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Psychotropic Substances of the Amfetamine Type Used by Drug Addicts in Bulgaria

Synthesis and Medicinal Forms

Analytical Methods of Identification

by Dafinka Dimova and Nenko Dinkov
Research Institute of Forensic Science and Criminology
Sofia, Bulgaria

LABORATORY OPERATIONS
RESEARCH AND SCIENTIFIC SECTION
TECHNICAL SERVICES BRANCH

Psychotropic Substances of the Amfetamine Type Used by Drug Addicts in Bulgaria

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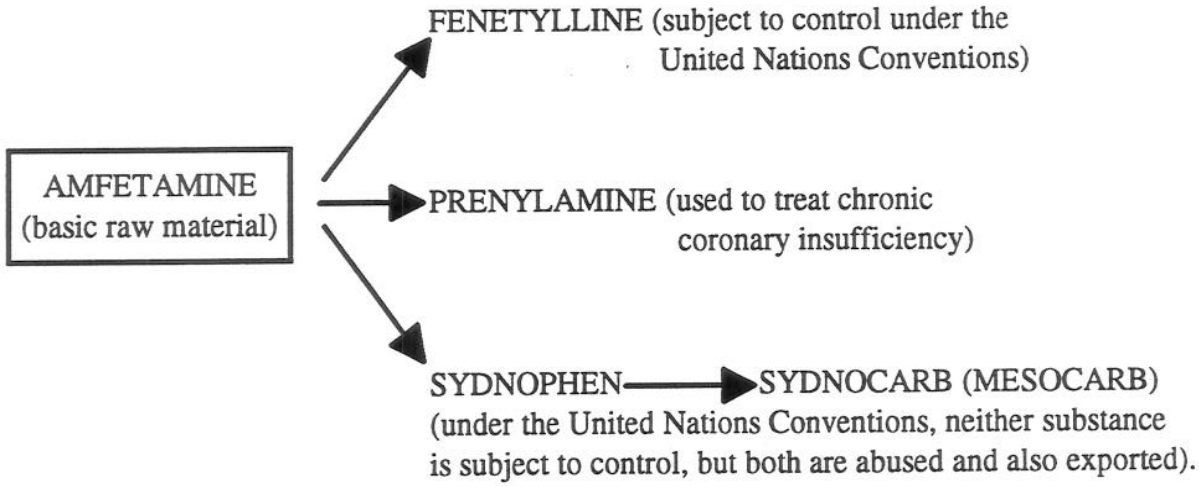
On the basis of the expert assessments carried out at the Research Institute for Forensic Sciences and Criminology in Sofia, it is possible to point to a number of trends as regards the use and spread of medicines among drug addicts in recent years. Some of these trends are in line with those observed throughout the world, whereas others are region-specific and depend on local sources of procurement including in Bulgaria the pharmaceutical industry. The first reports of the abuse of amfetamine-type substances (powder samples, "Phenamine" tablets, "Acetylsalicylic acid - Amfetamine" tablets, and the latest medicinal form "Capsasal-CO" - all containing amfetamine) date back to the beginning of the 1970s.

Amfetamine is also used as the basic raw material in the synthesis of other medicines, as illustrated in the following simplified diagram (see also figures 1 and 2):



Sydnocarb [*1*] is a psychotropic substance whose effect, in comparison to amfetamine, is slower to occur, but is longer lasting. Sydnophen [*1*] has, in comparison with sydnocarb, less of a stimulating effect on the central nervous system, but also works as an antidepressant.

In the course of 27 expert analyses carried out between 1990 and 1992 involving a total of over 100 samples (powders, individual tablets of unknown origin, tablets in blisters) an optimal method for the criminalistic identification of psychotropic substances (amfetamine, sydnophen, sydnocarb and fenetylline) was developed, taking into account the methods of analysis recommended in "Clarke's Isolation and Identification of Drugs" [2] and in "Recommended Methods for Testing Amphetamine and Methamphetamine" [3].

The comprehensive investigation makes it possible to determine:
- the nature of the active substance;
- the content of the active substance;
- whether the medicinal form corresponds to the description on the packing;
- the nature of the diluents (fillers).

The analysis begins with the microscopic investigation, followed by infrared spectroscopy and thin-layer chromatography, which are carried out simultaneously for the purpose of rapidly identifying the substance, gas chromatography and gas chromatography/mass spectrometry. The active substance can also be quantitated by the means of ultraviolet spectroscopy. When sufficient sample quantities are available, it is also advisable to carry out quality tests (determination of solubility, ion composition, sugar, starch, etc.).

Infrared (IR) Spectroscopy:

The potassium bromide disk technique was used.

Apparatus: PU 9800 FTIR Spectrometer
Sample preparation: 0.5mg of the samples were mixed with 100mg of potassium bromide and pressed to a disk of 13mm diameter.

Infrared spectra of sydnophen (as nitrate), sydnocarb, "Captagon" (Bulgaria) and "Captacola" appear as figures 3,4,5 and 6.

Thin-Layer Chromatography (TLC):

Plates: Glass plates (Merck), precoated with silica gel 60 F254, 20x20cm, layer thickness: 0.25mm
Developing solvents: System A: Methanol - conc. ammonia 100 : 1.5
System B: Chloroform - methanol 9 : 1

Preparation of sample solutions: The tablets are triturated to a fine powder. 50mg of the pulverized sample are suspended in 0.5ml of distilled water, alkalinized with ammonia to pH 10, transferred into a separatory funnel and extracted with 1ml of chloroform shaking intensively for one minute. The chloroform layer is separated and concentrated under vacuum to 100-150μl.
The alkalinization/extraction process is not necessary if it had been determined in the investigations preceding the chromatographic analyses that the substances are already present as bases.

Visualization methods: a) UV light at 254nm
b) Acidified potassium iodoplatinate reagent
c) Dragendorff's reagent

The latter does not detect amfetamine.

Rf-Values:		
Substance	**System A**	**System B**
Amfetamine	0.40	0.25
Sydnophen	0.85	0.25
Sydnocarb	0.90	0.90
Fenetylline	0.85	0.80

Gas Chromatography (GC) and Mass Spectrometry (MS):

GC:

Operating conditions:

Apparatus: Hewlett-Packard 5840A with flame ionization detector
Column: Glass, 1.8m x 2mm i.d., packed with 3% OV-17 on Chromosorb W-HP 100-120
Column Temperature Programme: from 100°C to 270°C at 5°C/min.
Injector/Detector Temperature: 280°C
Carrier gas: Helium, flow rate: 32ml/min.

Preparation of sample solutions: see TLC

A gas chromatogram of a mixture of amfetamine, ephedrine, phenmetrazine, sydnophen and fenetylline appears as figure 7.

GC/MS:

Apparatus: a) Hewlett Packard 5985B, data station Hewlett Packard 1000E
b) Shimadzu QP 5000
Preparation of sample solutions: see TLC

The chromatographic fractions separated under the aforementioned conditions are fed across an interface at 270°C to a quadrupole mass spectrometer with an electron ionization of 70eV and an ion source temperature of 200°C.

Direct MS Analysis:

Temperature of the ion source: 200°C
Electron ionization at 70eV

The samples are introduced to the source by means of a sample holder.

The results are indicated in the following table:

Substance	Gas chromatography		Molecular weight	Mass Spectrum (Major Peaks)
	$t_{Rmin.}$ *	$t_R \pm \frac{t \times \sigma}{\sqrt{n}}$ **		
Phenylisocyanate (from sydnocarb)	1.36	1.36 ± 0.02	119	119;91;64;120; 65;92;62;90
Amfetamine	2.80	2.80 ± 0.04	135	44;91;65;89; 120;92;115;63
Sydnophen	11.31	11.31 ± 0.04	203	91;173;65;92; 118;89;67;81
Fenetylline	27.56	27.56 ± 0.05	341	250;70;207;91; 251;119;148;56

* $t_{Rmin.}$ = retention time, calculated for n=7
n = number of analysis

** t_R = retention time
t = 2.45 for n=7 at P=95%
P = confidence level
n = number of analysis
σ = standard deviation

In the mass spectrum of sydnocarb obtained through direct analysis the main peaks occur at m/e 91, corresponding to the tropylium ion, $C_7H_7^{(+)}$, and at m/e 119, corresponding to the phenylisocyanate ion, $C_7H_5NO^{(+)}$. Sydnocarb decomposes, during the GC/MS analysis, into phenylisocyanate and sydnophen. The GC/MS and direct MS analysis of sydnophen yield similar spectra with an inadequate number of diagnostic masses, which can be explained by the decomposition of this substance at high temperatures.

Mass spectra of sydnocarb, sydnophen, "Captagon" and "Captacola" appear as figures 8-16.

On the basis of the aforementioned 27 expert analyses carried out between 1990 and 1992 involving a total of over 100 samples and using the analytical methodology developed, it can be concluded that medicinal forms of these amfetamine type drugs are often offered for sale to drug addicts whose actual active components are not as labelled. There are "Acetylsalicylic acid - Amphetemine"[1] tablets that contain sydnocarb instead of sydnophen and frequently, sydnophen instead of sydnocarb can be shown to be present in "Captacola" tablets, which is a trade name for the combination of sydnocarb with theophylline. Sydnocarb in combination with lactose is available under the name "Captagon".The combination of sydnocarb with paracetamol and caffeine represents an additional medicinal form. Sydnophen and sydnocarb are usually contained in an amount of 10mg (rarely more than 10mg but up to 18mg) per tablet.

In one third to one half of the seized preparations labelled "Captagon", the active component was proven to be sydnocarb or sydnophen, caffeine or quinine, but not fenetylline, - usually mixed with sugar of glucose as diluents. Especially in 1993 thousands of tablets of "Captagon" were seized containing quinine instead of fenetylline as the active component.

References:

[*1*] Maschkovskij, M.. Medicaments, Vol.1. Medizina Publishers, Moscow, Russia, 1985. p.113-114.

[*2*] Clarke's Isolation and Identification of Drugs. Moffat, A.C., Editor. The Pharmaceutical Press, London, U.K., 1986. p.613-614.

[*3*] Recommended Methods for Testing Amphetamine and Methamphetamine (Manual for Use by National Narcotics Laboratories), United Nations Manual, ST/NAR/9, 1987.

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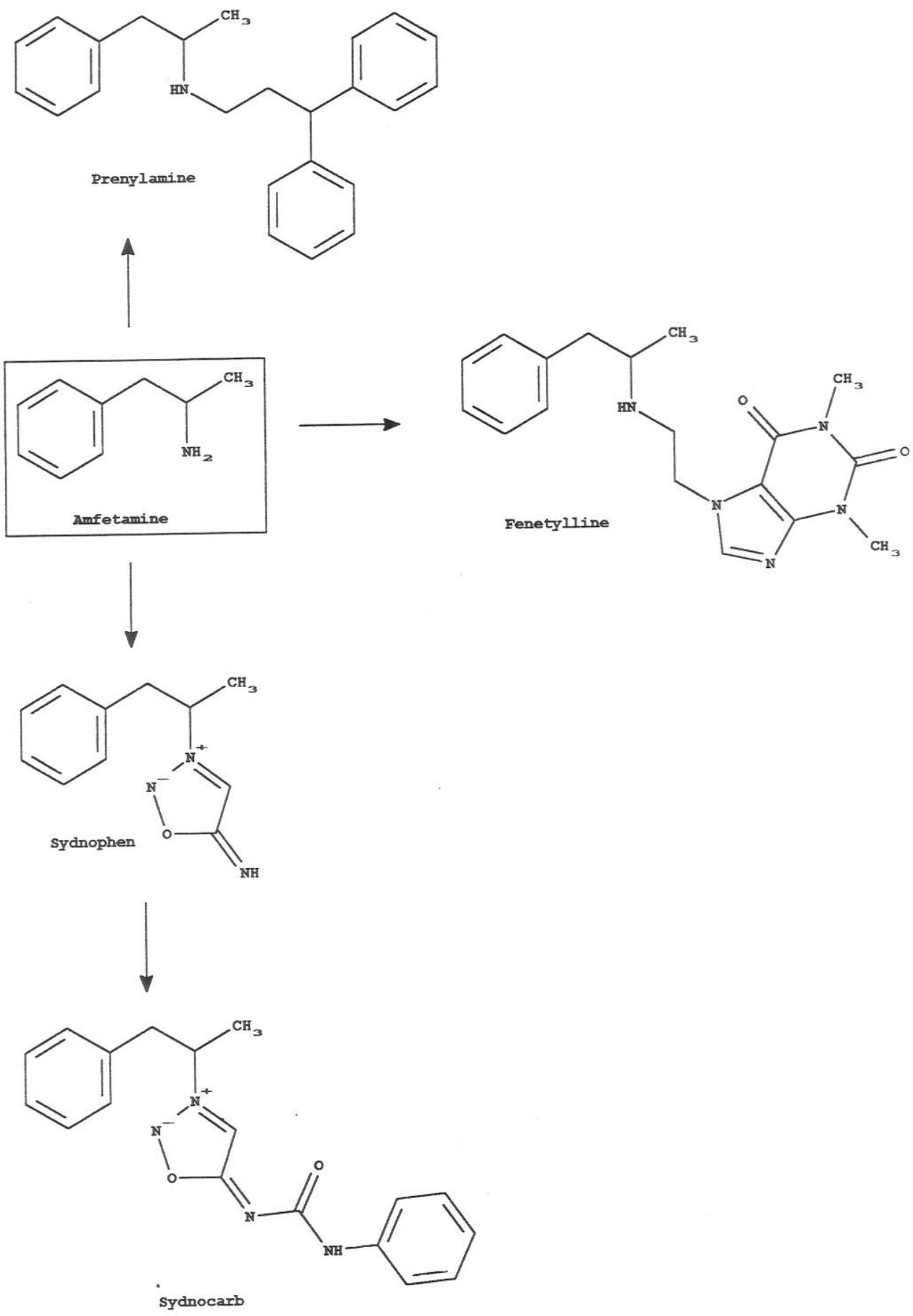
[1] Preparations presumed "Acetylsalicylic acid - Amphetemine" contained sydnophen or sydnocarb and those spelled with "a" contained amfetamine.

Figure 1


Prenylamine
Amfetamine
Fenetylline
Sydnophen
Sydnocarb

Synthesis of Sydnophen and Sydnocarb

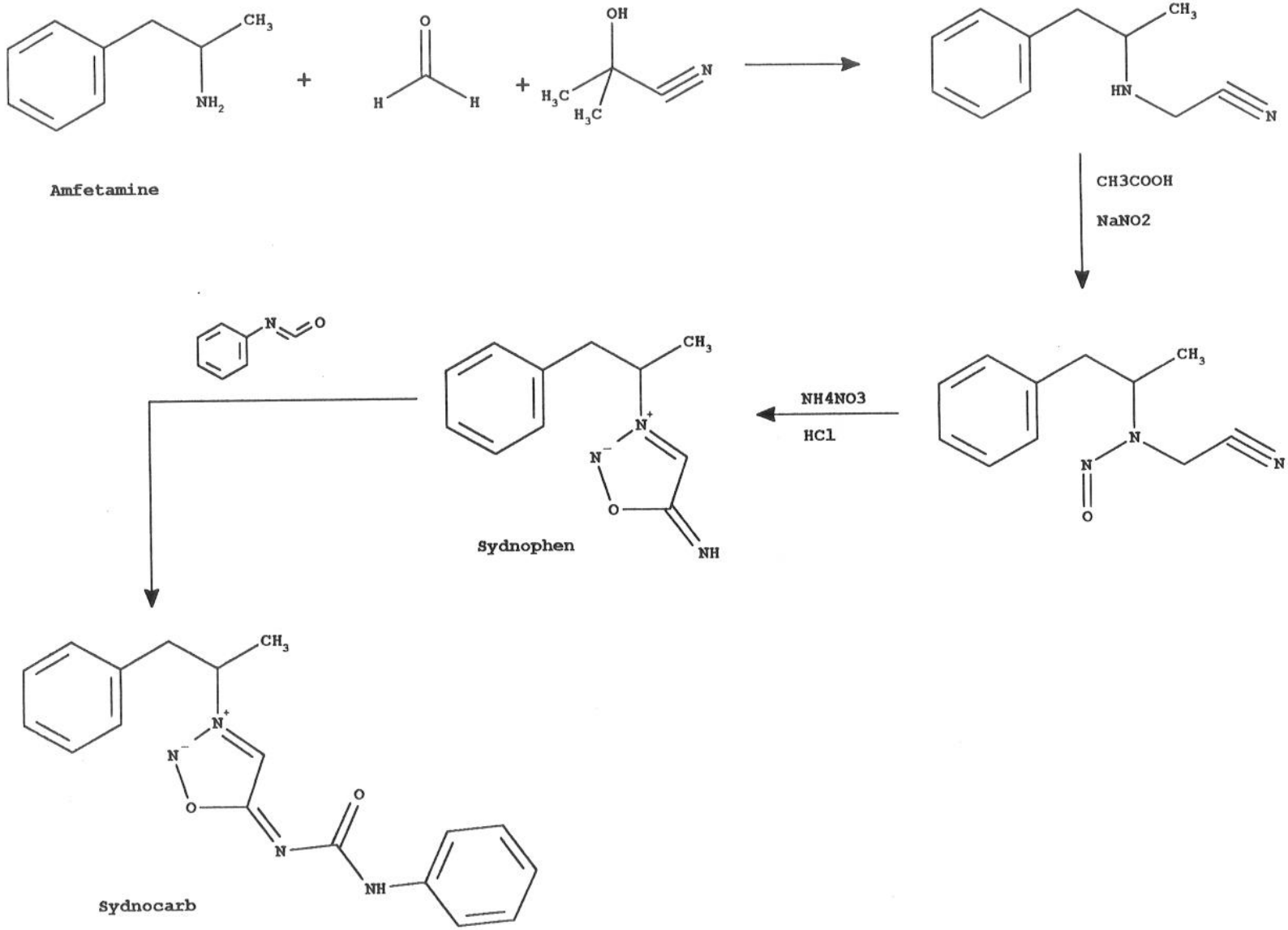
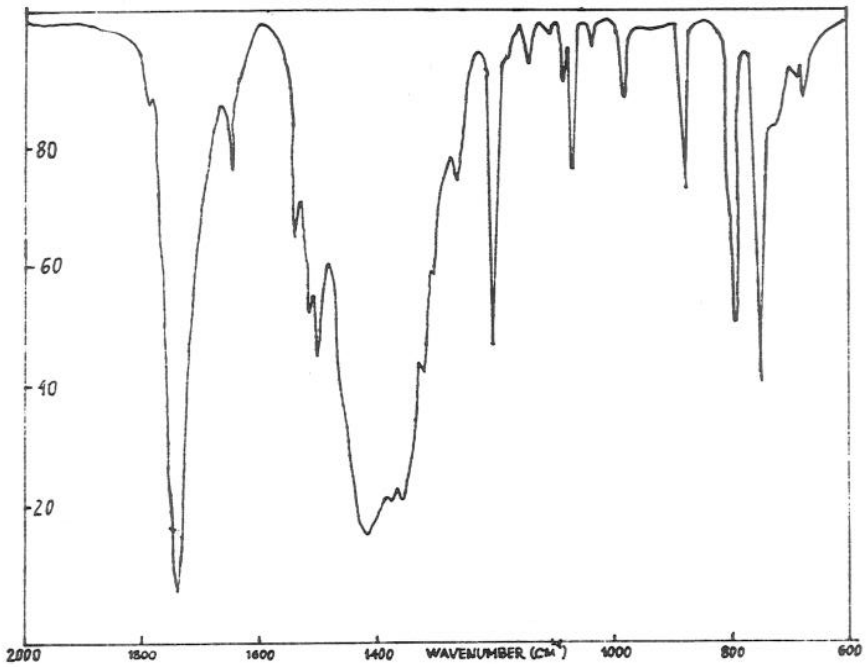


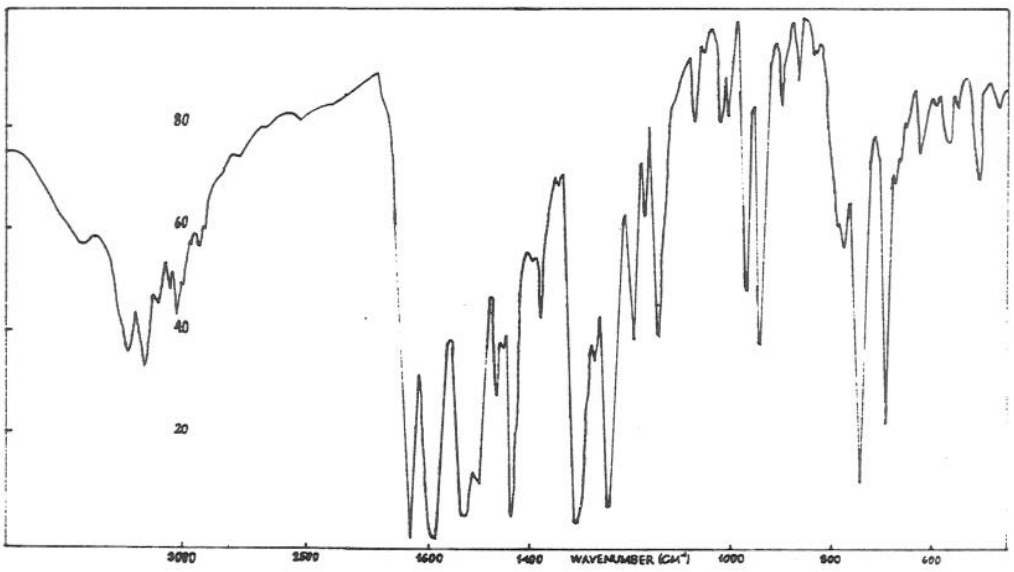
Figure 2

Figure 3



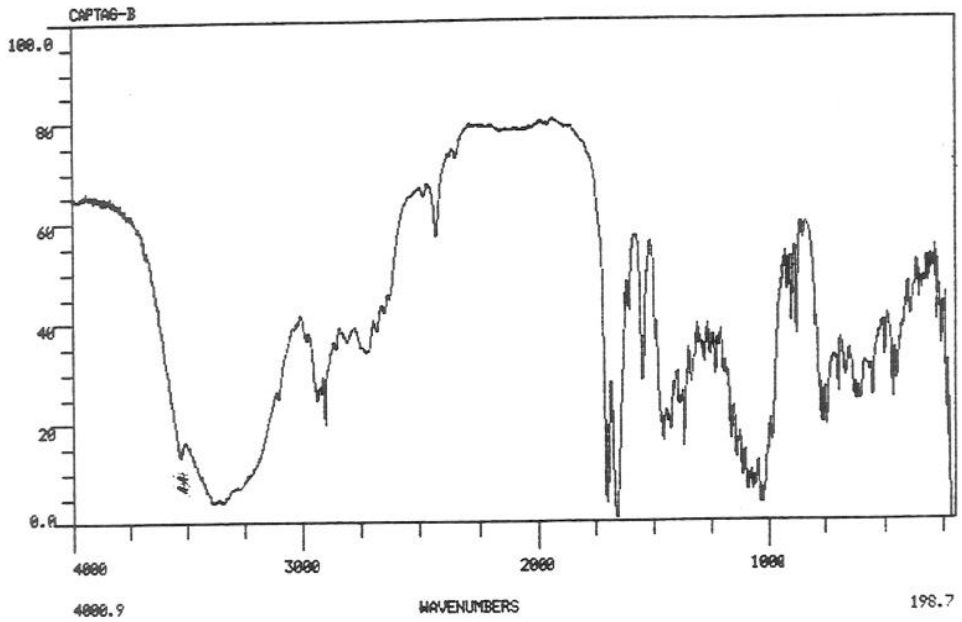
IR spectrum of sydnophen nitrate

Figure 4



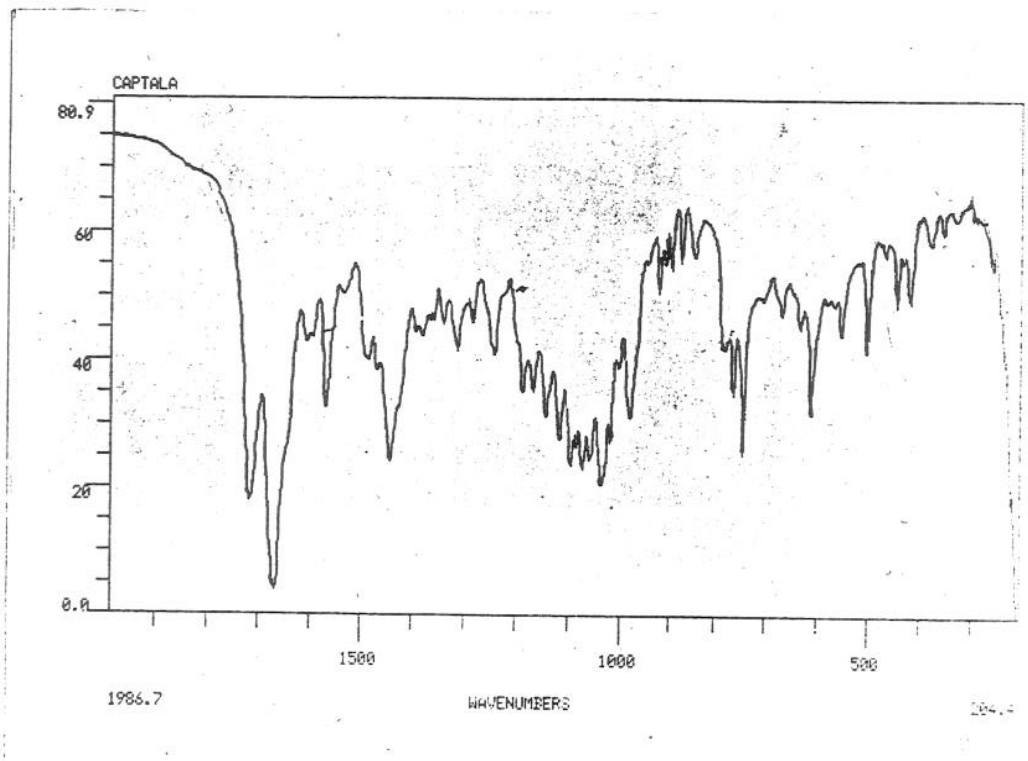
IR spectrum of sydnocarb

Figure 5



IR spectrum of "Captagon" (Bulgaria)

Figure 6



IR spectrum of "Captacola"

Figure 7

Gas chromatography of a mixture of amfetamine (1), ephedrine (2), phenmetrazine (3), sydnophen (4) and fenetylline (5).

Operating conditions as described on page 3.

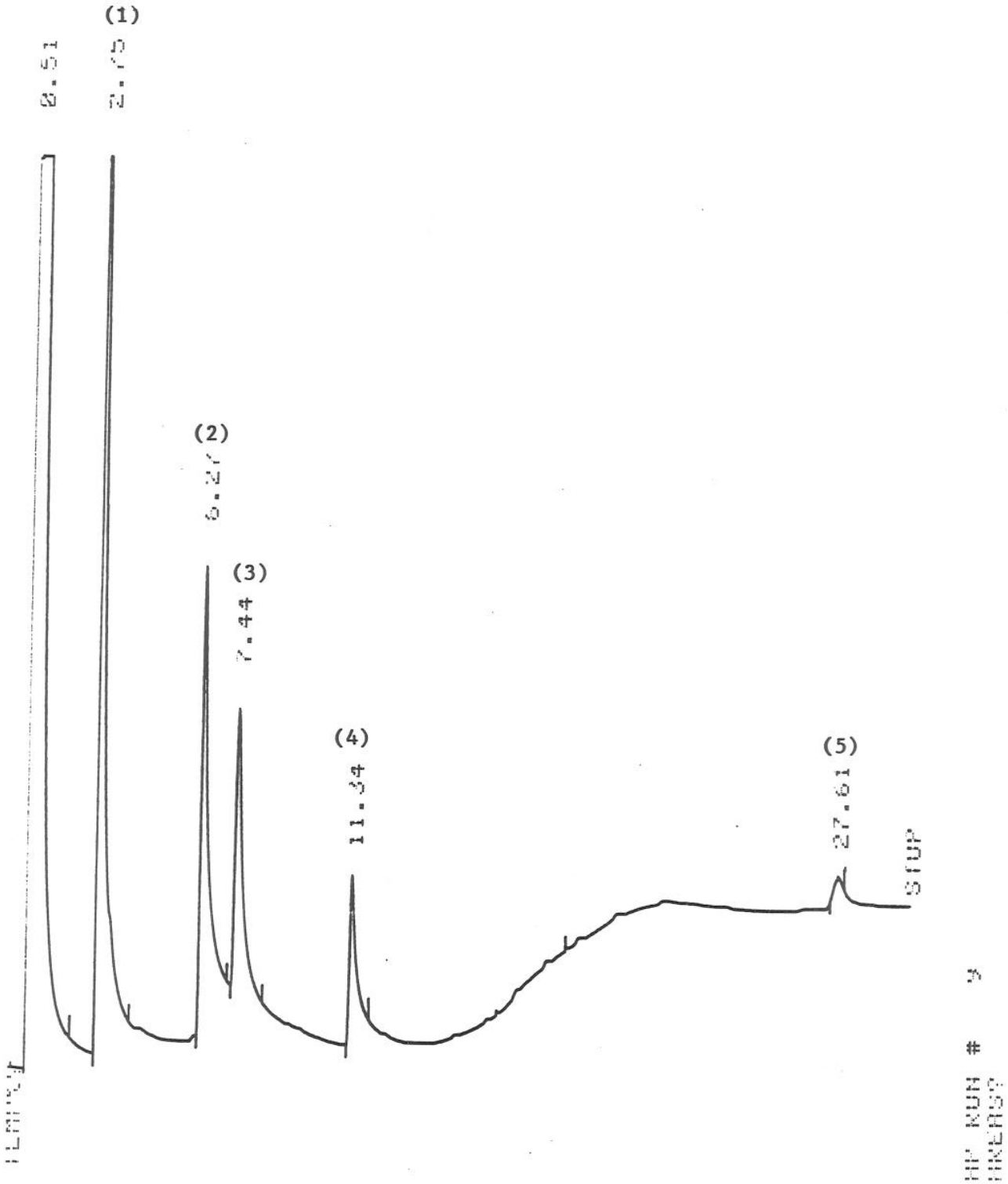
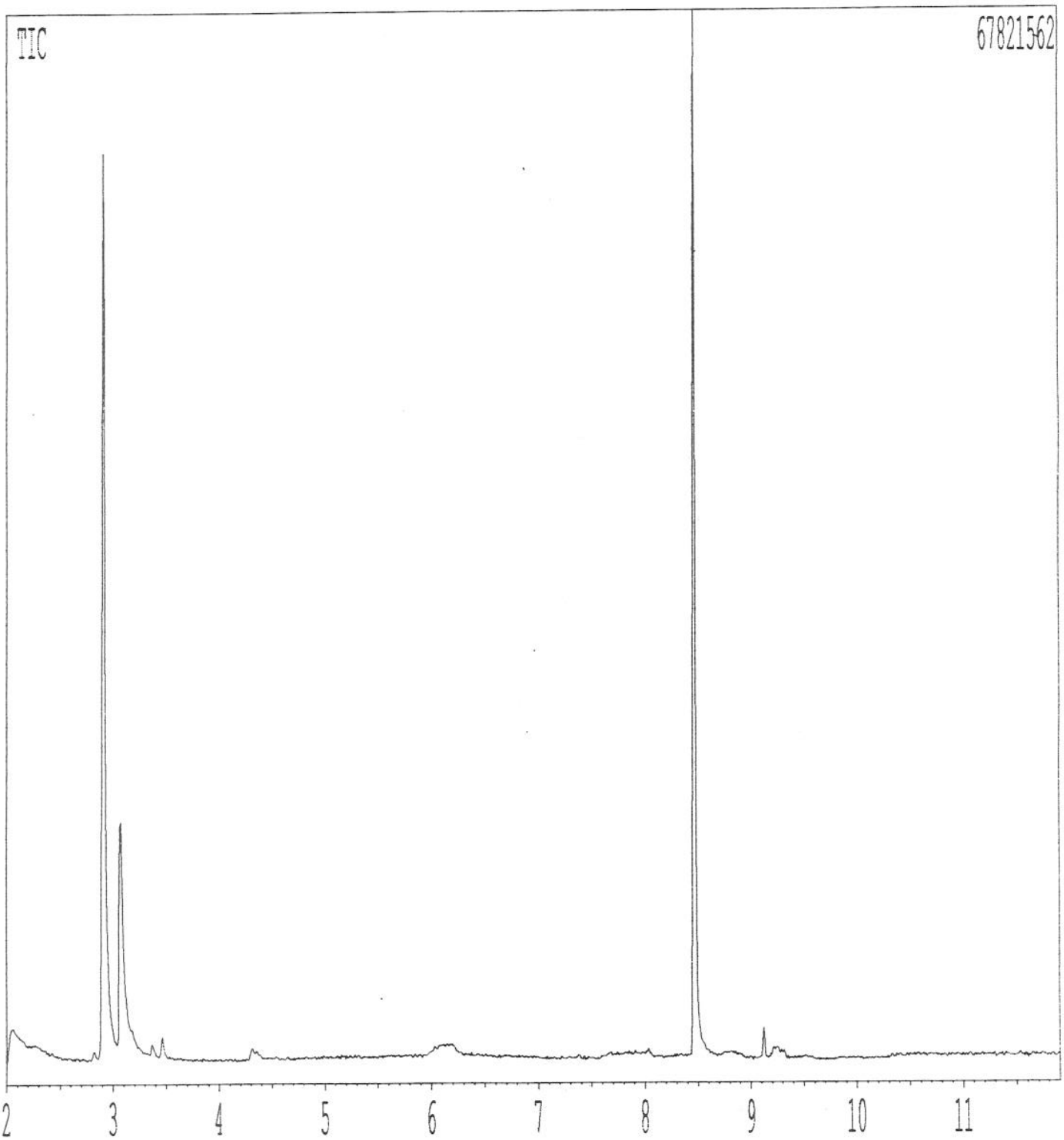


Figure 8a

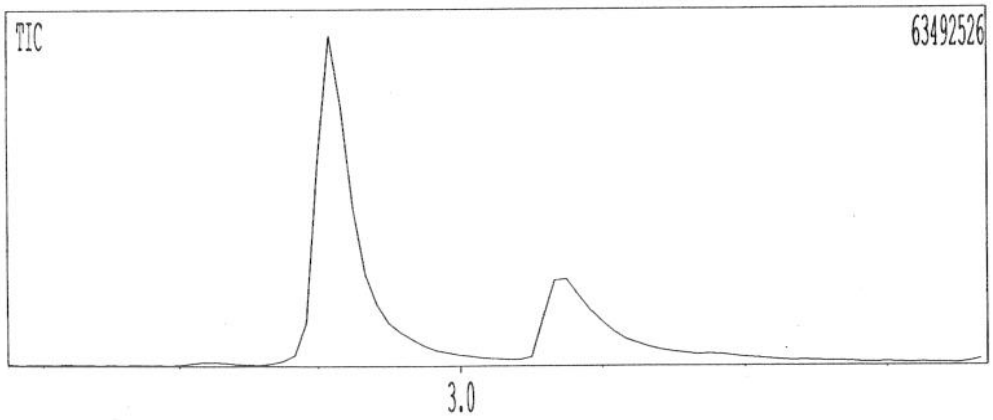
GC/MS of sydnocarb (on Shimadzu QP 5000)

*** CLASS-5000 *** Report No. = 1 Data : SAM.D06 94/07/12 11:53:40

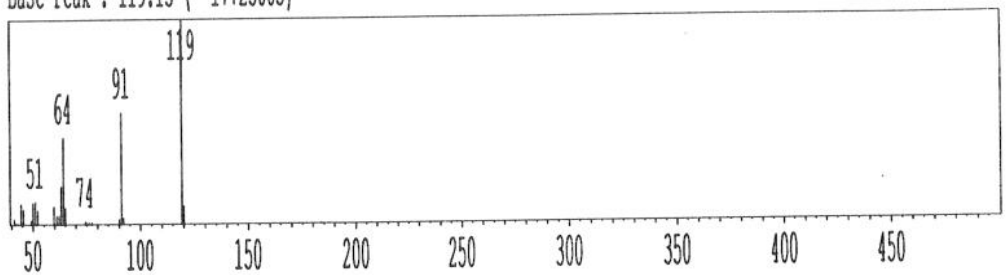


*** CLASS-5000 *** Report No. = 1 Data : SAM.D06 94/07/12 11:53:40

Sample : dafa
ID :
Sample Amount : 1
Dilution Factor : 1
Type : Unknown
Operator : dinkov
Method File Name : SAMPLE.MET
Vial No. : 1
Barcode :



Scan # : 110
Peak # : 24 Ret. Time : 2.908
Base Peak : 119.15 (17725005)



Scan # : 130
Peak # : 29 Ret. Time : 3.075
Base Peak : 93.15 (5371810)

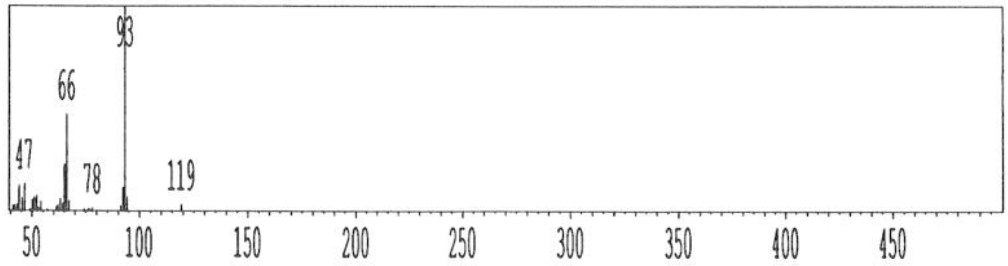
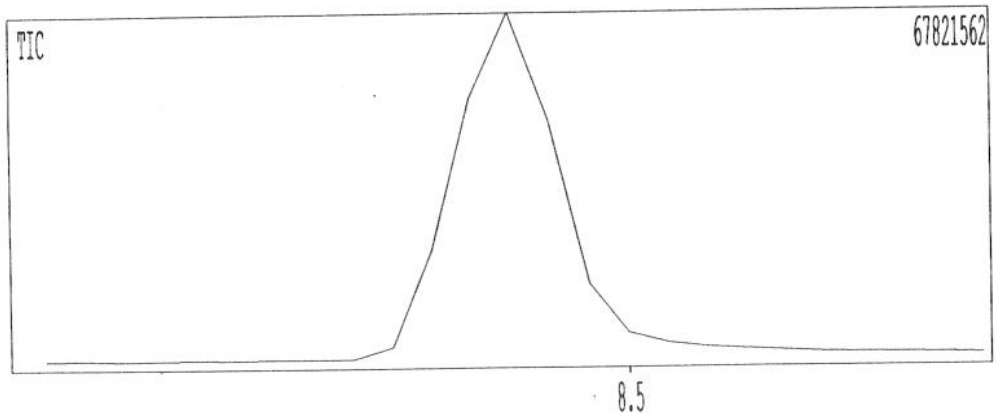


Figure 8b

*** CLASS-5000 *** Report No. = 1 Data : SAM.D06 94/07/12 11:53:40

Sample : dafa
ID :
Sample Amount : 1
Dilution Factor : 1
Type : Unknown
Operator : dinkov
Method File Name : SAMPLE.MET
Vial No. : 1
Barcode :



Scan # : 778 B.G. Scan # : 781
Peak # : 40 Ret. Time : 8.475
Base Peak : 91.15 (17594854)

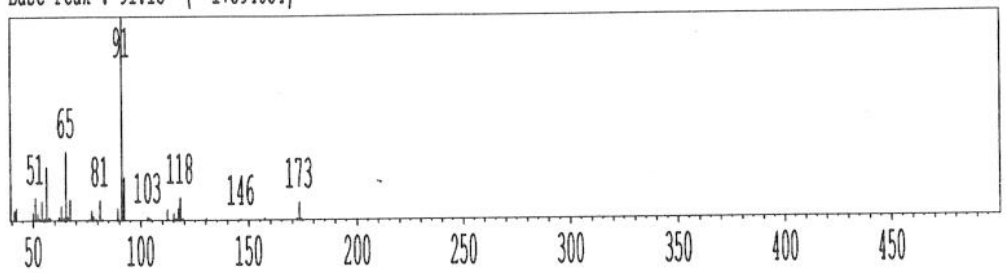


Figure 8c

Figure 9

Direct probe MS of sydnocarb (on Hewlett Packard 5985B)

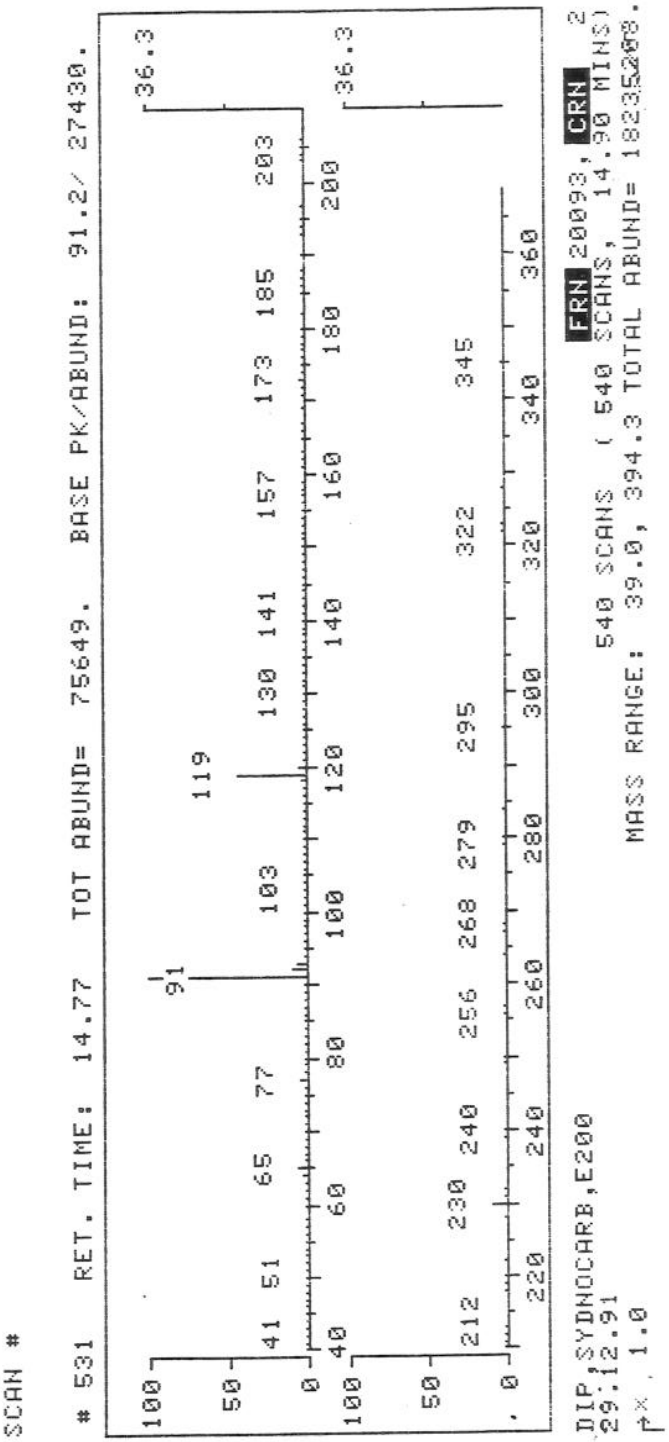
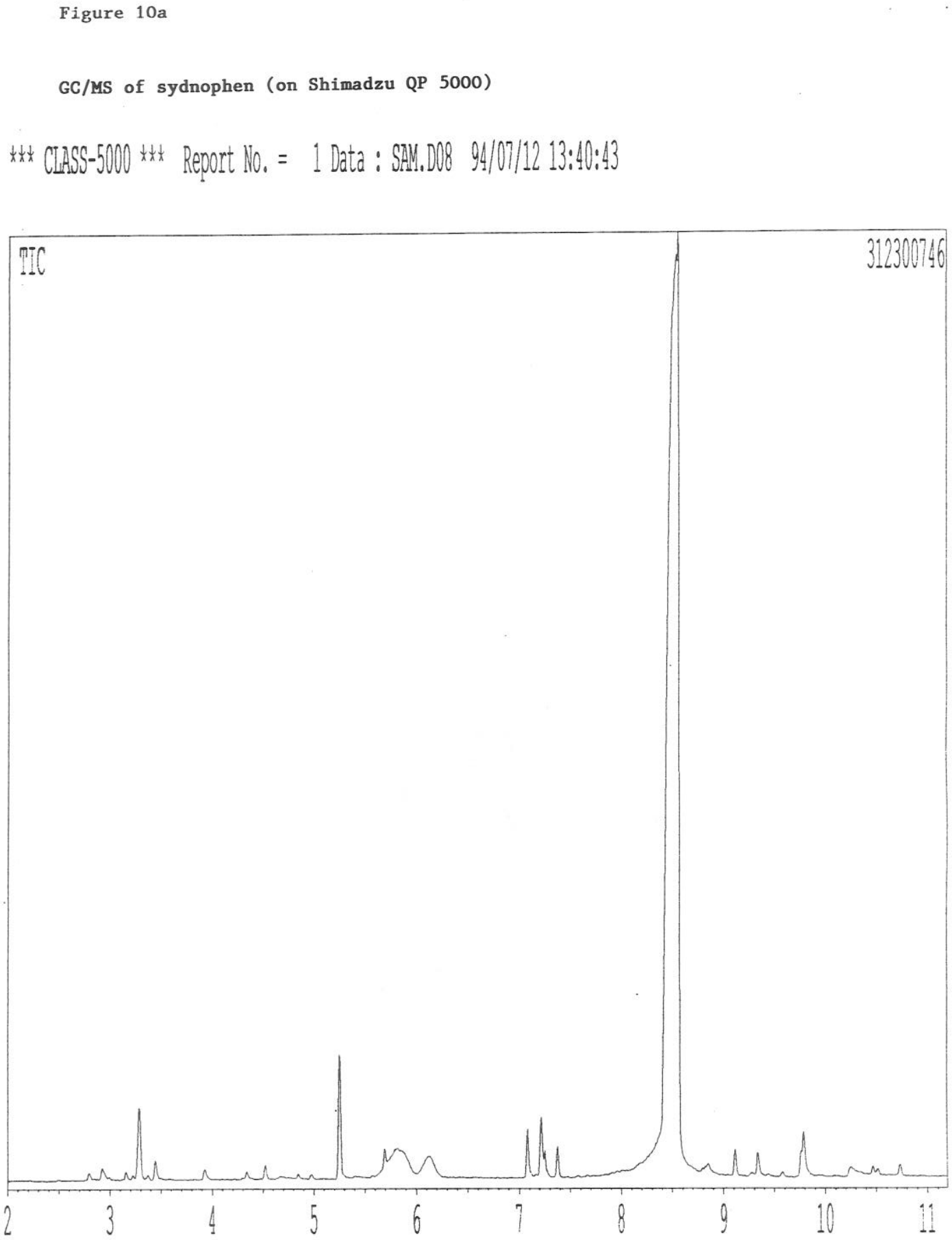
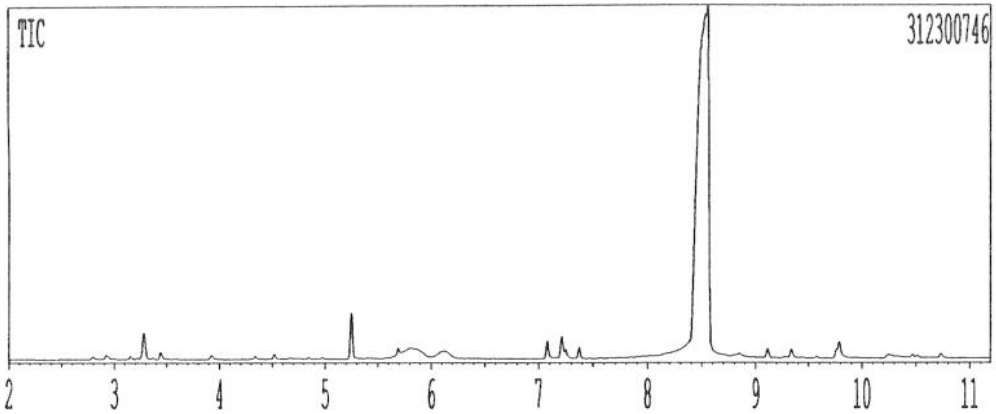


Figure 10a

GC/MS of sydnophen (on Shimadzu QP 5000)



*** CLASS-5000 *** Report No. = 1 Data : SAM.D08 94/07/12 13:40:43



Scan # : 785 B.G. Scan # : 733
Peak # : 54 Ret. Time : 8.533
Base Peak : 91.40 (46544767)

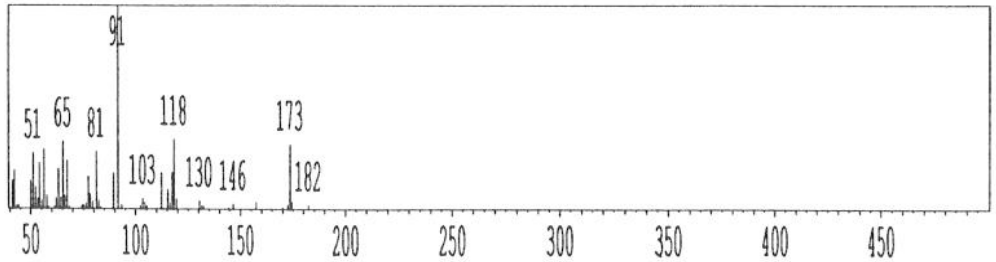
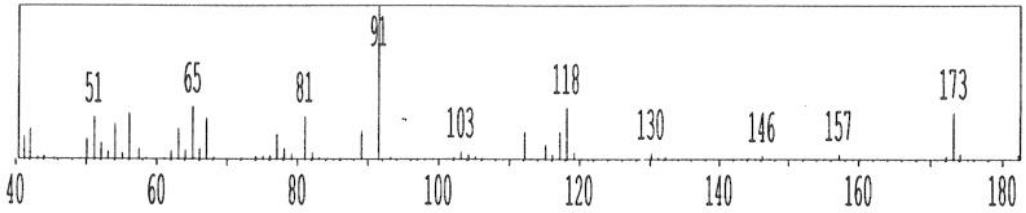


Figure 10b

Data1 SAM.d08
Scan # : 783 B.G. Scan # : 820
Peak # : 129 Ret. Time : 8.517 B.G. Time : 8.818
Base Peak : 91.45 (44361443)



Data2 PMW_TOX2.LIB
Entry : 54 CAS : 300-62-9 Mol.Wgt. : 135
Mol.Form. : C9H13N
Name : Amfetamine @ P509

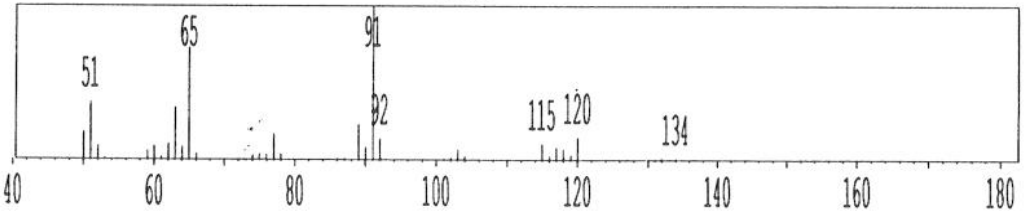
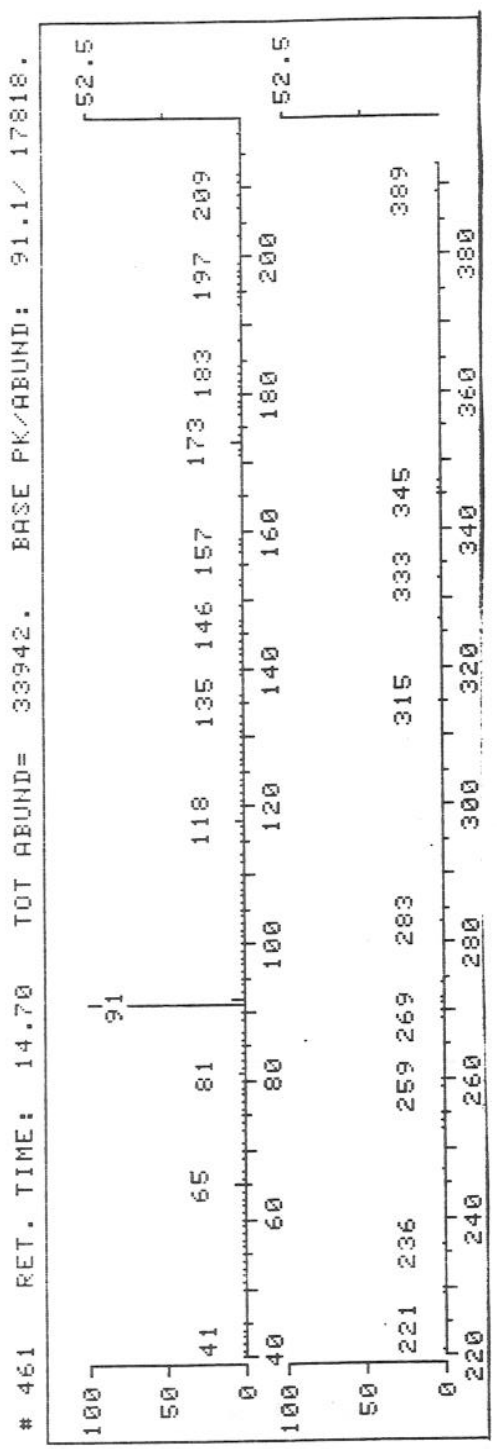


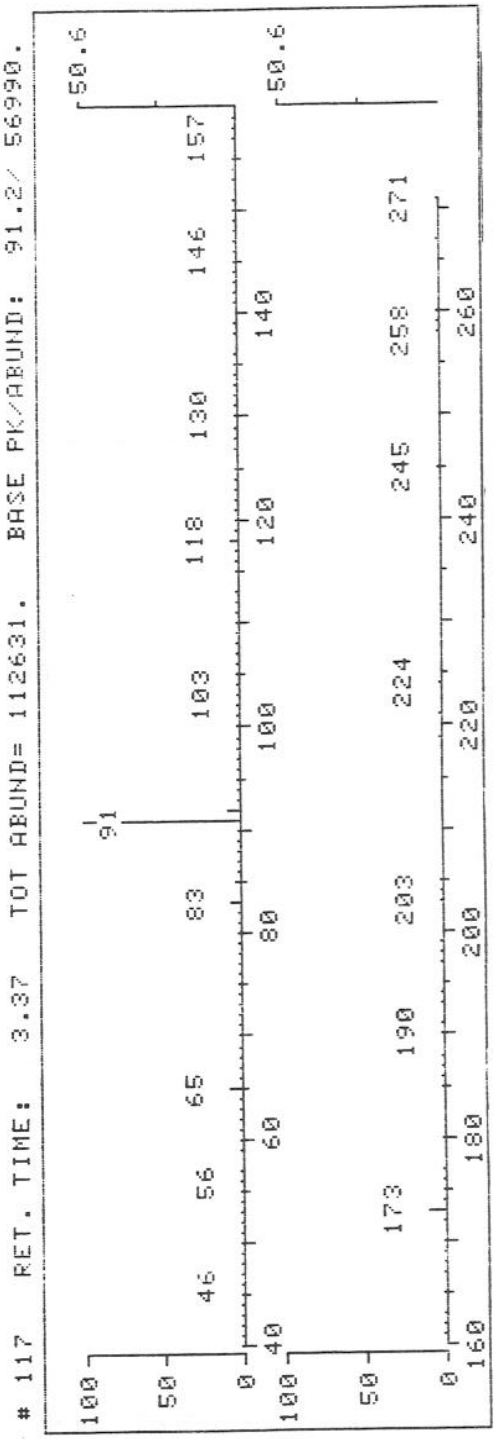
Figure 11

a) Mass spectrum from GC/MS of sydnophen (on Hewlett Packard 5985B)

b) Direct probe MS of sydnophen (on Hewlett Packard 5985B)



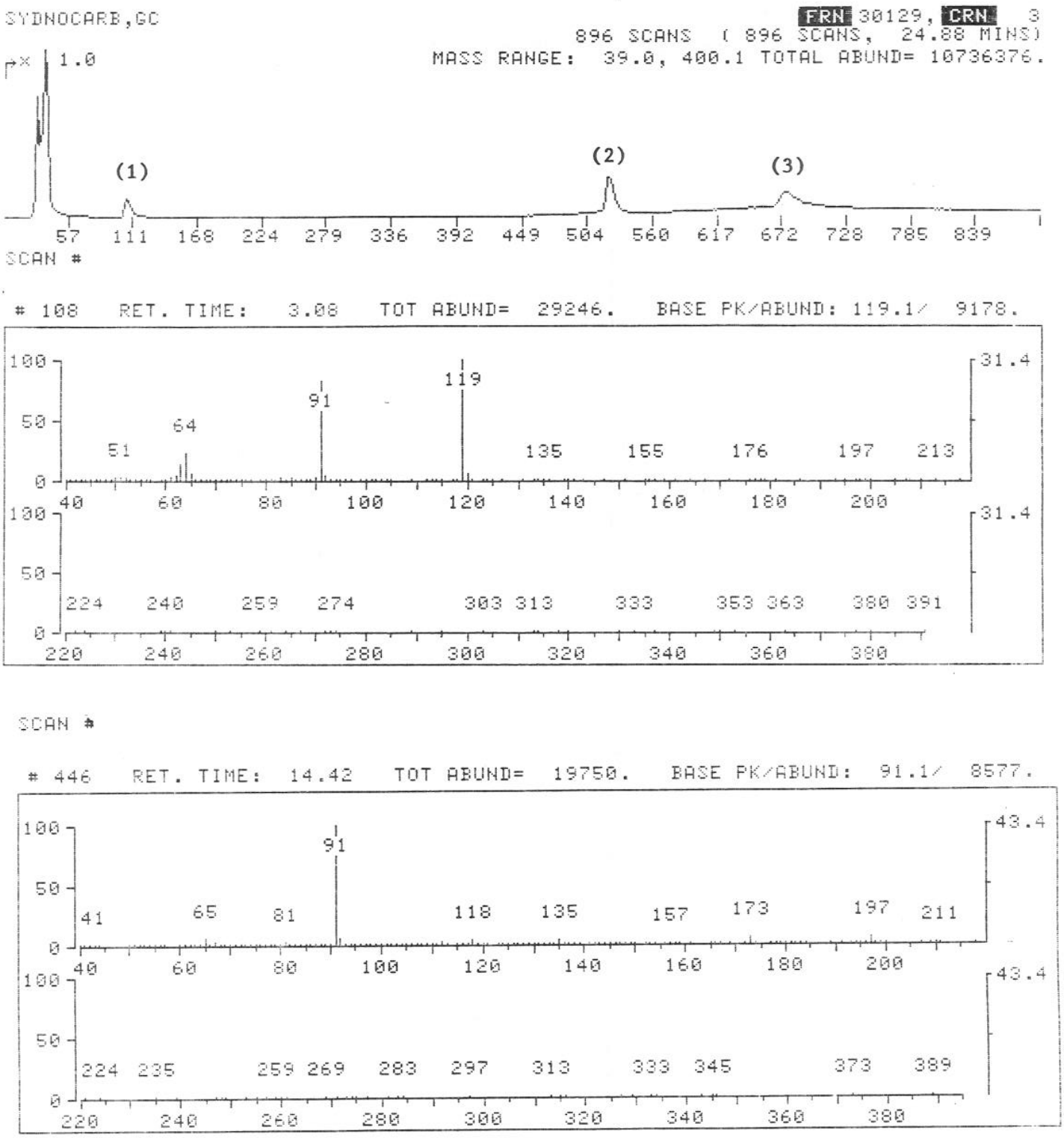
a)



b)

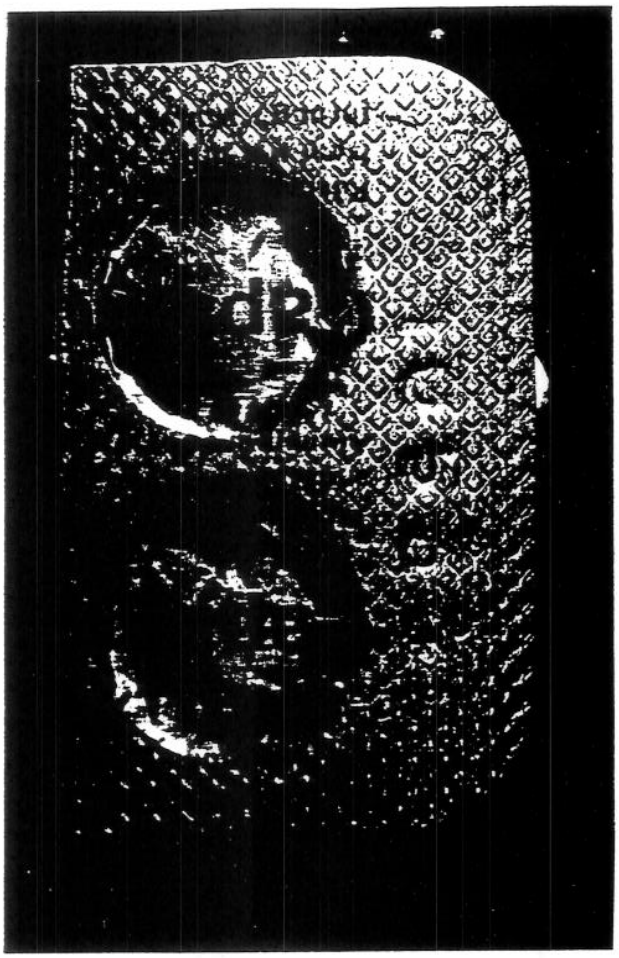
Figure 12

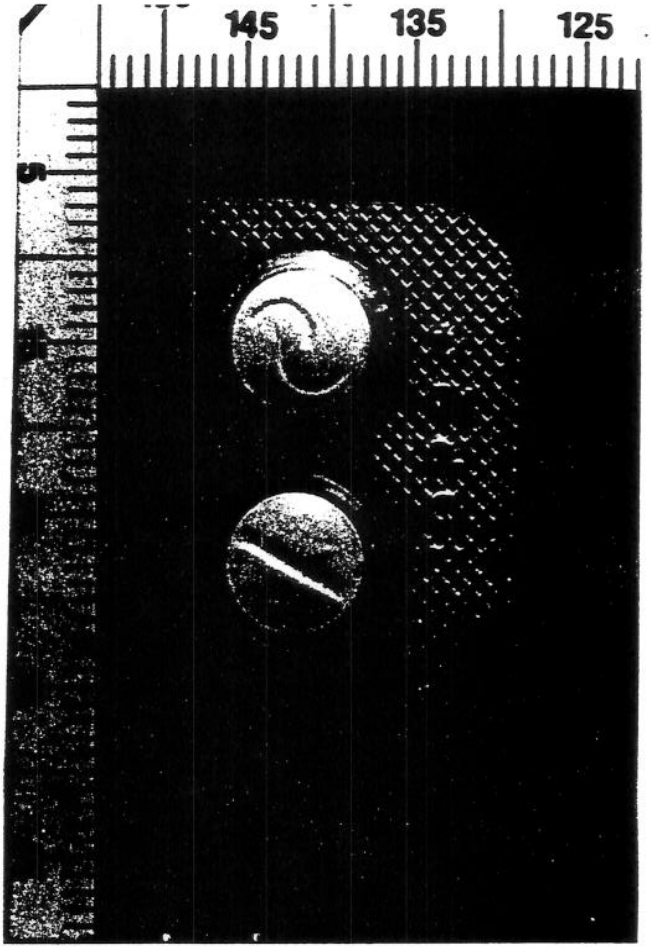
GC/MS of a sydnocarb street sample (powder) (on Hewlett Packard 5985B)

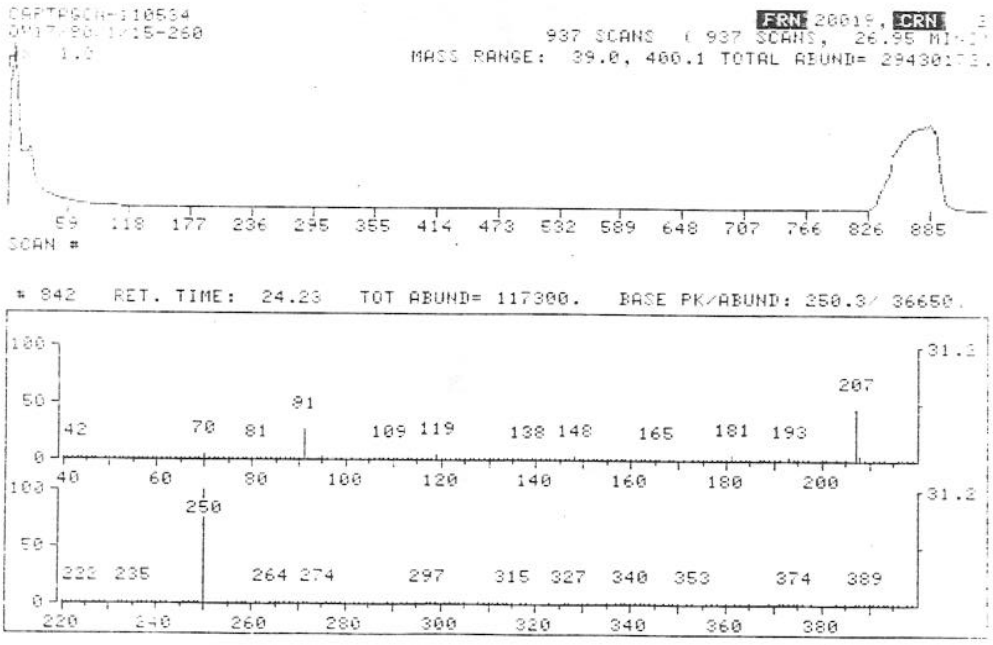


Peaks: Phenylisocyanate (1), sydnophen (2), theophylline (3)

Figure 13



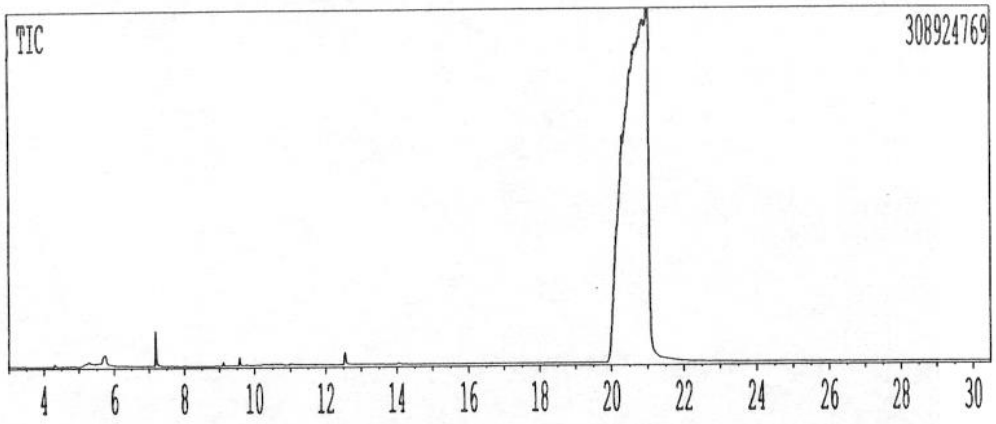




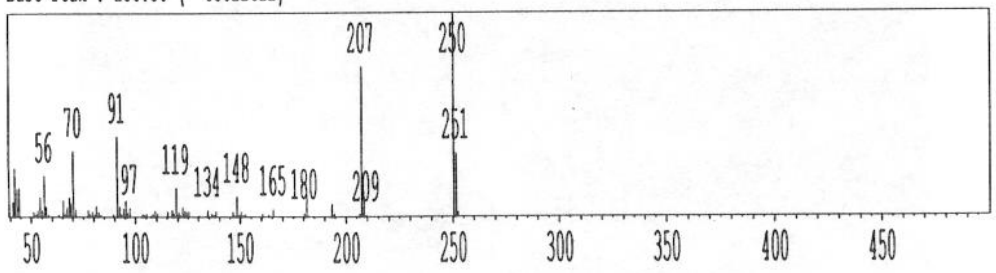
GC/MS of the "Captagon" tablets shown on the photos containing fenetylline as the active component (on Hewlett Packard 5985B).

GC/MS of a "Captagon" tablet containing fenetylline as the active component (on Shimadzu QP 5000)

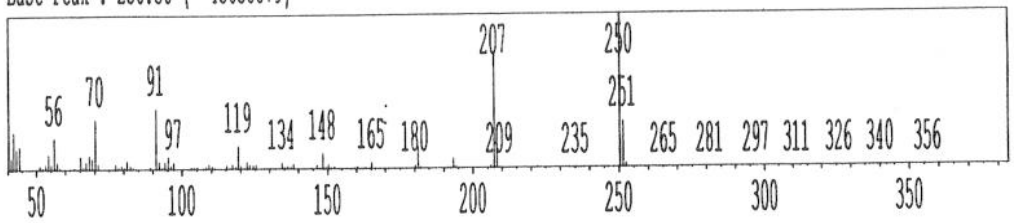
*** CLASS-5000 *** Report No. = 1 Data : SAM.D04 94/07/12 10:22:29



Scan # : 2154
Peak # : 79 Ret. Time : 20.942
Base Peak : 250.30 (45022412)



Data1 SAM.d04
Scan # : 2143
Peak # : 244 Ret. Time : 20.850
Base Peak : 250.30 (45038879)



Data2 PMW_TOX2.LIB
Entry : 778 CAS : 3736-08-1 Mol.Wgt. : 341
Mol.Form. : C18H23N5O2
Name : Fenetylline P1625

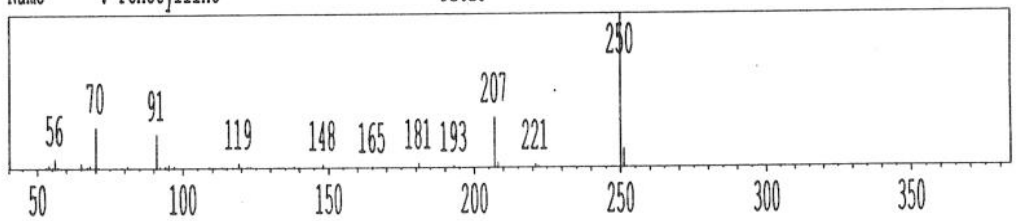
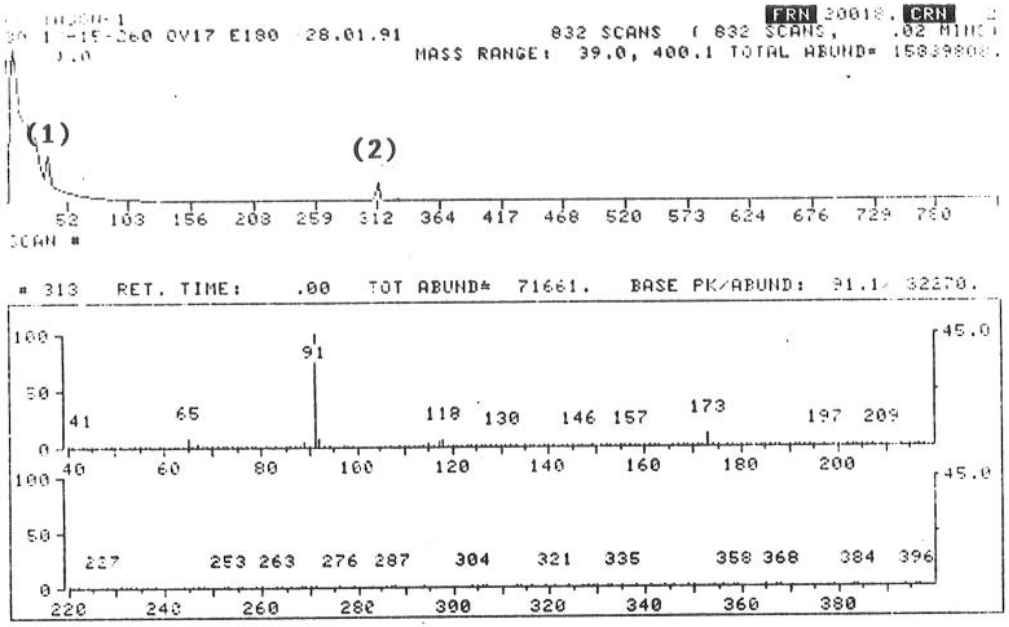
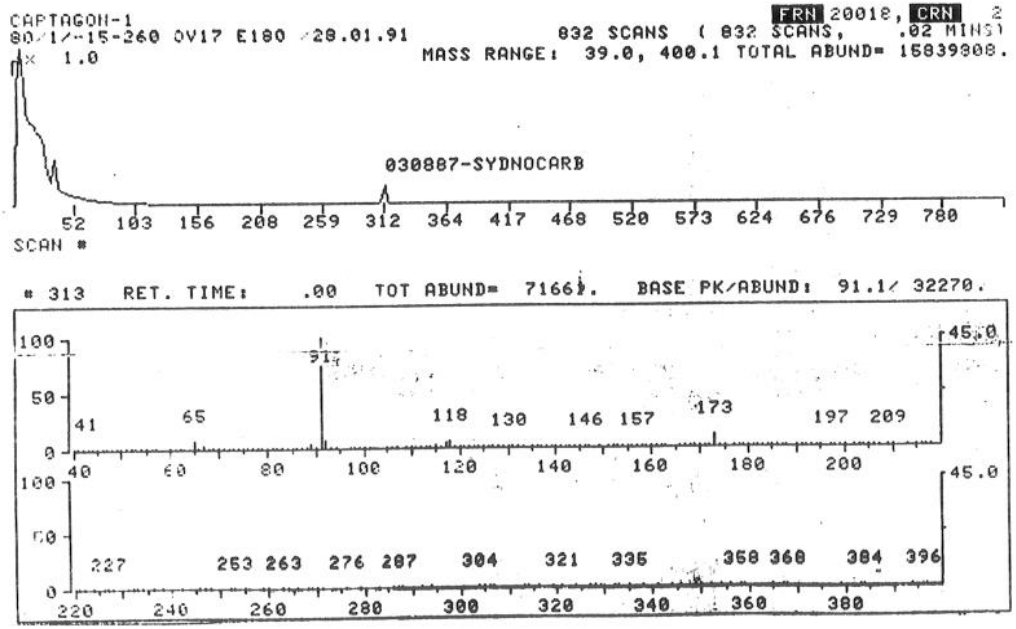
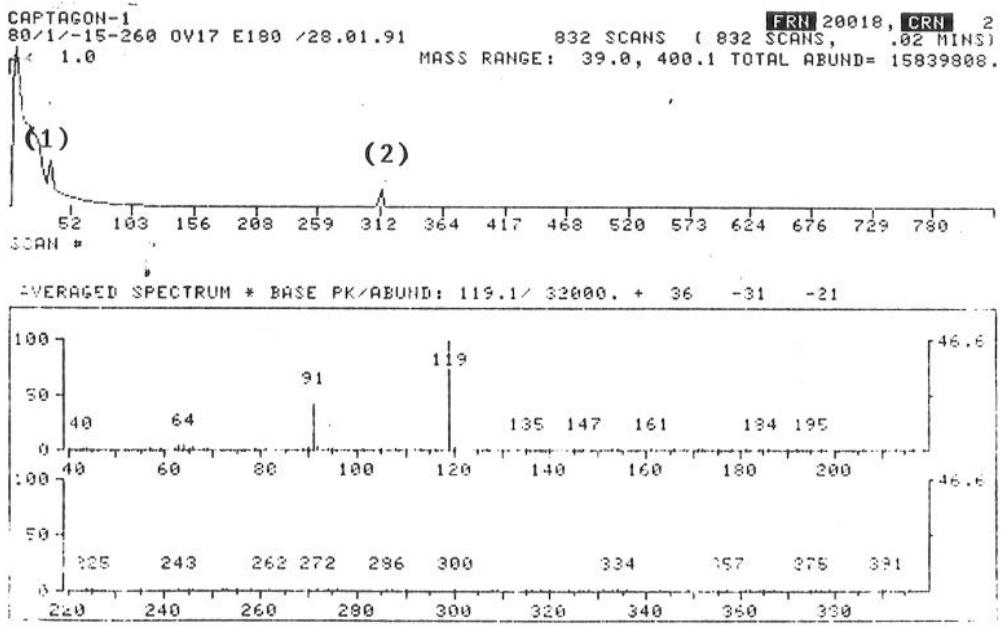


Figure 14

GC/MS of a tablet with the appearence of "Captagon", but with sydnocarb as the active component decomposing to phenylisocyanate (1) and sydnophen (2) during the analysis.







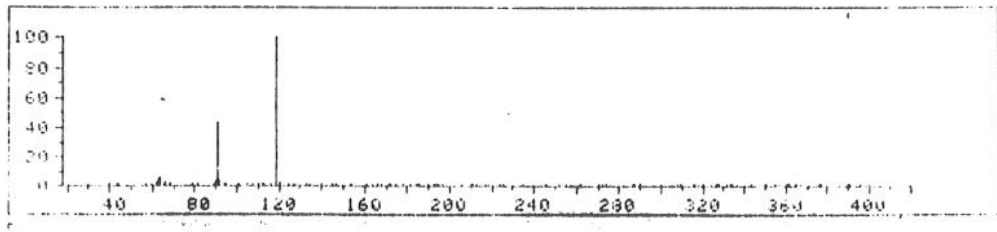
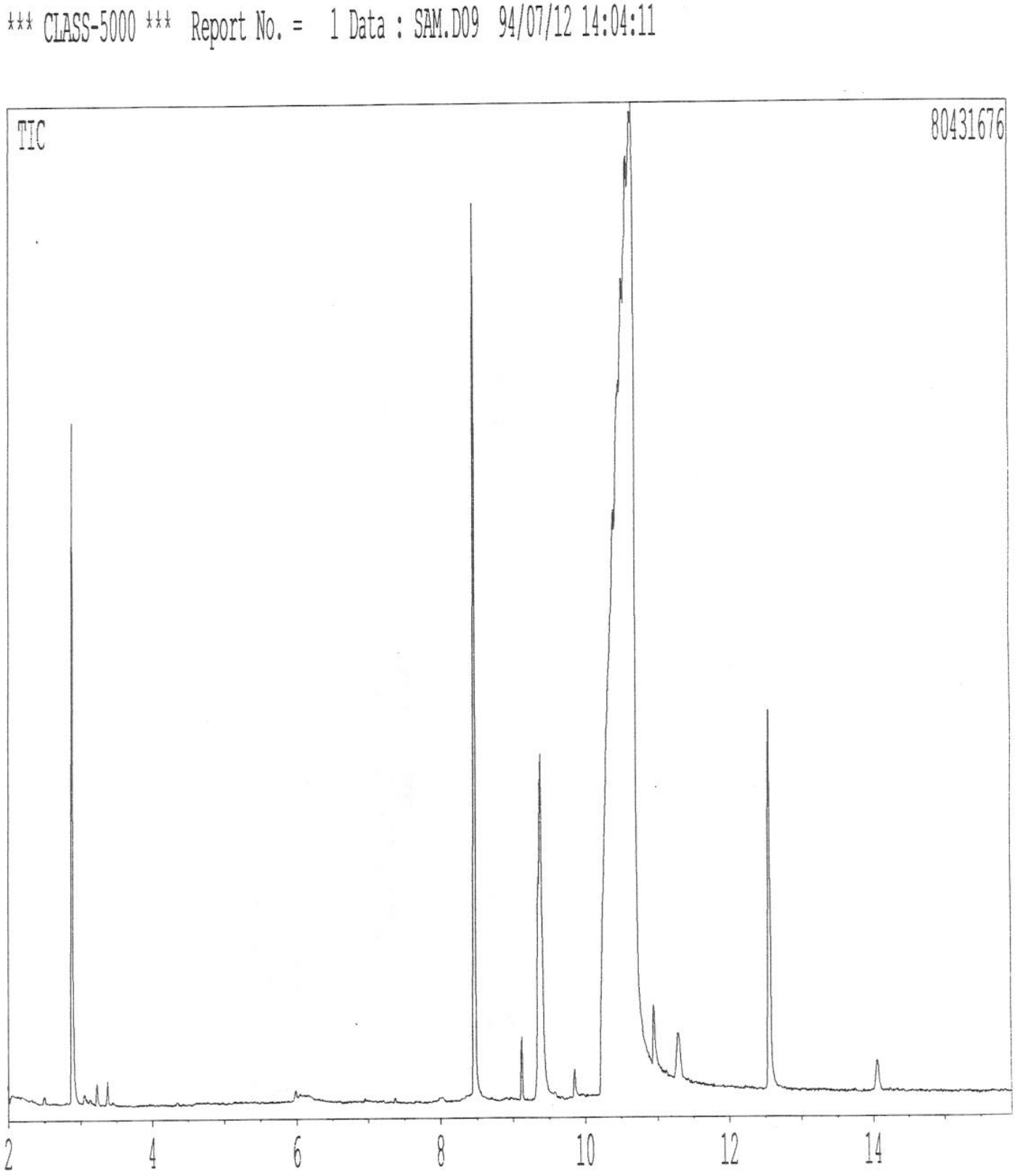


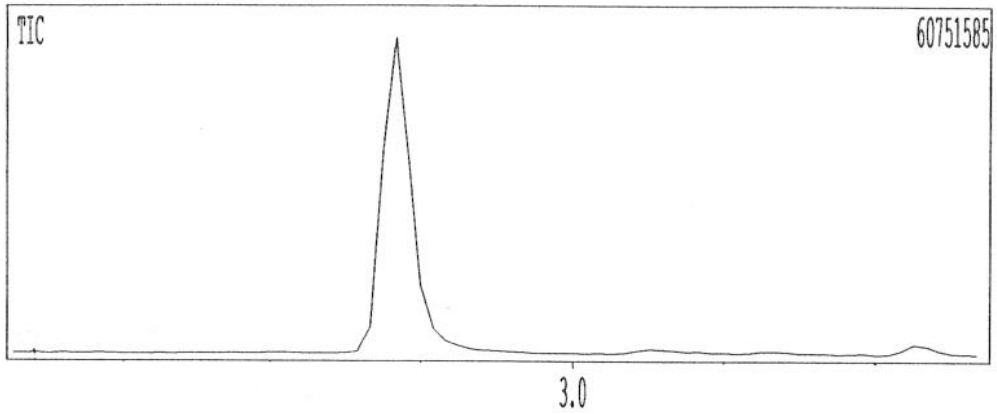
Figure 15

Figure 16a

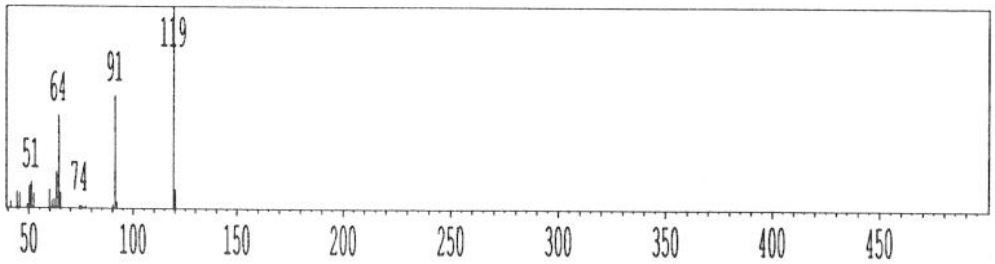
GC/MS of a "Captacola" tablet containing sydnocarb and theophylline as the active components (an Shimadzu QP 5000).



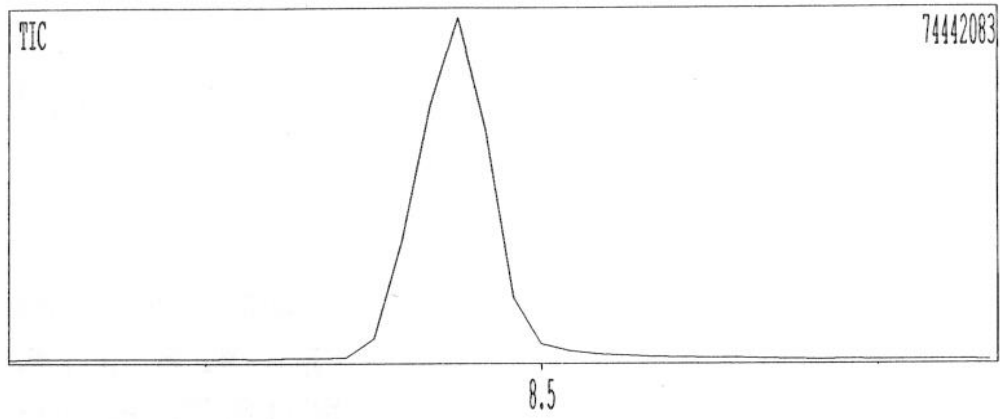
*** CLASS-5000 *** Report No. = 1 Data : SAM.D09 94/07/12 14:04:11



Scan # : 107 B.G. Scan # : 115
Peak # : 22 Ret. Time : 2.883
Base Peak : 119.15 (16009143)



*** CLASS-5000 *** Report No. = 1 Data : SAM.D09 94/07/12 14:04:11



Scan # : 778 B.G. Scan # : 786
Peak # : 38 Ret. Time : 8.475
Base Peak : 91.10 (19923121)

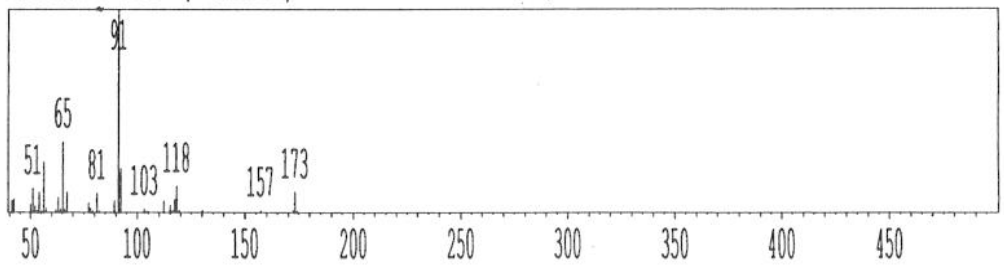
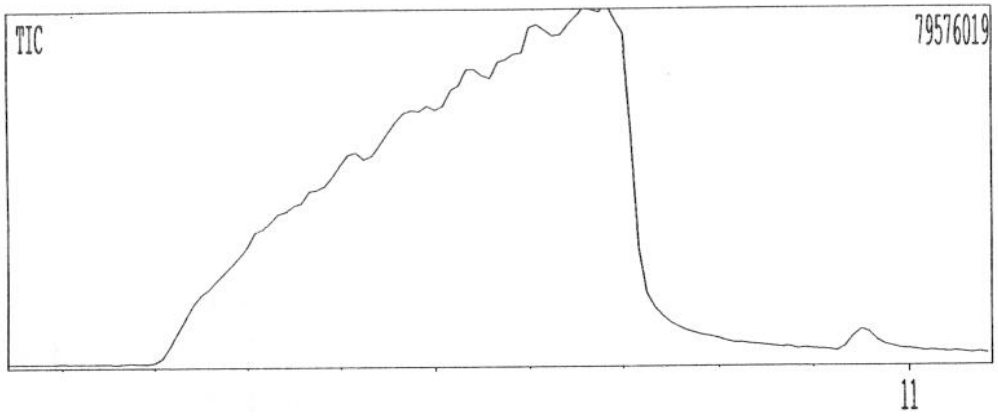
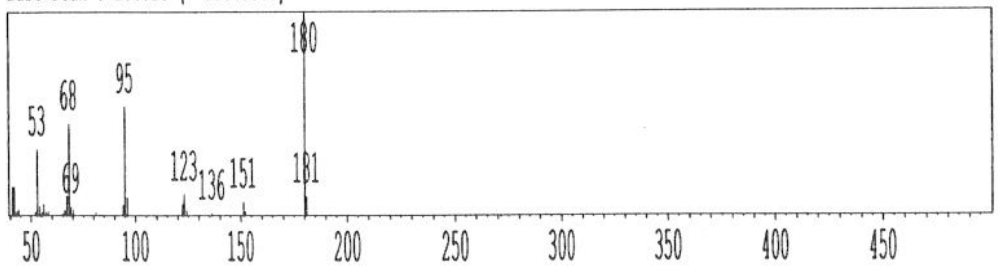


Figure 16b

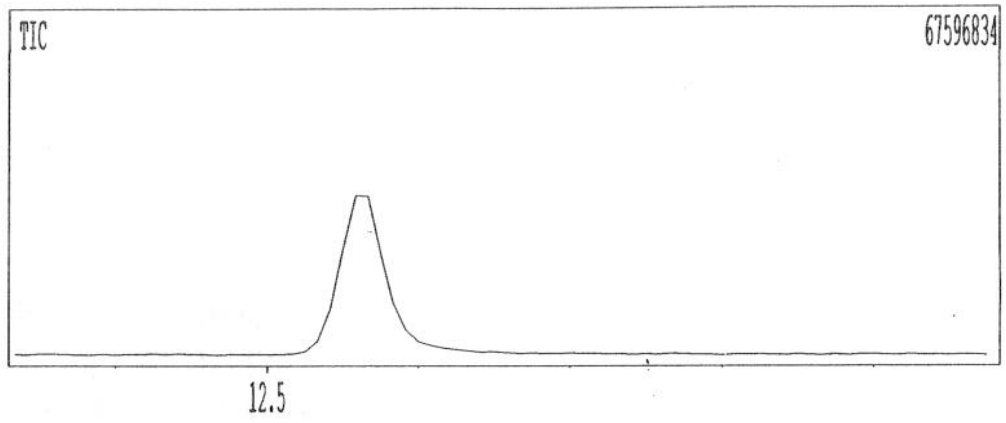
*** CLASS-5000 *** Report No. = 1 Data : SAM.D09 94/07/12 14:04:11



Scan # : 1042 B.G. Scan # : 1068
Peak # : 29 Ret. Time : 10.675
Base Peak : 180.10 (19343365)



*** CLASS-5000 *** Report No. = 1 Data : SAM.D09 94/07/12 14:04:11



Scan # : 1268 B.G. Scan # : 1284
Peak # : 41 Ret. Time : 12.558
Base Peak : 129.15 (5350355)

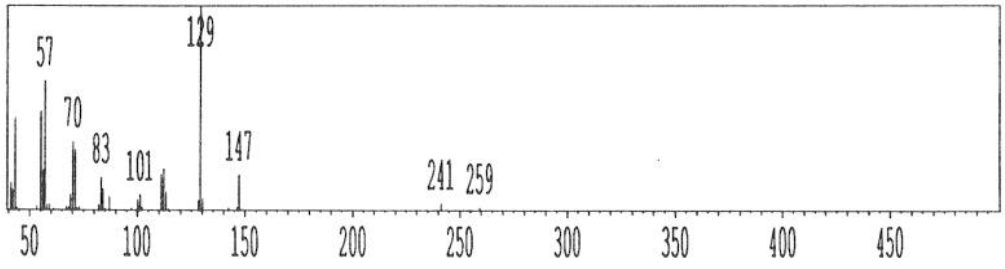


Figure 16c