DOKUZ EYLÜL UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

CHEMICAL PROFILING OF ECSTASY TABLETS

by
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İZMİR

CHEMICAL PROFILING OF ECSTASY TABLETS

A Thesis Submitted to the Graduate School of Natural and Applied Sciences of Dokuz Eylül University in Partial Fulfillment of the Requirements for the Degree of Master of Science in Chemistry

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M.Sc THESIS EXAMINATION RESULT FORM

We have read the thesis entitled **"CHEMICAL PROFILING OF ECSTASY TABLETS"** completed by **HASAN DURMUŞ** under supervision of **PROF. DR. MELEK MERDİVAN** and we certify that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science.

……

Prof.Dr. Melek MERDİVAN

Supervisor

…… ……

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Jury Member Jury Member

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Hasan DURMUŞ

CHEMICAL PROFILING OF ECSTASY TABLETS

ABSTRACT

Ecstasy is the most popular name which is given the tablets that are containing 3, 4-methylenedioxymethamphetamine (MDMA), a derivative of amphetamine. MDMA was synthesized by the German pharmaceutical company Merck in 1912 in order find and patent pathways leading to haemostatic substances not develop an appetite suppressor. In this study it is tried to make a link between the tablets collected between January 2005 and June 2006 from the seizures exceeding 100 tablets, by using Gas Chromatography-Mass Spectrometry (GC-MS). Scanning the former studies of subject and making a list of the impurities encountered helped to construct a cluster according the synthesis route and with this cluster analysis conclusion of synthetic pathways made. Also using hierarchical cluster analysis links between the seizures are investigated. As a result ecstasy tablets were classified into different groups. It is apparent that most used method of synthesis is reductive amination in the production of MDMA. Chemical profiling of ecstasy tablets is providing intelligence on clandestine laboratory networks.

Keywords: Ecstasy, MDMA, Chemical Profiling, Reductive Amination, GC-MS.

EKSTAZİ TABLETLERİNİN KİMYASAL PROFİLLENDİRİLMESİ

ÖZ

Ekstazi, bir amfetamin türevi olan 3,4-methylenedioxymethamphetamine (MDMA), içeren tabletlere verilen en popular isimdir. MDMA ilk olarak 1912 yılında Alman ilaç firması Merck tarafından, iştah bastırıcı geliştirmek için değil, kan durdurucu maddeleri oluşturmak için gereken maddelerin bulunması ve patentlenmesi sırasında sentezlendi. Bu çalışmada Gaz Kromatografisi-Kütle Spektrometresi kullanarak (GC-MS), Ocak 2005 ve Haziran 2006 tarihleri arasında yakalanan ve 100 adedi geçen yakalamalardan ele geçen tabletler arasında bir bağ kurmaya çalıştık. Bu çalışmadan önce yapılmış olan çalışmaları taranıp karşılaşılan safsızlıkların bir listesi oluşturularak, maddelerin ait olduğu sentezleme yöntemine göre kümeler oluşturuldu ve elde edilen safsızlıkları bu kümelere yerleştirilerek, incelenen örneğin hangi metot ile sentezlendiği tespit edilmeye çalışıldı. Ayrıca hiyerarşik küme analizi kullanılarak bu örnekler arasında ki ilişkide araştırıldı. Sonuç olarak incelenen ekstazi tabletleri iki ana grupta toplandı. Açıkça görüldü ki MDMA üretiminde en çok kullanılan yol indirgeyici aminleme reaksiyonudur. Ekstazi tabletlerinin kimyasal profillendirilmesi yasadışı laboratuar ağları hakkında önemli bilgiler sunmaktadır.

Anahtar Kelimeler : Ekstazi, MDMA, Kimyasal Profillendirme, İndirgeyici Aminleme, GC-MS.

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CHAPTER ONE

INTRODUCTION

1.1 What Is Ecstasy?

Ecstasy is the most popular name which is given the tablets that are containing MDMA, a derivative of amphetamine. Ecstasy is a semi synthetic psychedelic empathogen. Today these tablets are consumed by mostly young adults and teenagers in night clubs and streets. “The number of ecstasy labs dismantled fell by 40 % in 2005 to just 52 labs, 20 % less than in 2000. Seizures of ecstasy precursors also fell by 40 % in 2005. In parallel, global ecstasy seizures fell by one third in 2005. All of this suggests that global ecstasy production, after strong increases in the 1990s, is now shrinking, primarily because of production falling in Europe”(United Nations Office on Drugs and Crime (UNODC), 2007 World Drug Report, 2007). While ecstasy trafficking decreased in West and Central Europe, it increased in East and South-East Europe.(UNODC, 2007 World Drug Report, 2007)

1.2 History

1.2.1 Background

The most commonly repeated statement in the medical literature is that MDMA was synthesized by the German pharmaceutical company Merck in 1912 in order to develop an appetite suppressor (Gimeno, Besacier, Chaudron-Thozet, Girard and Lamotte, 2002). An explanation for the erroneous association of MDMA with appetite suppressors might be that MDMA’s analogue MDA was studied for its potential as an antidepressant and appetite suppressor by Smith, Kline and French Laboratories between 1949 and 1957. (Kline & French Laboratories, 1957) (Yensen, Di Leo, Rhead, Richards, Soskin, Turek et al, 1976)

However, in these documents there were no indications for plans to develop an appetite suppressant. MDMA was mentioned only casually and without being called ‘MDMA’. In the patent specification, MDM

A appeared only as a chemical formula and in the annual report it was referred to as ‘Methylsafrylamin’. The accurate background for the first synthesis of MDMA was that Merck wanted to find and patent pathways leading to haemostatic substances, not appetite suppressors. The company tried to evade an existing patent for the synthesis of a clotting agent called ‘Hydrastinin’ held by the German competitor Farbenfabriken Elberfeld und Decker or Bayer/Elberfeld, as stated explicitly by the head of Merck’s laboratory, Dr Walter Beckh (1870–1915) in the Annual Report for 1912.(Freudenmann, Öxler, Bernschneider-Reif, 2006)

Merck Co. started some toxicological tests with MDMA, when we were beginning of 50’s. But meanwhile at the University of Michigan there was the first formal animal study in five species using MDMA, with sponsorship of US army. (Shulgin, 1990)

1970 was the turnover fort the substance while it was starting to be used as a recreational drug in the streets of Chicago. (Gaston, Rasmussen, 1972) However it took a long time to become a controlled substance and banned to produce, sell and use of, till 1985.

1.2.2 Current Situation

Ecstasy production continues to be largely concentrated in Europe, though the expansion of ecstasy production, in recent years, has mainly taken place outside Europe, notably in North America and in East and South-East Asia. (UNODC, 2007 World Drug Report, 2007)

Global seizures of amphetamine type stimulants (ATS) are dominated by seizures of methamphetamine. Over the 2000-2005 period, 49 % of ATS seizures were in the form of methamphetamine, 15 % in the form of amphetamine, and 14 % in the form of ecstasy; the rest (23 %) was not properly defined. In the case of ecstasy, 38 % of global seizures in 2005 took place in West and Central Europe, 27 % in the Oceania region, 20 % in North America and 9 % in East and South-East Asia. (UNODC, 2007 World Drug Report, 2007)

"Total ATS production in 2005(rounded figures) was composed of 110 mt of ecstasy and 370 mt of 'amphetamines' (including 290 mt of methamphetamine and 80 mt of amphetamine)". (UNODC, 2007 World Drug Report, 2007)

Global seizures of ATS precursors in 2005 included: 3,4-MDP-2-P (also known as PMK) sufficient to produce 10 mt of MDMA (ecstasy), piperonal sufficient to produce 2 mt of MDMA; and small quantities of safrole and isosafrole sufficient to produce some 11 kg of MDMA.(UNODC, 2007 World Drug Report, 2007)

In terms of the origin of ecstasy seizures reported (''mentioned'') by Member States, more than a third of the reporting countries (35%)continue to mention the Netherlands as the main source country (2003-05 period), followed by Belgium (9%). Europe as a whole accounts for 81% of such mentions. There may be a statistical bias, however, as 60 % of the countries reporting on the origin of ecstasy were actually European countries (34 out 57), which are more likely to cite other European countries as the source of ecstasy found on their markets. Country origin mentions suggest that the role of the Netherlands as the key production centre for ecstasy is declining in importance. While over the 2002-04 periods, 39 % of all mentions referred to the Netherlands, this proportion fell to 32 % by 2005. Countries outside Europe which are frequently mentioned as sources of ecstasy include Canada, China, South Africa, USA as well as Hong Kong SAR of China. (UNODC, 2007 World Drug Report, 2007)

According to EUROPOL, illicit PMK prices rose in the European Union in 2005 and 2006, indicating an emerging shortage on the market. Ecstasy production at significant levels nonetheless continued. This has raised questions about the origin of ecstasy precursors in Europe. Some of them still appear to come from China, but a great variety of new routes have been identified, including overland by rail via Central & West Asia and East Europe, and by sea via Asia and Africa. (UNODC, 2007 World Drug Report, 2007)

1.3 Effects

MDMA is taken orally approximately 1-2 tablets, it starts to rise in the human blood in between 30-60 minutes, where at the and of this time period reaches a maximum level and lasts for 2-3 hours there.

When a person took couple of ecstasy pills he or she would feel himself or she more socialized more energetic, increased awareness and appreciation of music, and also feelings of comfort, belonging, and closeness to others. These are positive effects of MDMA on humans.

But also there are some other unwanted effects like appetite loss, nystagmus, change in body temperature regulation and visual distortion. However those given effects above are not so bad compared to effects coming up when people start taking higher doses and frequent use, which is finally ended up with nausea and vomiting, mild depression and fatigue for up to a week, possible psychological crisis requiring hospitalization, short-term memory scramble or loss & confusion, even small risk of death. Also long term abuse seems to cause brain damage and impairments in visual and verbal memory.(McCann, Szabo, Scheffel, Dannals, Ricaurte, 1998)(Bolla, McCann, Ricaurte, 1998) Additionally the permanent users can have erectile dysfunction and difficulty reaching orgasm, where ecstasy is a so called “love drug”.

1.4 Chemical Profiling

In general, chemical profiling methods are based on determining and quantifying the illicit substance and identifying the organic impurities present. Certain impurities may be route specific in the synthetic drugs. Because of poor chemical handling during synthesis, side reactions of the intermediates formed, inadequate purification procedures and contamination, in the reagents, the adulterants and diluents added or due to packaging and handling of the final tablets, impurities are present in illicit drugs.

The production of ecstasy in Europe is becoming ever more sophisticated, characterized by increased professionalism and efficiency in production. Trends

> such as the participation of more specialized staff, companies and facilitators, have been identified. The subsequent distribution of ecstasy end products however, may be more ad hoc. It is thought to be undertaken by a large number of rather small drug trafficking groups of various nationalities. They typically purchase the ecstasy in the Netherlands, Belgium or other producing countries (the Baltic countries, Poland, Balkan region etc.) and then traffic the drugs to their respective home countries. (UNODC, 2007 World Drug Report, 2007)

Because of these reasons, finding the synthesis route and the correlation between the seizures needs a little bit more sophisticated work with the tablets of investigation.

Early attempts to link illicitly produced tablets were based on physical descriptions. Today, conventional profiling of illicit drugs relies on a combination of physical, chemical and statistical techniques to establish links among seizures originating from a common source. (Daéid & Waddell, 2005)

In the case of synthetic drugs, links between the seizures, unfortunately can not be build by targeting one or two compounds, i.e. precursors, starting materials. In stead of that one should be select a group of chemicals, since most of the synthesis routes have same starting materials and there is a possibility of contamination where we deal with trace evidence.

Because of the fact that illegally synthesized drugs probably are distributed in more than one country, there is need for us as forensics and law enforcements for a universal cooperation and method development in impurity profiling.

1.5 Synthesis Methods of MDMA

There are three main routes for the synthesis of MDMA, which are reductive amination, safrole bromination and Leuckart method. The last one claimed as the most used synthesis method of producing amphetamine. 3, 4-methylenedioxy-

phenyl-2-propanone MDP2P is precursor for the reductive amination and Leuckart route, where isosafrole for the safrole bromination. But all three procedures must start with sassafras oil, or as named safrole.

> Very little safrole is actually required to make MDMA. Ocotea cymbarum is an essential oil - distilled from the trunk bark of a tropical tree native to Brazil, Colombia, and Paraguay - that typically contains between 80 and 94 percent safrole, a precursor for MDMA and MDA (3,4-methylenedioxyamphetamine). An MDMA producer with access to the proper chemicals can use a 500-milliliter quantity of Ocotea cymbarum to produce an estimated 1,300 to 2,800 tablets containing 120 milligrams of MDMA. (Microgram, 2005)

1.5.1 Reductive Amination

The reaction carried out is simply attack of the amine group to carbonyl in order to form an imine intermediate by loss of water and continuing with reducing nitrogen-carbon double bond with an appropriate reducing agent, like $NaBH_4$ or Al(Hg) amalgam. As this manner the reaction called indirect reductive amination. However, it is also possible to carry out the same reaction all in one pot, with the imine formation and reduction occurring concurrently. This is known as direct reductive amination and is carried out with reducing agents that are more reactive toward imines than ketones, such as $NaBH_3CN$.

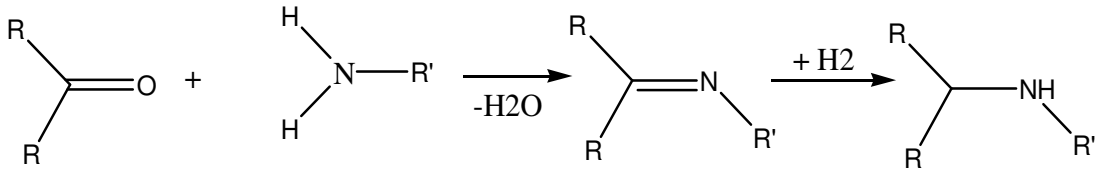


Figure 1.1 Simple scheme of the reductive amination.

In the case of MDMA synthesis safrole reacted with methylamine in the presence of reducing agents which are Al(Hg) amalgam, $NaBH_4$ or $NaCNBH_3$.

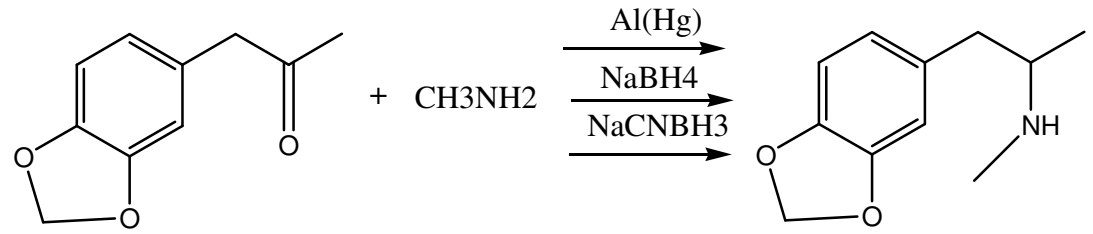


Figure 1.2 The scheme of reductive amination for MDMA synthesis.

1.5.2 Safrole Bromination

Safrole Bromination is based on Markovnikov's Rule, which says that with the addition of H-X to an alkene, the acid hydrogen (H) becomes attached to the carbon with the greatest number of hydrogen, and the Halide (X) group becomes attached to the carbon with the least hydrogen. As a result we have a more reactive compound with an easy leaving group.

This method is the bromination of cis-isosafrole with HBr and debromination of the intermediate with methylamine.

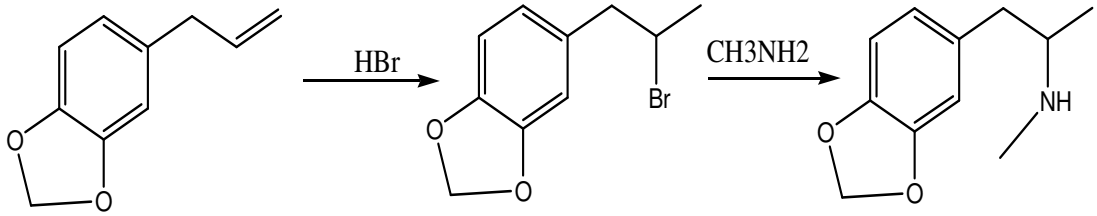


Figure 1.3 The scheme of safrole bromination for MDMA synthesis.

1.5.3 Leuckart Reaction

Leuckart Reaction is reductive alkylation of ammonium (or amine) salts of formic acid or formamides by aldehydes or ketones.

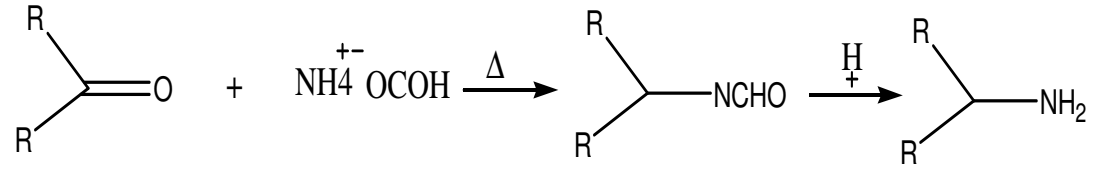


Figure 1.4 The scheme of Leuckart reaction.

For MDMA production, safrole reacted with $HCONHCH_3$ in the presence of formic acid followed by hydrolysis of intermediate.

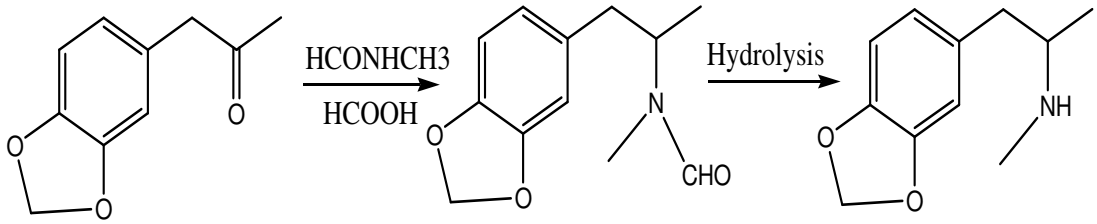


Figure 1.5 The scheme of Leuckart Reaction for MDMA synthesis.

1.6 Main Precursors

There are four main precursors to synthesize MDMA, which are isosafrole, 3, 4-methylenedioxyphenyl-2-propanone (MDP2P or PMK), piperonal and safrole. Also HBr, HCl, methylamine, ethanol, potassium hydroxide, hydrogen peroxide, formic acid, sulphuric acid, aluminum and mercury chloride used in the synthesis of ecstasy. However safrole is the starting material for isosafrole, piperonal and MDP2P, that we can say it is the main starting material.

1.6.1 Safrole

Safrole (5-(2-Propenyl)-1, 3-benzodioxole) is an oil extracted from the plant sassafras. The plant can be found in different species at America and South Asia. But the sassafras plants raised in North America contain less oil, and extraction procedure is difficult. Sassafras oil is obtained mainly from South America (for example from *Ocotea cymbarum*, which is sassafras plant grow in Brazil) and South Asia.

Safrole is used in perfumery; denaturing fats in soap manufacture; in manufacture of heliotropin (piperonal); also formerly as flavoring agent in foods, drugs and beverages. It is anticipated to be human carcinogen.

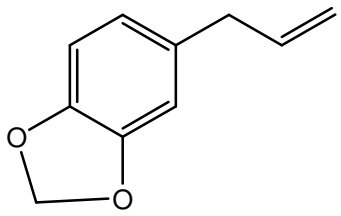


Figure 1.6 Safrole.

1.6.2 Isosafrole

Isosafrole (5-(1-Propenyl)-1, 3-benzodioxole) is a substance produced by isomerizing safrole with addition of ethanol and potassium hydroxide. It is also found in some essential oils, but in small amounts.

Isosafrole is used in manufacture of heliotropin; to modify oriental perfumes; to strengthen soap perfumes; in small quantities together with methyl salicylate in root beer and sarsaparilla flavors.

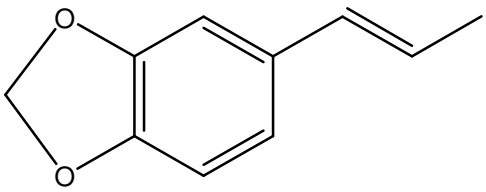


Figure 1.7 Isosafrole.

1.6.3 Piperonal (Heliotropin)

Piperonal (1, 3-Benzodioxole-5-carboxaldehyde) can be used to produce safrole and isosafrole, with further reactions amphetamine type stimulants.

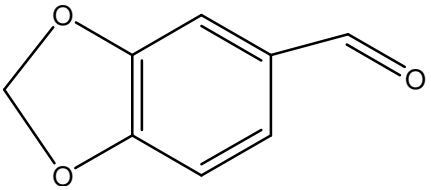


Figure 1.8 Piperonal

Chloromethylation of methylenedioxybenzene (1, 3-benzodioxole) to piperonylchloride (3, 4-methylenedioxybenzyl chloride), followed by reaction with the sodium salt of 2-nitropropane in an alcoholic solvent can be used to synthesize piperonal.

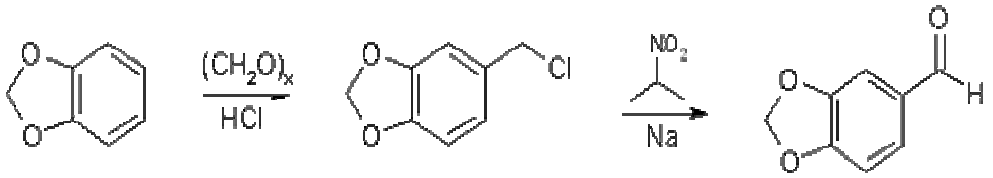


Figure 1.9 Synthesis of piperonal starting from methylenedioxybenzene.

It is used in many areas as in perfumery, cherry and vanilla flavors and organic syntheses. It also has been used for killing lice.

1.6.4 MDP2P (PMK)

MDP2P (3, 4-methylenedioxy-phenyl-2-propanone) is obtained through oxidation of safrole or isosafrole using hydrogen peroxide, formic acid and sulphuric acid. It has no other industrial or medicinal use, than production of amphetamine type stimulants.

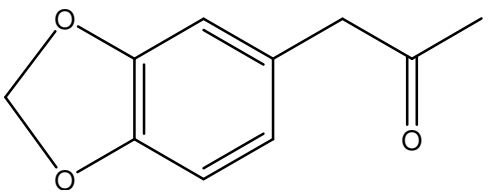


Figure 1.10 MDP2P

1.7 Adulterants and Diluents

As this work deals with chemical profiling, adulterants and diluents are also in its scope, since they are sources of impurities somehow. In most of the seized MDMA cases, it is in the tablet form. In order to make tablets, producers put some adulterants like caffeine and to increase number of tablets some diluents (cutting agents) like saccharose, lactose, starch and mannitol. Additionally stearic acid and N-hexadecanoic acid powders added in to MDMA powder in tabletting process.

Detection of adulterants and diluents are secondary proofs for the linking seizures, in most cases. But some situations like detecting other types of drugs in ecstasy tablets may lead to a good result, where it can be proved it is not a cross contamination.

1.8 Literature Cited Impurities

Compared to the studies on amphetamine tablets, there is much less work on MDMA pills. Because of that first of all it is needed to scan previous works and collect the compounds that authors detected.(Gimeno, et al, 2002), (Gimeno, Besacier, Chaudron-Thozet, 2003), (Gimeno, Besacier, Bottex, Dujourdy, Chaudron-Thozet, 2005), (Świst, Wilamowski,Zuba, Kochana, Parczewski, 2005), (Świst, Wilamowski, Parczewski, 2005a), (Świst, Wilamowski, Parczewski, 2005b)

The impurities detected by authors are given in the table 1.1. In the table the letters L, R and B stands for the synthesis method. However in the works mentioned above, authors deal with reductive amination much more than the other routes, that is why letter R was given with a number with it, which is representing the specific reductive amination route.

Also mass spectra of some compounds are useful for comparison retrieved in these works. So that it will prevent to mismatch of the spectra and let to make a better identification.

Table 1.1 The impurities identified in cited studies. (L=Leuckart, B=Safrole bromination, R=Reductive amination R1= Reductive amination with Al/Hg R2= Reductive amination with $NaBH_3CN$ R3= Reductive amination with $NaBH_4$)

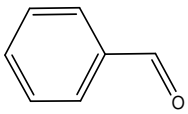
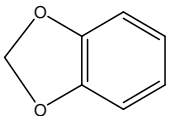
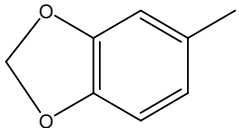
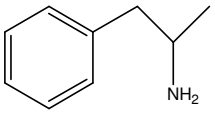
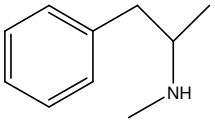
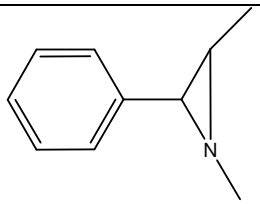
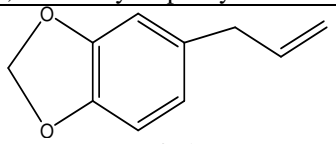
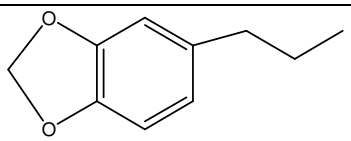
	Compound	Source	References
1	 Benzaldehyde	Chemical precursor of ephedrine	(Gimeno, et al, 2002)
2	 1,3-Benzodioxole	Impurity present in safrole	(Gimeno, et al, 2002) (Gimeno, et al, 2003)
3	 3,4-methylenedioxy toluene	Impurity present in safrole, isosafrole and piperonal	(Gimeno, et al, 2002) (Gimeno, et al, 2003)
4	 Amphetamine	Contamination	(Gimeno, et al, 2002)
5	 Methamphetamine	Contamination	(Gimeno, et al, 2002)
6	 1,2-Dimethyl-3-phenyl-aziridine	Methamphetamine impurity	(Gimeno, et al, 2002)
7	 Safrole	Chemical precursor of MDMA B, R	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, et al., 2005b)
8	 3,4-(Methylenedioxy)-phenylpropane	Chemical reduction of safrole or isosafrole R	(Gimeno, et al, 2002) (Gimeno, et al, 2003)

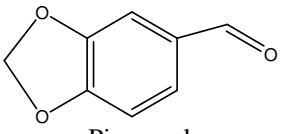
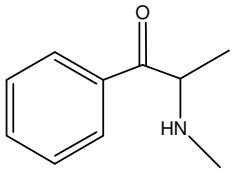
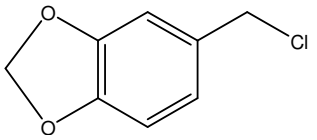
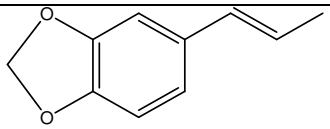
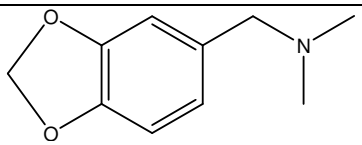
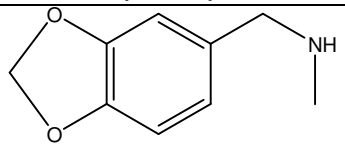
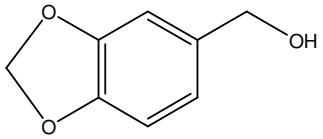
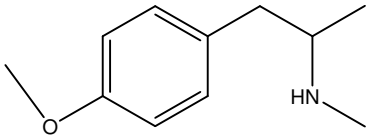
Table 1.1 continued.			
9	 Piperonal	Chemical precursor of MDMA R	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, Zuba, et al, 2005) (Świst, et al., 2005b)
10	 2-Methylamino-1-phenyl-1-propanone	Methamphetamine impurity	(Gimeno, et al, 2002)
11	 Piperonylchloride	Nucleophilic substitution of piperonyl alcohol by HCl R	(Gimeno, et al, 2002) (Gimeno, et al, 2003)
12	 Isosafrole	Chemical precursor of MDMA R	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, et al., 2005b)
13	 3,4-Methylenedioxy-N,N-dimethylebenzylamine	MDMA by product L, R1, R2, R3	(Gimeno, et al, 2002) (Świst, Zuba, et al, 2005) (Świst, et al., 2005a) (Świst, et al., 2005b)
14	 3,4-Methylenedioxy-N-methylebenzylamine	MDMA by product L, R1, R3	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, et al., 2005a) (Świst, et al., 2005b)
15	 Piperonyl alcohol	Chemical reduction of piperonal R	(Gimeno, et al, 2002) (Gimeno, et al, 2003)
16	 p-Methoxymethamphetamine	MDMA by product B, R	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, Zuba, et al, 2005) (Świst, et al., 2005b)

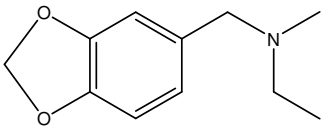
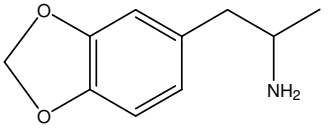
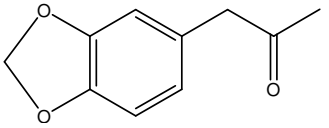
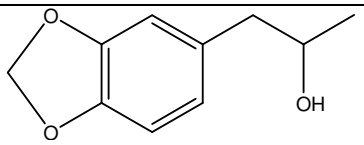
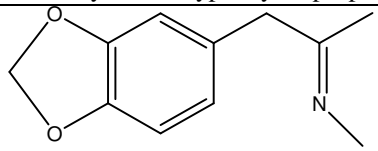
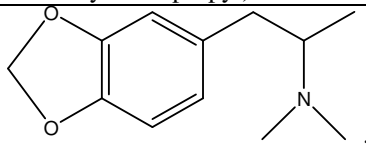
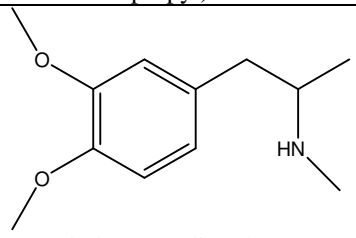
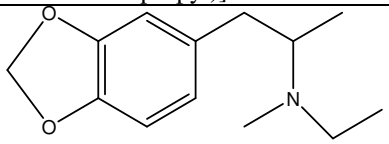
Table 1.1 continued.			
17	 3,4- Methylenedioxy-N-ethyl-N-methylebenzylamine	MDMA by product	(Gimeno, et al, 2002) (Świst, Zuba, et al, 2005)
18	 3,4-methylenedioxyamphetamine	MDMA by product R	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, Zuba, et al, 2005)
19	 3,4-methylenedioxyphenyl-2-propanone	MDMA intermediate or precursor R	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, et al., 2005b)
20	 1-3,4-methylenedioxyphenyl-2-propanol	Chemical reduction of MDP2P R3	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, Zuba, et al, 2005) (Świst, et al., 2005b)
21	 1,2-methylendioxy-4-(2-N-methyliminopropyl)benzene	MDMA intermediate R2	(Gimeno, et al, 2002) (Gimeno, et al, 2003) (Świst, Zuba, et al, 2005) (Świst, et al., 2005b)
22	 , N,N-dimethyl-(1,2-methylenedioxy)-4-(2-aminopropyl)benzene	MDMA by product Synthesis of MDMA from piperonal R	(Gimeno, et al, 2002) (Gimeno, et al, 2003)
23	 N-methyl-1-[1,2-dimethoxy-4-(2-aminopropyl)]benzene	MDMA by product R	(Gimeno, et al, 2002) (Gimeno, et al, 2003)
24	 N-ethyl-N-methyl-1,2-dimethoxy-4-(2-aminopropyl)benzene	MDMA by product	(Gimeno, et al, 2002)

Table 1.1 continued.

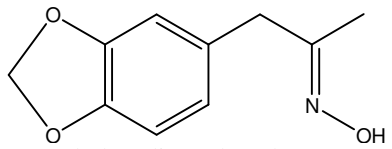
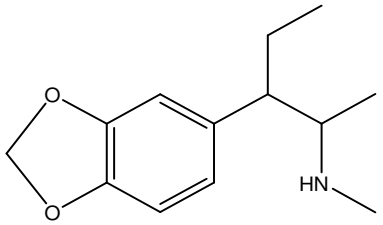
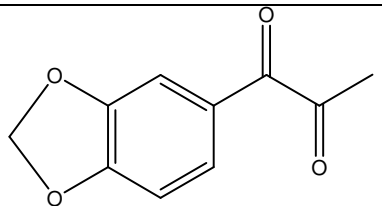
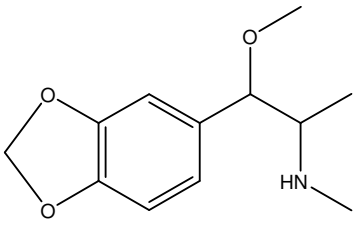
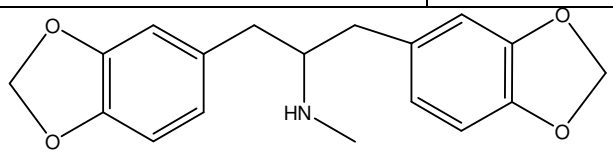
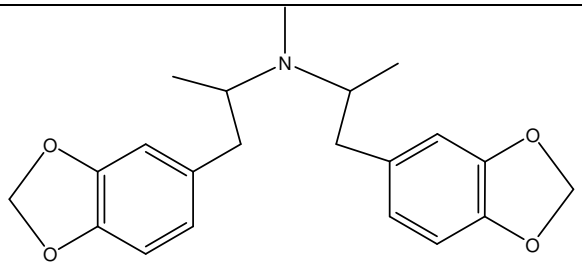
25	 1-(3,4-methylenedioxyphenyl)-2-propanone oxime	Chemical reduction of nitroisosafrole Synthesis of MDMA from piperonal and isosafrole B	(Gimeno, et al, 2002) (Świst, Zuba, et al, 2005) (Świst, et al., 2005b)
26	 N-methyl-(1,2-methylenedioxy)-4-(1-ethyl-2-aminopropyl)benzene	Unknown L, B, R1, R2, R3	(Gimeno, et al, 2002) (Świst, et al., 2005a) (Świst, et al., 2005b)
27	 1-(3,4-methylenedioxyphenyl)-1,2-propanedione	Synthesis of MDMA from piperonal R1	(Świst, Zuba, et al, 2005) (Świst, et al., 2005b)
28		Synthesis of MDMA from isosafrole L, R1, R2, R3	(Świst, Zuba, et al, 2005) (Świst, et al., 2005a) (Świst, et al., 2005b)
29	 R1		(Świst, et al., 2005b)
30	 L, B		(Świst, et al., 2005a) (Świst, et al., 2005b)

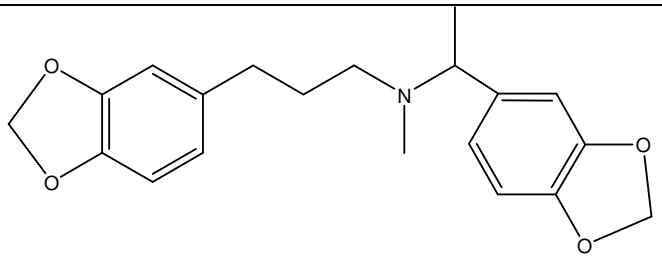
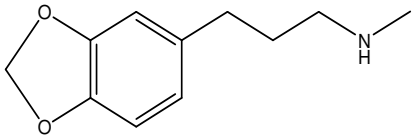
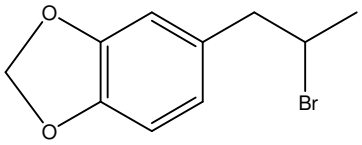
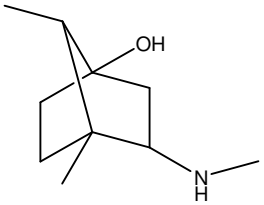
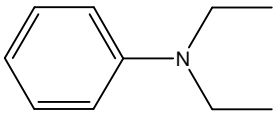
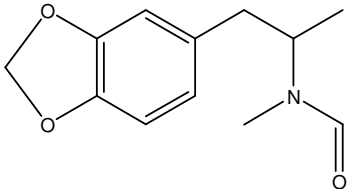
Table 1.1 continued.			
31	 B		(Świst, et al., 2005a) (Świst, et al., 2005b)
32	 1-(1,3-Benzodioxol-5-yl)-N-methyl-1-propanamine	B	(Świst, et al., 2005a) (Świst, et al., 2005b)
33		B	(Świst, et al., 2005b)
34		B	(Świst, et al., 2005b)
35	 N,N-diethyl-Benzenamine	L	(Świst, et al., 2005b)
36	 N-formyl MDMA	Synthesis of MDMA from piperonal L, R	(Świst, Zuba, et al, 2005) (Świst, et al., 2005a) (Świst, et al., 2005b)

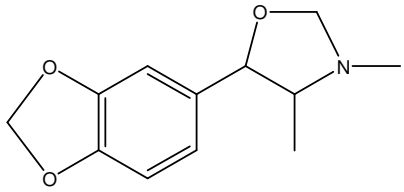
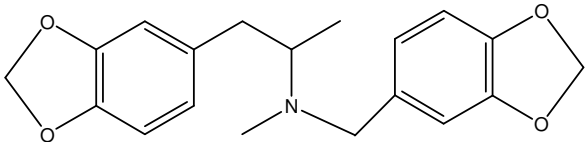
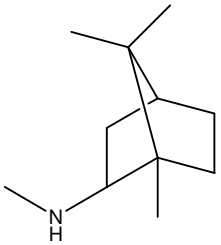
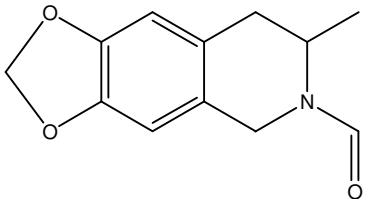
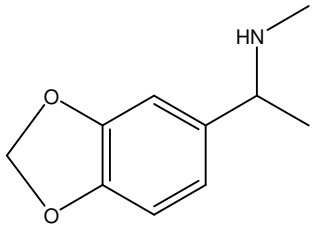
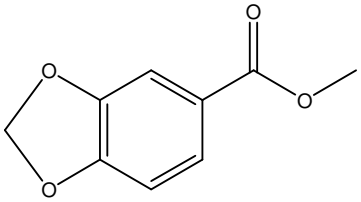
Table 1.1 continued.			
37		L, R3	(Świst, et al., 2005b)
38	 L, R, R3		(Świst, et al., 2005a) (Świst, et al., 2005b)
39	 N,1,7,7-tetramethyl-Bicyclo[2.2.1]heptan-2-amine	L, R	(Świst, et al., 2005a) (Świst, et al., 2005b)
40		L	(Świst, et al., 2005b)
41		L R2	(Świst, et al., 2005a) (Świst, et al., 2005b)
42	 1,3-Benzodioxole-5-carboxylic acid, methyl ester	R2	(Świst, et al., 2005b)

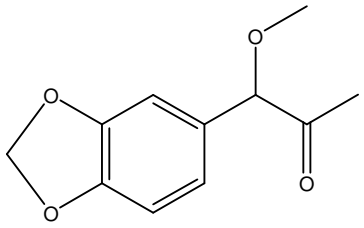
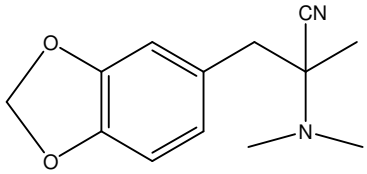
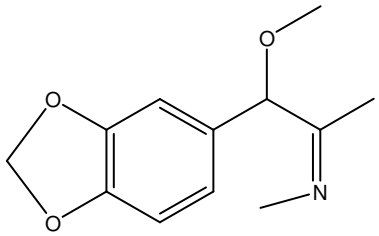
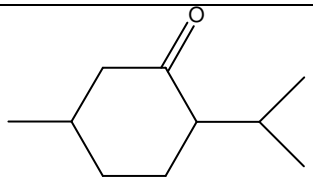
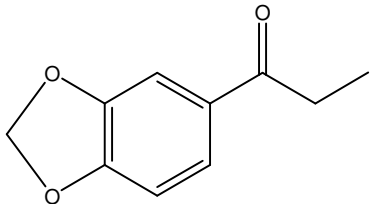
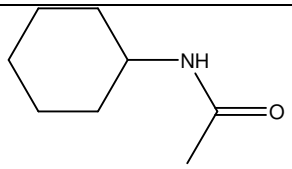
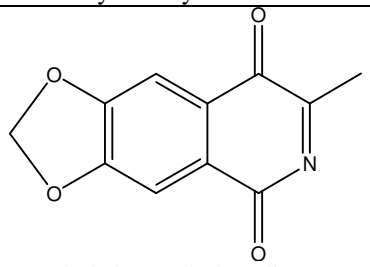
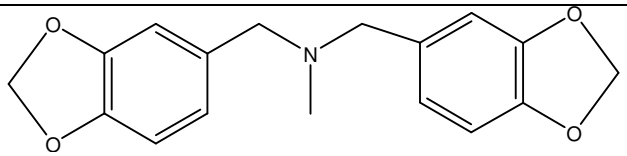
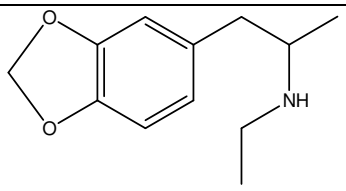
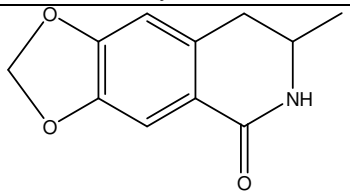
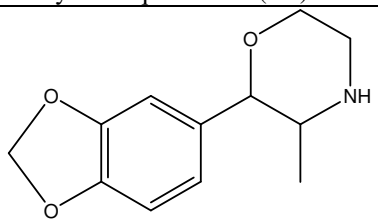
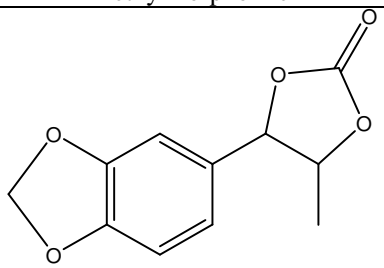
Table 1.1 continued.			
43		R2	(Świst, et al., 2005b)
44		R2	(Świst, et al., 2005b)
45		R2	(Świst, et al., 2005b)
46	 trans-5-methyl-2-(1-methylethyl)-Cyclohexanone	R2	(Świst, et al., 2005b)
47	 3,4-Methylenedioxypropiophenone	R2	(Świst, et al., 2005b)
48	 N-Cyclohexyl-acetamide	Synthesis of MDMA from piperonal R3	(Świst, Zuba, et al, 2005) (Świst, et al., 2005b)
49	 3-methyl-6,7-methylenedioxy-3,4-dihydroisoquinoline-1,4-dione	Synthesis of MDMA from piperonal R3	(Świst, Zuba, et al, 2005) (Świst, et al., 2005b)

Table 1.1 continued.			
50	 R3		(Świst, et al., 2005b)
51	 N-ethyl-MDA	Synthesis of MDMA from piperonal Synthesis of MDMA from isosafrole	(Świst, Zuba, et al, 2005)
52	 3-methyl-6,7-methylenedioxy-3,4-dihydroisoquinoline-1(2H)-one	Synthesis of MDMA from piperonal and isosafrole	(Świst, Zuba, et al, 2005)
53	 2-methyl-(6,7-methylenedioxyphenyl)-3-methylmorpholine	Synthesis of MDMA from piperonal	(Świst, Zuba, et al, 2005)
54	 4-methyl-5-(3,4-methylenedioxyphenyl)-[1,3]dioxolan-2-one	Synthesis of MDMA from isosafrole	(Świst, Zuba, et al, 2005)

There are 54 compounds detected and identified by authors in the cited studies. Some of the impurities are only mentioned at the corresponding team's works. But in the other hand there are compounds detected by both of the groups.

According to these works;

-impurity number 9, 12, 19 and 22 are the most encountered impurities in MDMA. (Świst, et al., 2005a), (Świst, et al., 2005b).

-Compound 13 found in only piperonal made samples, but unfortunately it is not detected in all samples that authors worked. (Gimeno, et al., 2005)

-Number 18, 22, 14, 44, 45 are impurities found in MDMA synthesized by reductive amination also. (Gimeno, et al, 2002), (Gimeno, et al, 2003), (Świst, Zuba, et al, 2005), (Świst, et al., 2005a), (Świst, et al., 2005b)

-No 22, 18, 14 and 53 are both found in Leuckart and reductive amination. (Świst, Zuba, et al, 2005)

-Compound 21 is reductive amination route specific impurity. (Gimeno, et al, 2005)

-26 are formed in all methods but different amounts, which leads distinction of Leuckart and safrole bromination from reductive amination. (Świst, et al., 2005a)

-Comparison done with 13 help us to differ Leuckart from safrole bromination since it is absent in safrole bromination. (Świst, et al., 2005a)

-16 presence shows that synthesis started from commercial safrole (means safrole bromination), where absence shows that synthesis started from commercial isosafrole (means Leuckart and reductive amination). (Świst, et al., 2005a)

-Compounds 48, 49, 13, 18, 14 and 53 are found MDMA samples which are synthesized by reductive amination from MDP-2-P which is also made by reduction of 1-(3,4-methylenedioxyphenyl)-2-nitropropene. (Świst, et al., 2005a)

-48 and 49 are route specific impurities (only found in reductive amination). Instead of 48 we can see (N-alkylacetamide) corresponding to amine used as catalyst. (Świst, et al., 2005a)

1.9 Aim of the Study

The aim of this study is to take a picture of chemical profiles of seized ecstasy tablets in the region İzmir, starting with detection of the synthesis route and after that trying to find a connection between them in order to help law enforcements.

Constructing a cluster collected from previous works, and replacing the impurities identified in the subject tablets will lead to a conclusion about the synthesis route that MDMA synthesized by the clandestine laboratory. Also targeting some synthesis

based impurities and comparing their ratios in the tablets will show the connection between the different batches of the tablets.

CHAPTER TWO

MATERIALS AND METHODS

2.1 Instrument and Chemicals

2.1.1 GC-MS

The studies of impurity profiling on ecstasy tablets mostly done by using GC-MS. Because of the reliable results, efficient data and definitive identification for the molecules from the corresponding mass spectrum, it has been used in this study.

In this work a Hewlett-Packard 6090 gas chromatogram with an auto sampler combined with quadropole mass filter 5973 mass spectrometer was used. Carrier gas was helium (99,999%) and gas flow set to 1 mL/min. The inlet, interface and MS temperatures are as follow: 200, 220, and 280 ^{0}C. Column is HP5-MS ((5%-Phenyl)-methylpolysiloxane, 30 m x 0,25 mm x 0,25 μm). The injection as 2 μL was made splitless by the auto sampler. The following temperature program was applied: 50 ^{0}C maintained for 2 min, then ramped at 10 ^{0}C/min up to 150 ^{0}C, maintained 5 min, and again increased to 300 ^{0}C at 10 ^{0}C/min ramp, and maintained for the final 10 min in order to clean up the column as post run. Mass spectrometer is operated in positive ion mode. Before the analysis an auto tune done every day. Full scan spectra 40 to 700 amu are obtained. The method used in this study is a modified version of the used by Świst et al. in their works. (Świst, et al., 2005a), (Świst, et al., 2005b)

2.1.2 Chemicals Used

Diethyl ether (Merck, analytical grade), sodium bicarbonate anhydrous (Merck, analytical grade), androstene (Sigma-Aldrich >98%), sodium hydroxide (Merck, analytical grade), MDMA (Lipomed) were

used throughout the studies. The water was used throughout the work was deionized by a Millipore Milli-Q system (Van Nuys, Ca 91406 USA).

2.1.3 Preparation of the solutions

pH 10 carbonate buffer is prepared from anhydrous sodium bicarbonate and sodium hydroxide. 3.75 g of $NaHCO_3$ and 3.1 g NaOH weighed and dissolved in 1000 mL deionized water separately. After the complete solution, 21.4 mL of NaOH solution added to 100 mL of carbonate solution and mixed well in order to get a pH 10 carbonate buffer.

There is no purification needed for diethyl ether, and the diethyl ether containing internal standard is simply prepared by dissolving 40 mg of androstene in the solvent.

2.2 Sample Preparation

2.2.1 Sample Collection

The 28 samples of ecstasy tablets presented in the study are representative of seizures made between January 2005 and June 2006. Ten randomly chosen tablets were sampled from each seizure of over 100 tablets. The samples stored in refrigerator at 4 ^{0}C but not frozen.

Table 2.1 Tablets collected for the study.

Number	Color	Shape	Logo	Weight (mg)	Picture
yl13	Tile color		None	302.3	

Table 2.1 continued.

yl14	Blue	Round	Heart	294.2	
yl15	Green	Round	Club	202.0	
yl16	Yellow	Round	Tulip	249.5	
yl18	White	Round	Dino	300.5	

Table 2.1 continued.

yl20	Orange	Round	Tulip	251.8	
yl21	Cream	Round	Duck	252.3	
yl22	White	Round	Bird	298.7	
yl23	White	Round	Star of David	294.0	

Table 2.1 continued.					
yl25	White	Round	Cherry	301.2	
yl26	White	Round	Kangaroo	297.8	
yl27	White	Round	Star of David	296.5	
yl28	Green	Round	Question Mark	285.3	

Table 2.1 continued.

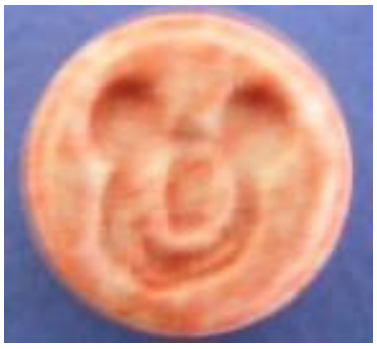
yl29	White	Round	Martin	303.5	
yl30	White	Round	Armani	199.4	
yl31	Red	Round	Mickey Mouse	202.6	
yl32	Green	Heart	none	250.7	

Table 2.1 continued.

yl33	White	Round	Cherry	299.1	
yl34	Orange	Round	Martin	299.4	
yl35	Yellow	Round	Tulip	250.3	
yl36	White	Round	Bird	297.8	

Table 2.1 continued.					
yl37	White	Round	Rolex	290.7	
yl38	Blue	Round	Women	303.2	
yl39	White	Round	Kangaroo	298.3	
yl40	White	Round	Cherry	301.2	

Table 2.1 continued.						
yl41	White	Round	Cherry	301.0		
yl42	White	Round	Cherry	299.8		
yl43	White	Round	Cherry	300.4		

2.2.2 Extraction Procedure

Among the tablets collected, two tablets for each group were finely grounded powder in mortar and an amount about 200 mg weighed. The powder was then transferred to a test tube and added 3 mL of pH 10 carbonate buffer. The solution stirred with a vortex for 15 min. After that 2 mL of diethyl ether was added the solution and stirred for another 15 min. Then the solution was waited till the layers were separated. Organic layer was collected and evaporated to dryness under a minimum nitrogen flow. Soon 1 mL of diethyl ether containing androstene as an

internal standard was putted in the test tube, and the final solution transferred to a 2 mL vial. The final extracts were injected GC-MS by using automatic liquid sampler. The procedure was repeated two times for each tablet group.

2.3 Statistical analysis

After collection of the mass spectra of tablets, the impurities are identified and their peak area ratios to internal standard were calculated. 16^{th} version of SPSS (Statistical Package for the Social Sciences) for Windows, a well known statistical analysis program, for the data analysis, was used. The ratios calculated were analyzed by hierarchical cluster analysis.

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 Tablets collected

The tablets subject to this work were collected from the seizures containing at least 100 tablets at the same shape, logo and color. Because of the uncertainty of the production processes, tablets from different seizures but same shape, logo and color are also chosen for the study. Among 28 tablets there are 6 different white colored cherry marked, 2 different white colored Star of David marked, 2 different white colored kangaroo marked, 2 different white colored bird marked and 2 different yellow colored tulip marked Tablets from the seizures.

Additionally the samples 40, 41 and 42 are from one big seizure with different packages. The reason of this selection is to test both the reproducibility of the method used and whether the samples different sourced or not. Also sample 43 has the same color, logo and mean weight with the samples 40, 41 and 42.

The diameter of the Tablets is varied from 5 to 8 mm and they are weighed as 200 to 350 mg. All of the Tablets analyzed come up with one active ingredient as a controlled substance. Seven of the Tablets contain caffeine as an adulterant and one of them contains ketamine which is unexpected but reported previously (Verweij, 1992). Also Cheng et al. said that 80% percent of the Tablets analyzed contain ketamine, but additionally they explained in that ketamine abuse is popular in Hong Kong (Cheng, Chan, M.F., Chan, T.W., Hung, 2006).

3.2 Extraction Procedure

3.2.1 Extraction Solvent

Different solvents tested in this work for the efficiency of the extraction procedure. These are chloroform, n-hexane and diethyl ether, which are used in many studies (Gimeno, et al, 2002), (Gimeno, et al, 2003), (Świst, Zuba, et al, 2005), (Świst, et al., 2005a), (Świst, et al., 2005b). The same extraction method was used for all tested extraction solvents and also extractions were performed tablets collected from a one big seizure.

The extracts collected were injected to GC-MS with the same conditions (GC-MS method, injection volume and duration before the sample introduction) and then the collected chromatograms were compared to each other. Within the tested three solvents, by diethyl ether the highest efficiency for impurities was obtained. Additionally, diethyl ether was easily handled during the extraction procedure. As a result, diethyl ether was chosen as the extraction solvent for this study.

3.2.2 Effect of pH

According to earlier works done by Gimeno et al. and Świst et al. the effect of pH on extraction procedure was investigated.(Świst, Wilamowski, Parczewski, 2005b), (Gimeno, et al, 2003). At the work of Gimeno et al. pH range from 8.4 to 12.6 was compared with respect to impurity area-internal standard area ratio. They concluded that pH 10.5-11.0 had a maximum for this ratio. However, they suggested that a buffer pH of 11.5 for extraction because of the similarity in the reproducibility of extraction with buffer pH between 10.8 and 12.0 (Gimeno, et al, 2003). On the other hand, Świst et al. use pH 10 buffer in all their studies. (Świst, Zuba, et al, 2005), (Świst, Wilamowski, Parczewski, 2005a), (Świst, Wilamowski, Parczewski, 2005b).

In this study; two buffer solutions, pH 10 and pH 11.5, were tried out for the extraction procedure with the selected solvent. Carbonate buffer pH 10 provided some improvements on the area of the impurities. As a result, buffer pH 10 was chosen for this study.

3.3 Impurities Identified

The impurities have been located in to the clusters according to their synthesis route that they are belonged (Figure 3.1). After detecting and identifying organic impurities found in MDMA tablets, using this cluster it is simple to decide synthesis route of the drug.

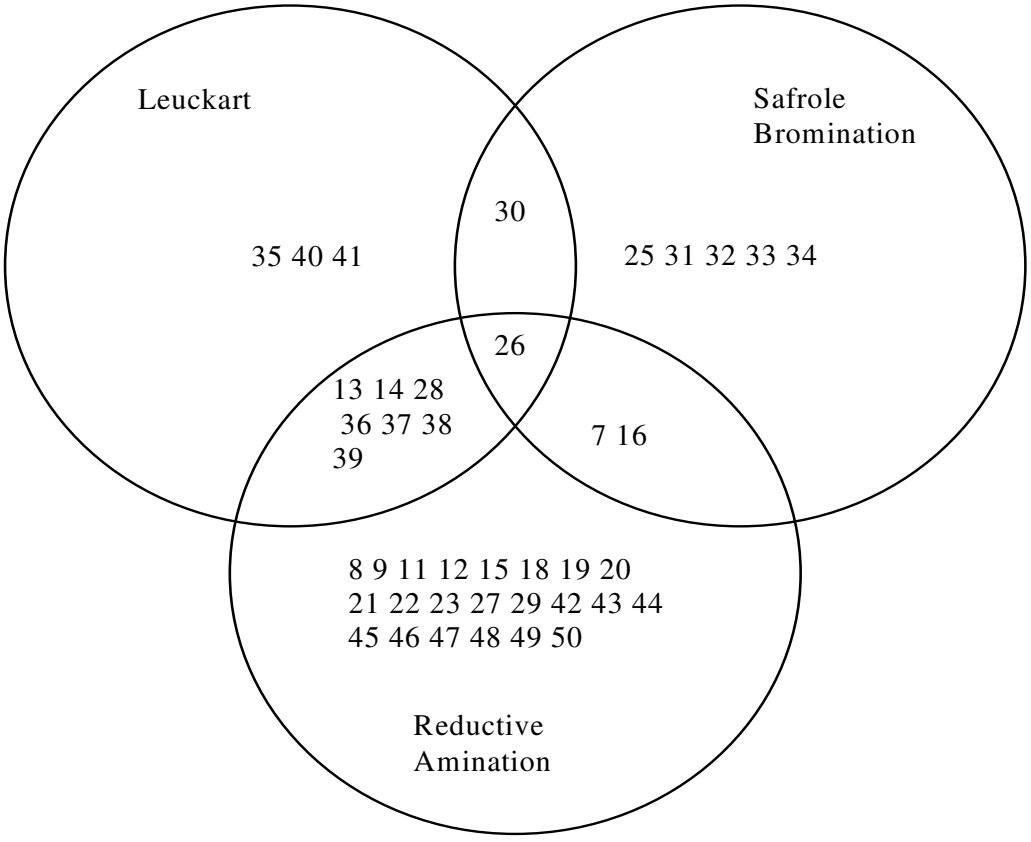


Figure 3.1 Cluster of the impurities according to their synthesis method.

Over the 28 tablets analyzed for the profiling 30 impurities were identified which were mainly sourced by the synthesis steps (Table 3.1). The others were sourced from cutting agents, adulterants and lubricants. The compounds identified in the

tablets were numbered by their retention times. They are given a number starting with “comp” in order to distinguish them that the compounds listed in table 1.1.

Table 3.1 Impurities identified in the Tablets.

No (No from table 1.1)	**Retention Time**	**Name of the peak**
Comp1 (5)	09.10	Methamphetamine
Comp2 (9)	11.27	Piperonal
Comp3	12.32	2-Carbomethoxy-8-methyl-8-azabicyclo[3.2.1]oct-2-ene
Comp4 (13)	12.37	3,4-Methylenedioxy-N-N-methylbenzylamine
Comp5	12.95	3-chloro-N,N-dimethyl-1-propanamine
Comp6 (19)	13.85	3,4-Methylenedioxyphenyl acetone
Comp7 (20)	14.11	1-(3,4-Methylenedioxyphenyl)-2-propanol
Comp8	14.50	Butyl Hydroxy Toluene
Comp9	15.34	3,4-Methylenedioxymethamphetamine
Comp10 (17)	17.20	N,N-dimethyl–3,4-methylenedioxyamphetamine
Comp11	18.06	N-methyl-N-nitroso-ethanamine
Comp12	19.46	1-((1,2-dimethyl-1-azacycloprop-2-yl)methyl)-3,4-methylenedioxybenzene
Comp13	19.56	Phenacetin
Comp14	19.81	Methyldiethanolamine
Comp15	20.30	chlorophenylpiperazine
Comp16	20.51	Tetradecanoic acid
Comp17	21.70	6-Methylthieno[2,3-b]pyridine
Comp18	22.00	Caffeine
Comp19	22.20	1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester
Comp20	22.39	Ketamine
Comp21	22.70	Naphtol
Comp22 (36)	23.08	N-Formyl-N-methyl-3,4-methylenedioxyamphetamine
Comp23	23.35	n-Hexadecanoic acid
Comp24	23.40	N-Acetyl-3,4-methylenedioxymethamphetamine
Comp25	25.52	Octadecanoic acid
Comp26	23.79	3,7-dihydro-1,3-dimethyl-1H-Purine-2,6-dione
Comp27	26.43	Cocaine
Comp28	29.99	Androst-4-ene-3,17-dione
Comp29	30.93	p-Phenylenediacetone dioxime
Comp30	31.82	2',6'-Dimethyl-4'-propoxyacetophenone

The GC chromatograms and mass spectrum of some ecstasy tablet samples were given in Figure 3.2-3.4 and 3.6-3.8. Among the 30 compounds found in ecstasy tablets (Table 3.2), 13 of them were considered as impurities that were comp1-7, comp10-12, comp14, comp22 and comp24. Fifteen of those, comp8, comp13, comp15-21, comp23, comp25-27, comp29 and comp30, were found as contaminations due to cutting agents, adulterants and lubricants. Additionally, comp28 was seen as an internal standard.

The identification of the compounds was done by MS. Mass spectrum library provided by the instrument was used. But when it is not sufficient, mass spectrum of the peaks were compared with the mass spectra of the cited works in order to identify impurities (Gimeno, et al, 2002), (Gimeno, et al, 2005), (Świst, Zuba, et al, 2005), (Świst, et al, 2005a)

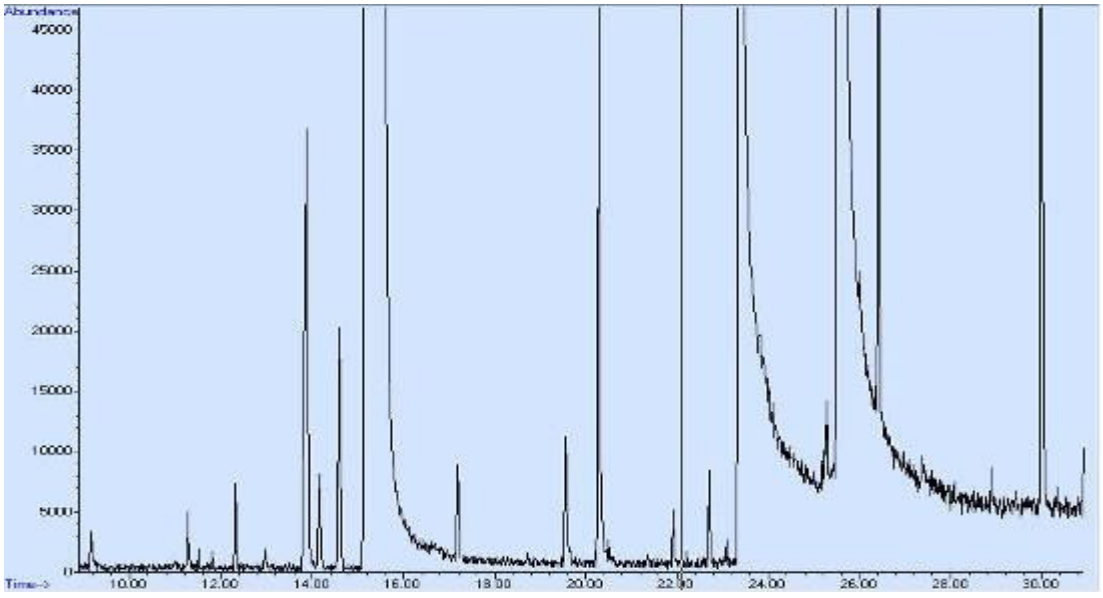


Figure 3.2 Chromatogram obtained for the sample yl28

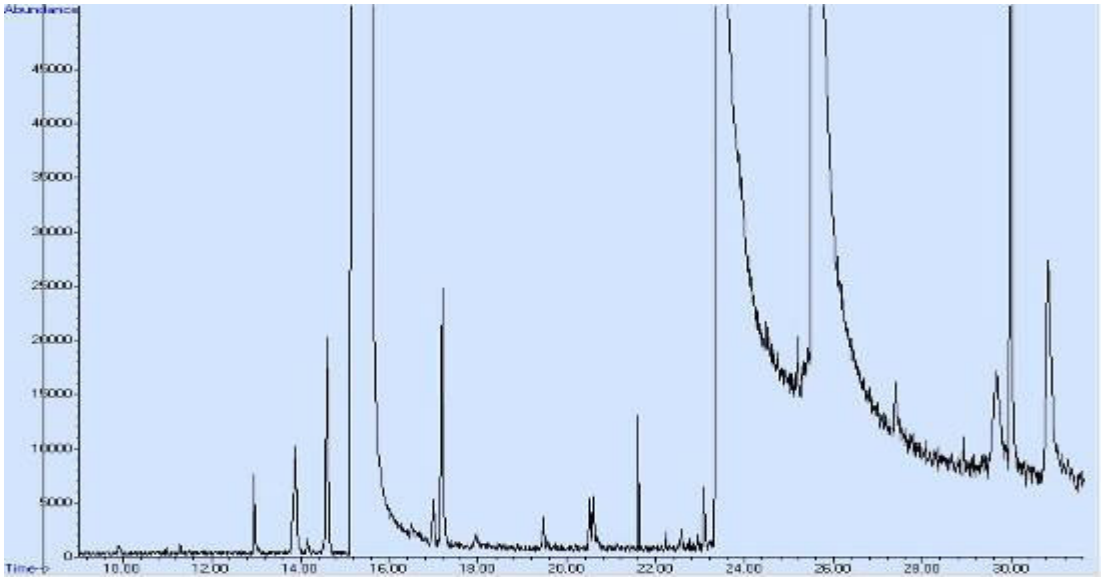


Figure 3.3 Chromatogram obtained for the sample yl32

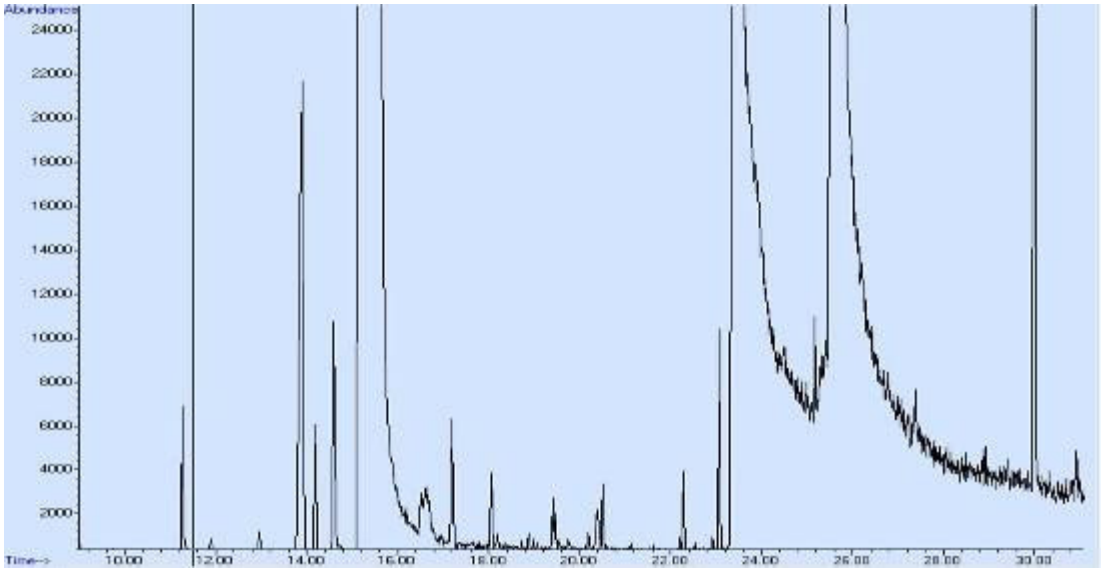


Figure 3.4 Chromatogram obtained for the sample yl36

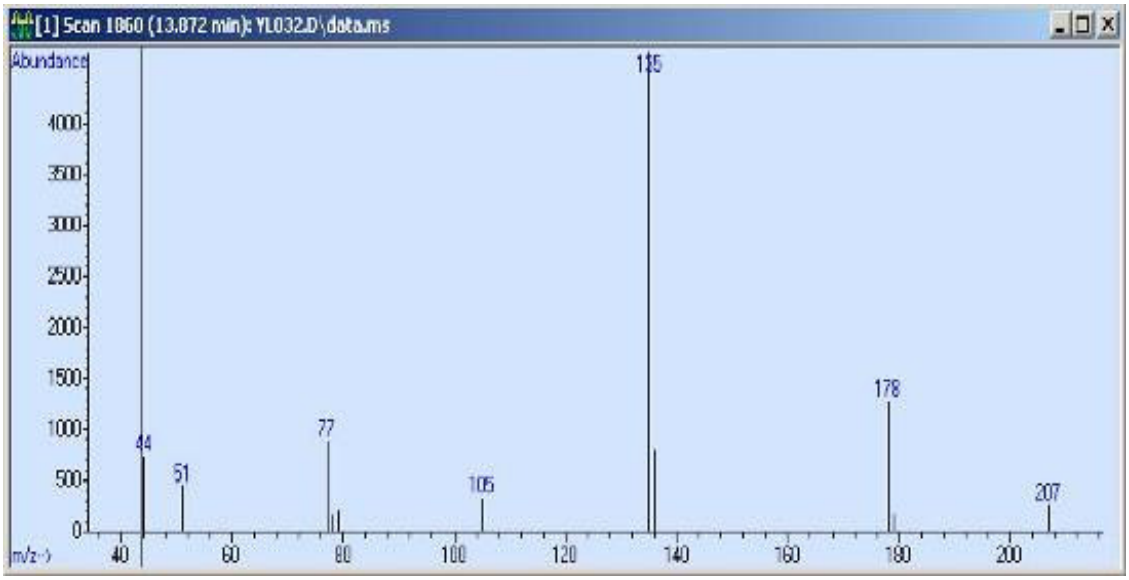


Figure 3.5 Mass Spectrum of comp6 (3, 4-Methylenedioxyphenyl acetone)

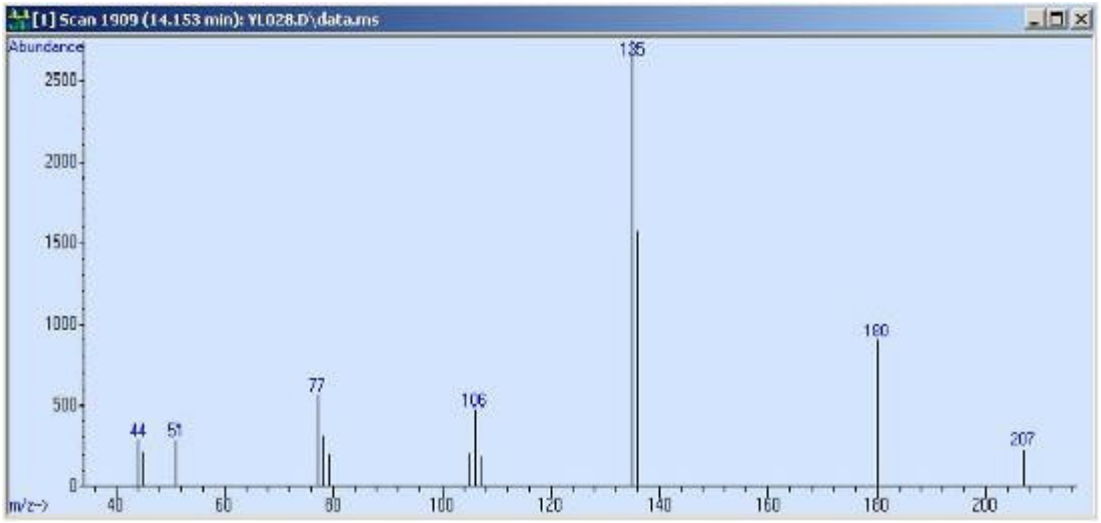


Figure 3.6 Mass spectrum of comp7 (1-(3, 4-Methylenedioxyphenyl)-2-propanol)

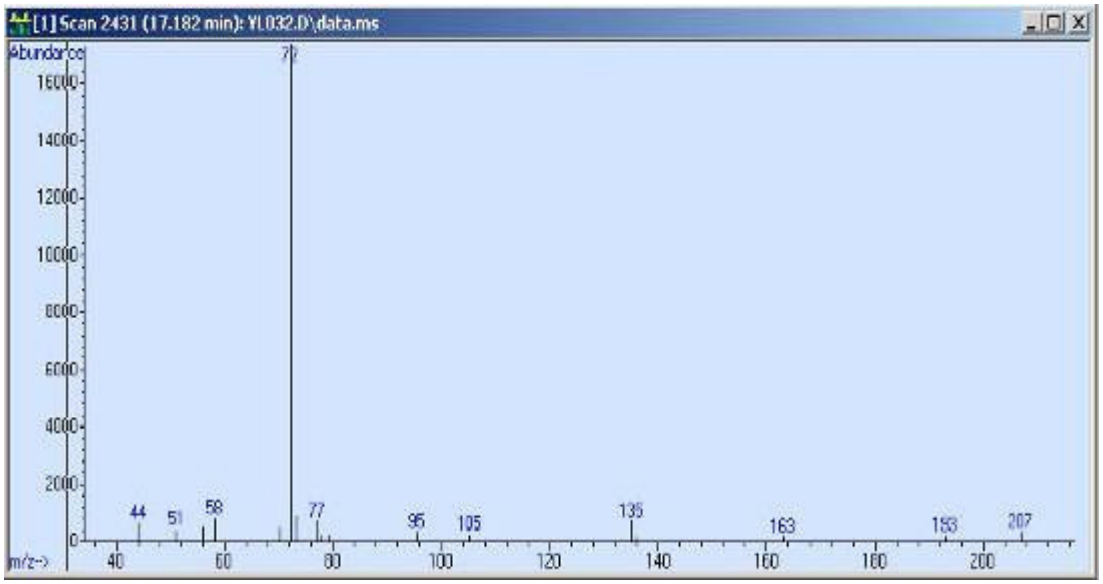


Figure 3.7 Mass Spectrum of comp26 (N-Acetyl-MDMA)

Table 3.2 Impurities found in the studied seizured tablets. (Numbers corresponding to table 3.1)

Sample No	Impurity	Contamination
yl13	6, 7, 24	8, 23, 26
yl14	4, 5, 24	8, 26
yl15	2, 6, 7, 24	8, 18, 26
yl16	6, 7, 10, 24	8, 26
yl18	6, 11, 24, 25	8, 26
yl20	1, 2, 4, 6, 10, 14, 22, 24	8, 15, 18, 25, 26, 29, 30
yl21	2, 6, 7, 24	8, 26, 29, 30
yl22	2, 6, 7, 22, 24	8, 16, 17, 18, 25, 26, 27, 29, 30
yl23	2, 6, 7, 22, 24,	8, 16, 17, 18, 25, 26, 29, 30
yl25	2, 6, 7, 10, 24	8, 18, 26
yl26	6, 7, 22, 24	8, 16, 26
yl27	6, 7, 22, 24	8, 16, 26
yl28	3, 6, 7, 10, 15, 22	8, 13, 18, 21, 26, 27
yl29	5, 6, 7, 10, 22, 24	8, 26
yl30	5, 6, 22, 24	8, 26
yl31	2, 6, 7, 10, 12, 22, 24	8, 16, 19, 26, 30

Table 3.2 continued		
yl32	6, 7, 10, 12, 22, 24	8, 16, 19, 26
yl33	6, 7, 10, 22, 24	8, 16, 19, 26
yl34	6, 7, 10, 11, 12, 22, 24	8, 19, 26, 29
yl35	6, 7, 10, 22, 24	8, 20, 26, 29
yl36	2, 5, 6, 7, 10, 11, 12, 22, 24	8, 16, 26
yl37	2, 5, 6, 7, 10, 11, 12, 22, 24	8, 16, 26
yl38	2, 5, 6, 7, 10, 11, 22, 24	8, 26
yl39	6, 10, 11, 12, 22, 24	8, 16, 18, 26
yl40	2, 6, 10, 11, 12, 22, 24	8, 16, 26
yl41	2, 6, 10, 11, 12, 22, 24	8, 16, 26
yl42	2, 6, 10, 11, 12, 22, 24	8, 16, 26
yl43	2, 6, 10, 11, 12, 22, 24	8, 16, 26

3.4 Determination of the Synthetic Route

As building a cluster of the impurities collected from cited studies at Figure 3.1, when the identified impurities are placed in this cluster one can determine synthetic route of the MDMA analyzed.

A comparison was done between the impurities listed at Table 3.1 with compounds listed at Table 1.1. After that the numbers replaced for the tablets and finally comparing the cluster of the tablets with the cluster at the Figure 3.1 gave the synthesis route of MDMA.

According to our analysis, reductive amination route was used in the synthesis of MDMA in twenty-three of twenty-eight tablets investigated. Actually decision of synthetic route for the remaining five MDMA samples could not be done. As a result it could be clearly said that MDMA samples analyzed for the chemical profiling in this work were synthesized according to reductive amination route, which is mentioned as the most popular route that clandestine laboratories using.

3.5 Statistical analysis

After the decision about the synthetic route, peak area ratios according to the internal standard were analyzed by SPSS using hierarchical cluster analysis (HCA). The impurities found in the analysis were the ones coming from the production step. Other kind of impurities could be useful for route determination but there is a chance to mislead because of the lack of standardization. As a result comp4, comp5, comp6, comp7, comp10, comp22 and comp24 found as impurities were used in the cluster analysis. The dendogram obtained by HCA was shown at Figure 3.9.

The percent content of MDMA in the tablets and the weight of the powdered sample are not taken account. Because the study of Cheng et al. shows that even if the percentage of MDMA changes 2 times, it will not effect categorization in hierarchical cluster analysis. (Cheng, et al., 2006)

3.6 Comparison of impurity profiles

As it is seen from Figure 3.8 our ecstasy tablet samples were grouped in two main clusters. These were MDMA samples which were synthesized by reductive amination, where it was decided at the section 3.4.

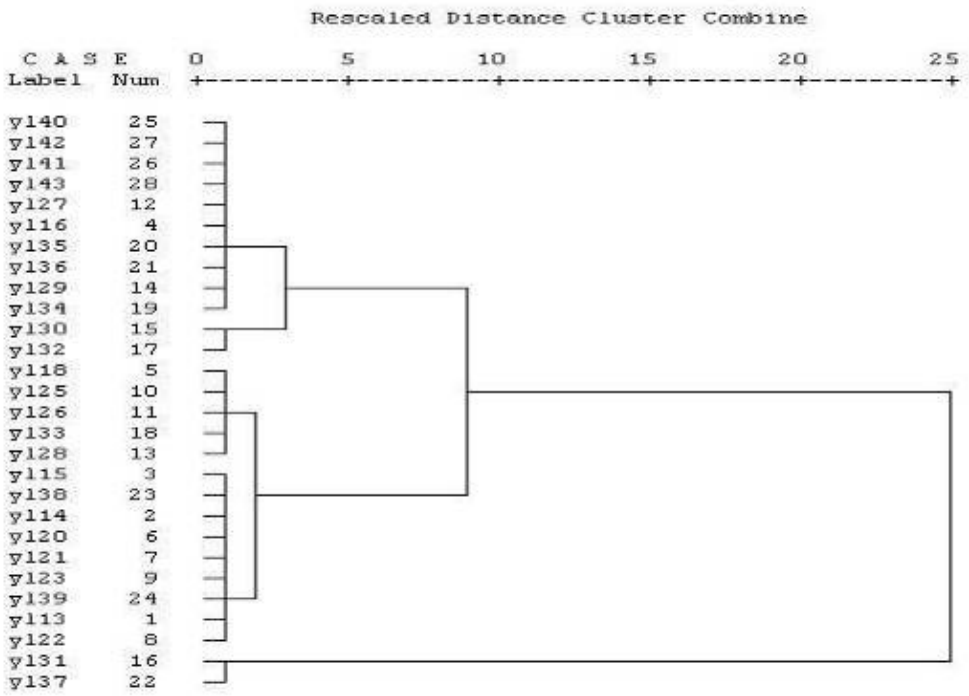


Figure 3.8 Dendogram obtained using Average Linkage Between Groups

On the other hand, the samples 13, 14, 18, 26 and 27 also seems to be synthesized by reductive amination, where it couldn't be decided the synthesis route previously. The reason for that is most likely not selecting all the impurities related to synthesis. But the peak purity and availability of impurities in samples should be taken account while calculating peak area ratios and HCA.

Looking the first group at the dendogram, it is seen that sample 40, 41 and 42 are closely related with each other and so it is confirmed that the method used is working. Also these three samples were closely related with sample 43 and 32 which were white colored and cherry marked (Figure 3.9). These three seizures occurred in one month period. As a result it might be concluded that these tablets were smuggled by one drug syndicate in different batches. However sample 23, which was also white colored and cherry marked, seized one year after these three groups, was different from them as there were main differences in their chromatograms.

Samples 16 and 34 (Figure 3.10), yellow tablets with tulip logo, seized in a short time period could be considered as to be from same source, where they were in the

same group. Additionally samples 31 and 37, grey colored with Versace logo and green heart shaped tablets seems to be prepared with much more different methods. Even if there are some differences in their chemical profiles, the similarities are much more than that.

Samples 25 and 26 were both with colored pills with a different logo, were seized together. They have seemed to be originated from the same source. However samples 28 and 33 (Figure 3.11) which have same logo, martin, with one orange and the other white, were seized long after the samples 25 and 26. It is possible for the tablets with a martin logo, but relation with the white tablets could be only explained by suggesting them as old stock, which is unexpected.

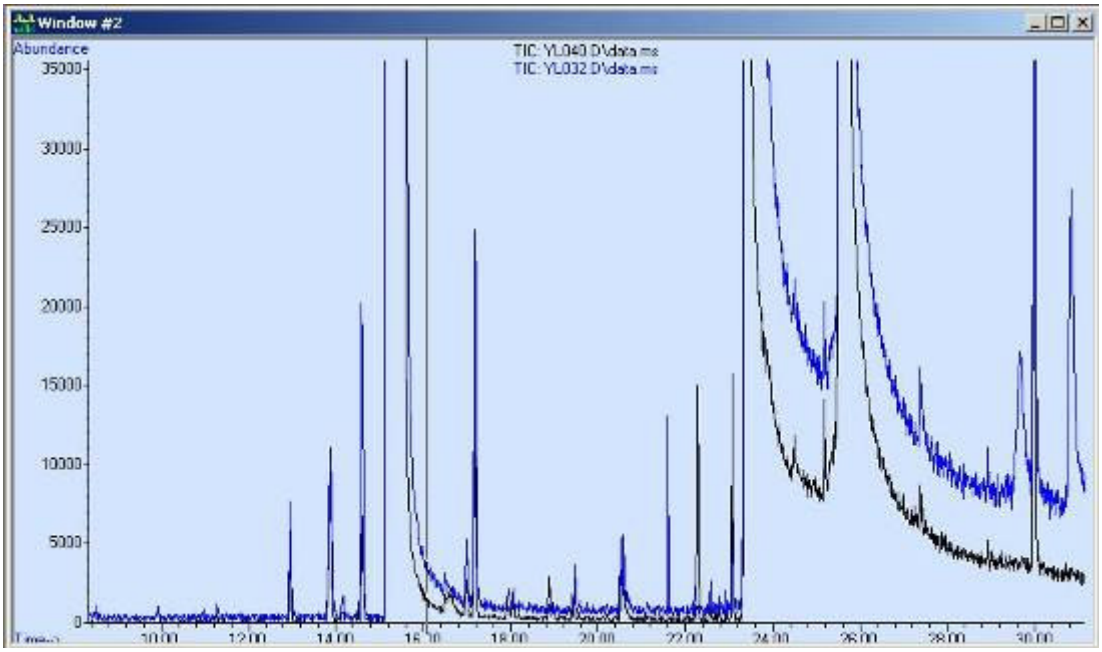


Figure 3.9 Chromatograms of samples 43 and 32.

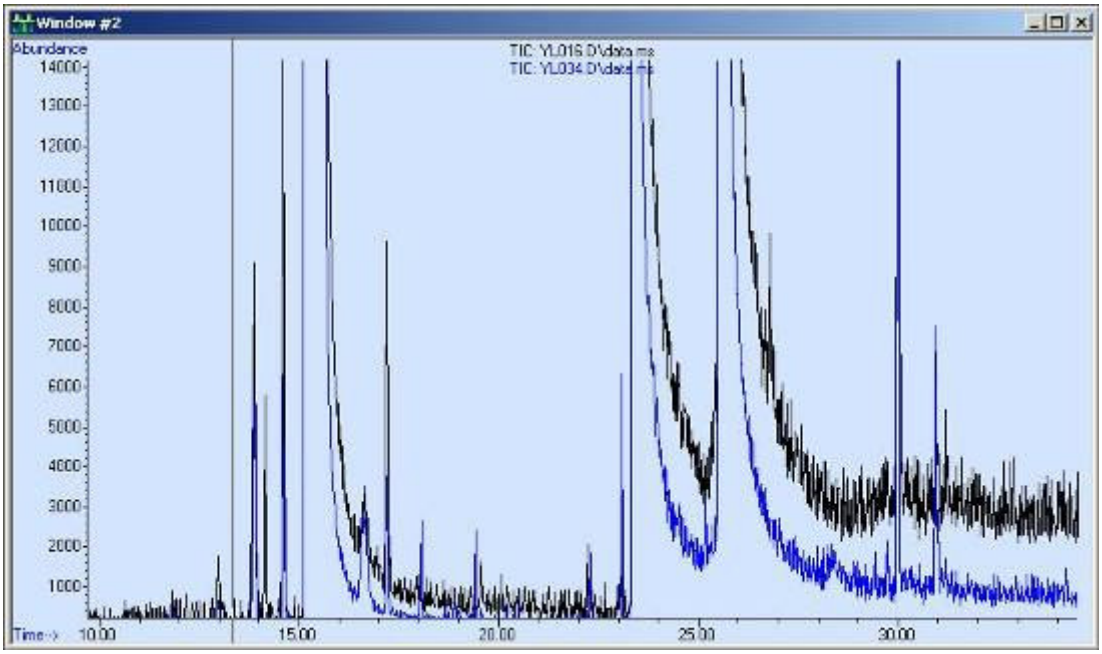


Figure 3.10 Chromatograms of samples 16 and 34.

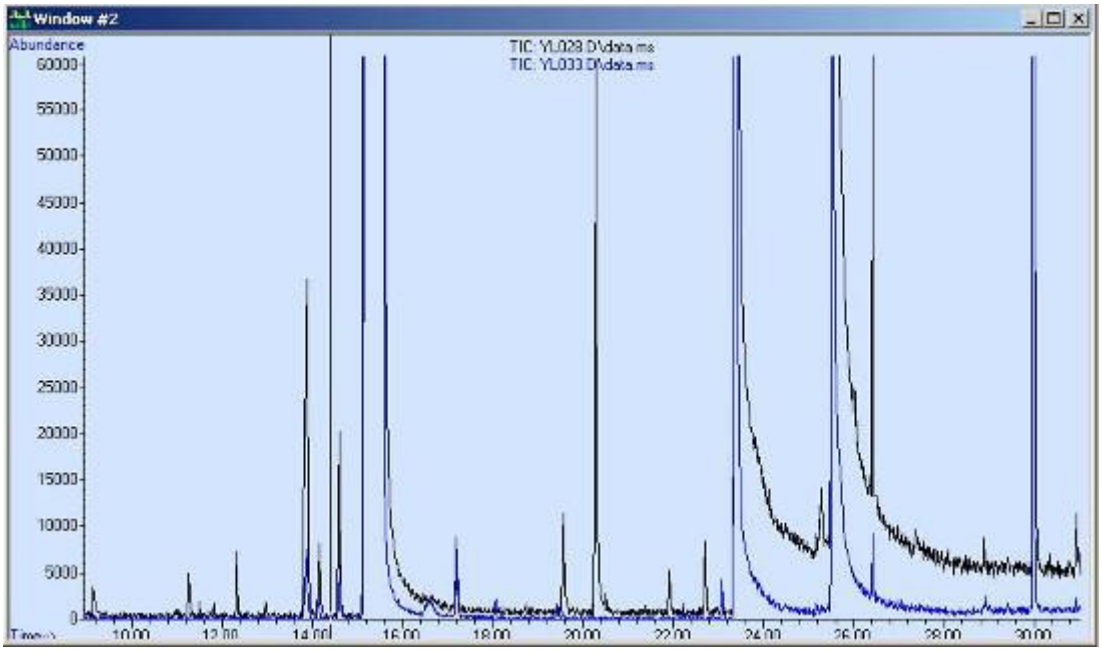


Figure 3.11 Chromatograms of samples 28 and 33.

The analyzed samples lead us two different groups of MDMA type, which can be caused by main source drug. As a matter of fact it is well known by law agencies that ecstasy tablets are smuggled as a return of the heroin seizures passed from Turkey. The results are also consequent with that, where the source of the MDMA seizures is mainly European countries as mentioned in UNDOC World drug report 2007.

CHAPTER FOUR

CONCLUSION

Impurity profiles of ecstasy tablets seized in between January 2005 and June 2006 showed that the major MDMA synthesis method was reductive amination. It is possible to say that it is plausible to correlate unrelated seizures showing off any similarities in physical appearance. As contrary, also one can distinguish seizures that have similar in physical appearance from each other. The information obtained with chemical profiling would help law enforcement agencies in the operations, and make easier to trace the source of MDMA.

In this study, it is proved that for another time that reductive amination is the most popular synthesis method for MDMA. Approximately 80 % of tablets analyzed come up with this results by using cluster formed as collecting data from previous works. This study can be useful for the proceeding works which will try to correlate MDMA containing tablets.

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