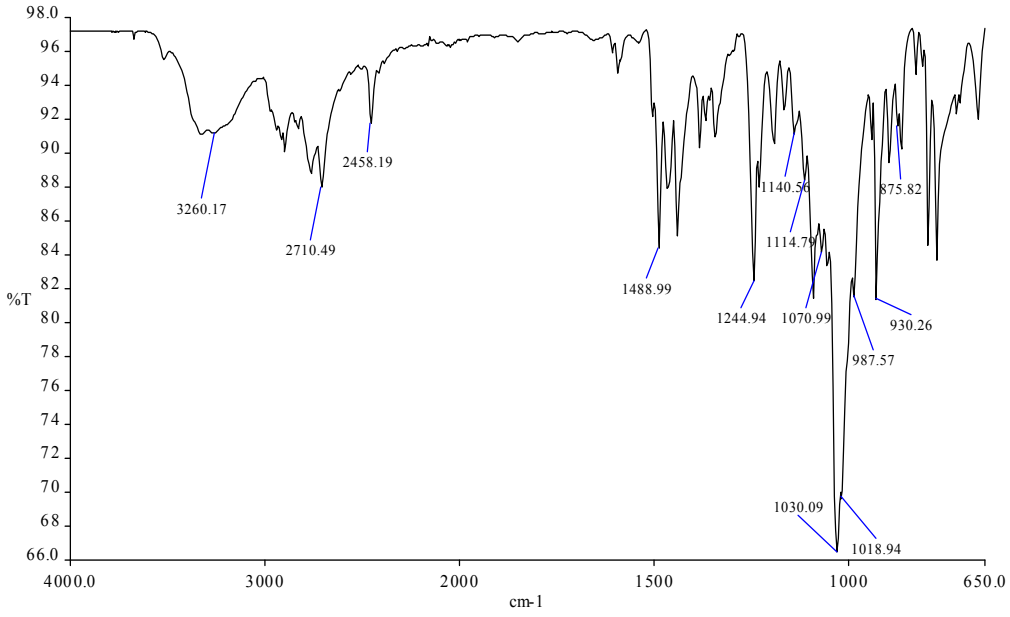


Figure C-66 IR-ATR Spectrum of S66
(32.9 % MDMA, Lactose)

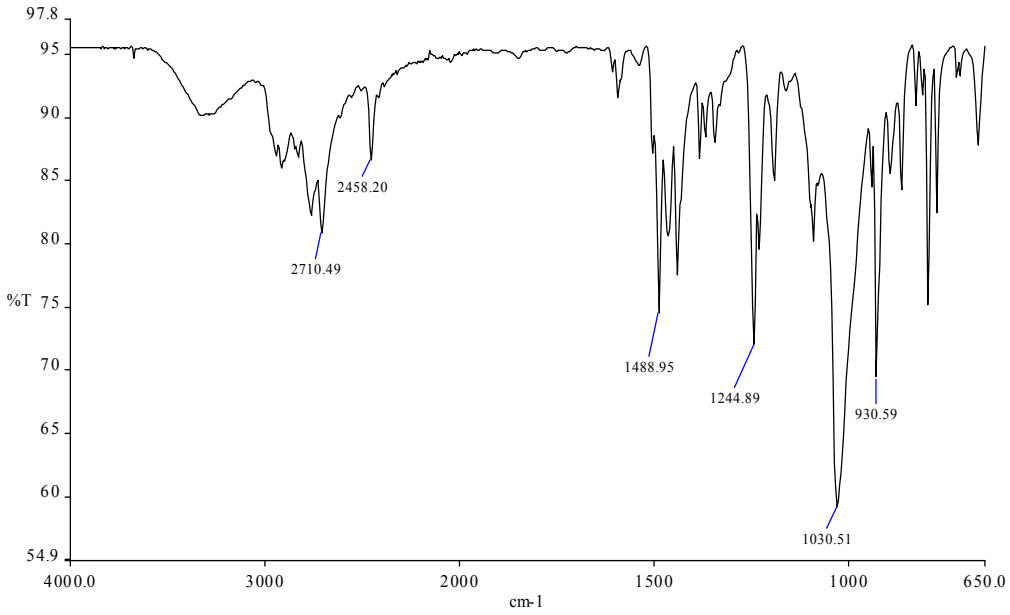


Figure C-67 IR-ATR Spectrum of S67
(41.5 % MDMA)

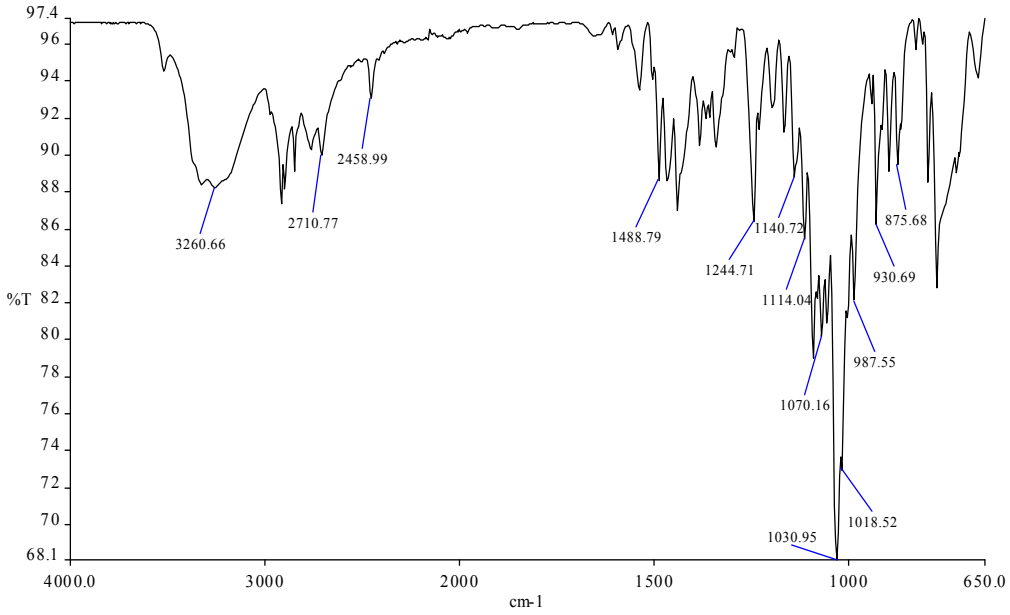


Figure C-68 IR-ATR Spectrum of S68
(20.7 % MDMA, Lactose)

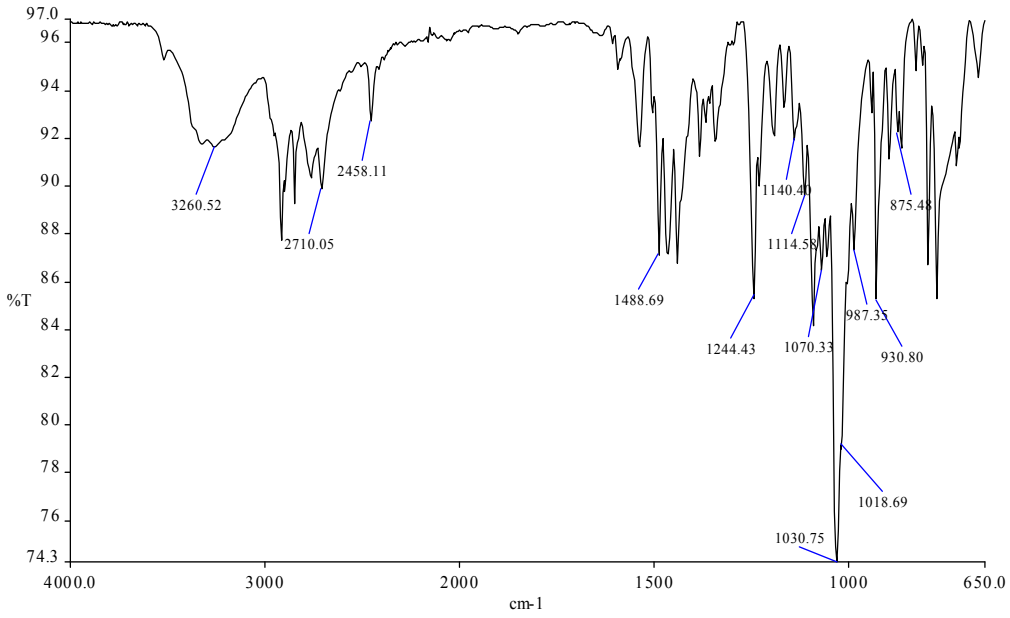


Figure C-69 IR-ATR Spectrum of S69
(31.6 % MDMA, Lactose)

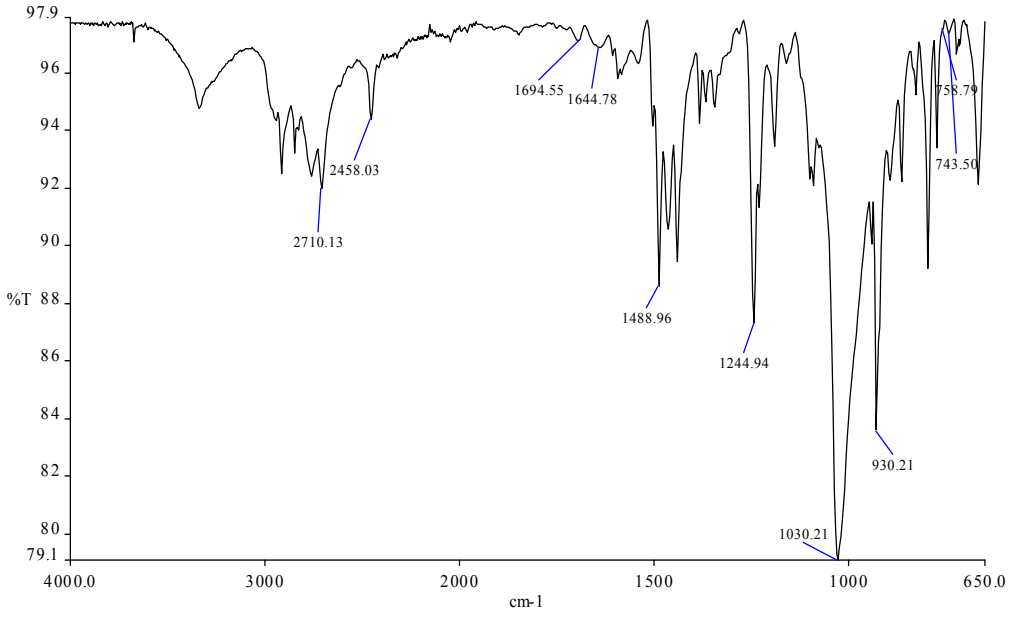


Figure C-70 IR-ATR Spectrum of S70
(26.2 % MDMA, 1.8 % Caffeine)

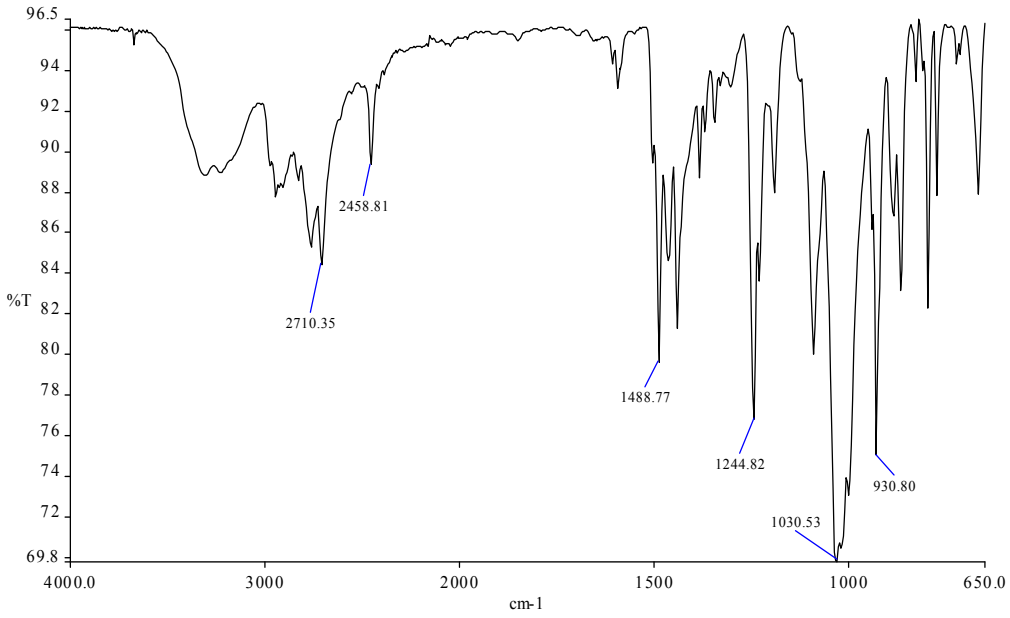


Figure C-71 IR-ATR Spectrum of S71
(25.6 % MDMA, 0.6 % Caffeine)

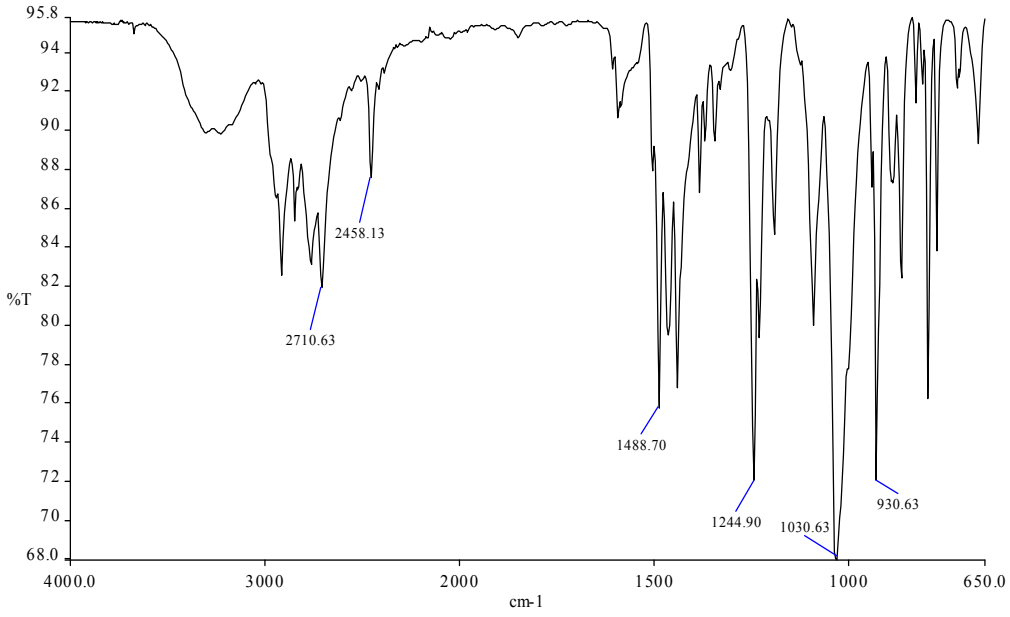


Figure C-72 IR-ATR Spectrum of S72
(35.9 % MDMA)

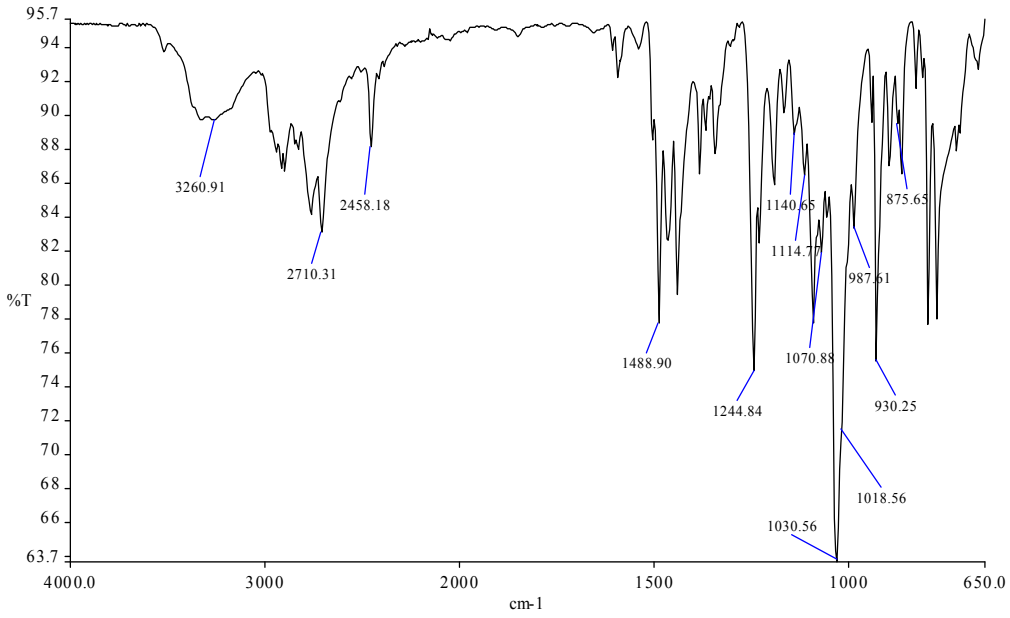


Figure C-73 IR-ATR Spectrum of S73
(60.4 % MDMA, Lactose)

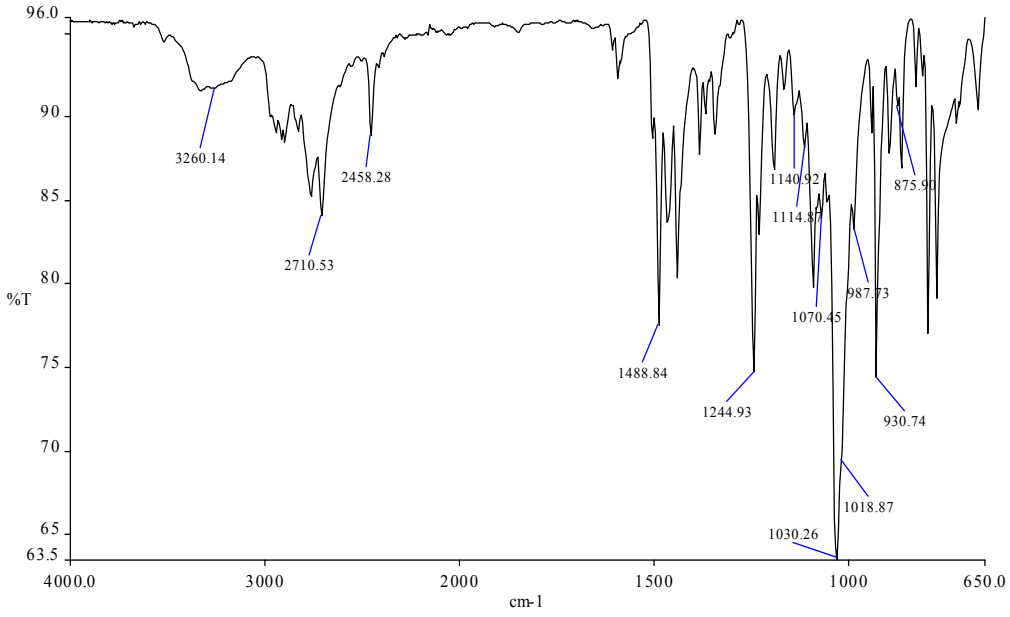


Figure C-74 IR-ATR Spectrum of S74
(55.9 % MDMA, Lactose)

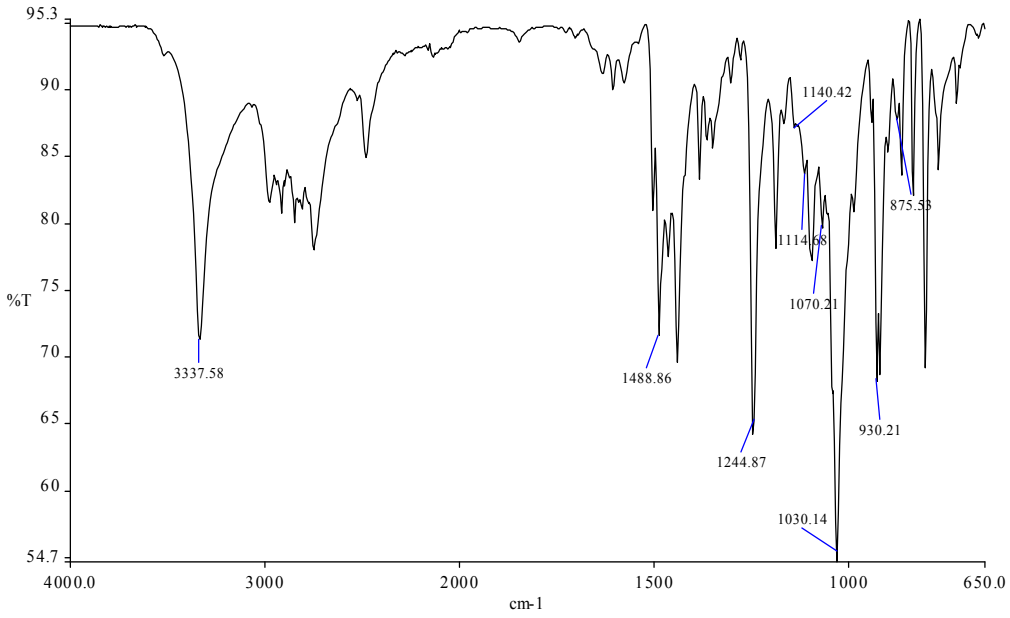


Figure C-75 IR-ATR Spectrum of S75
(40.3 % MDMA, Lactose)

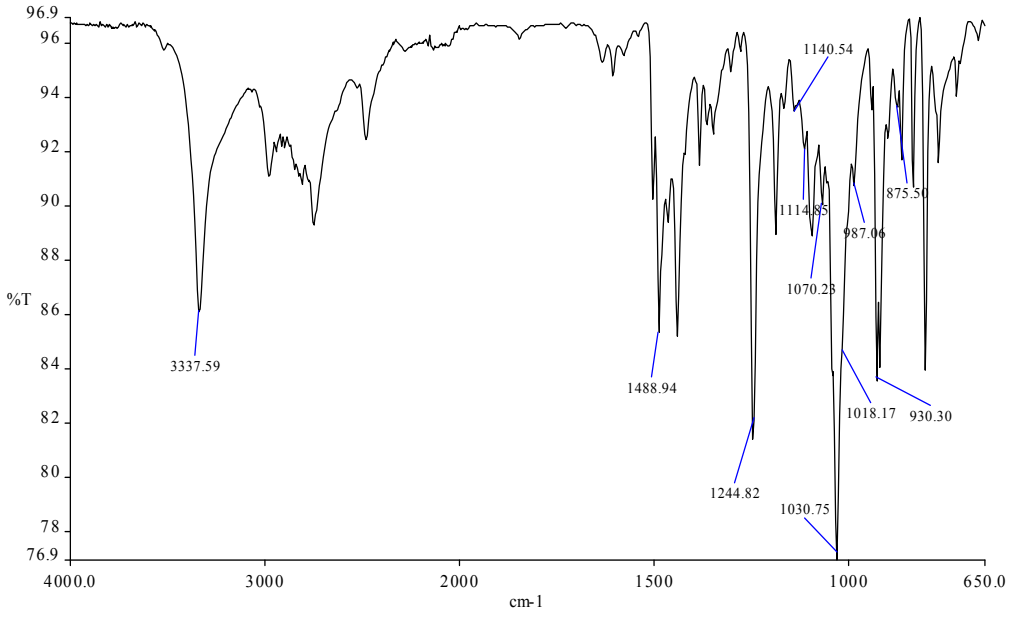


Figure C-76 IR-ATR Spectrum of S76
(39.1 % MDMA, Lactose)