

# MICROGRAM

Laboratory Operations Division  
Office of Science and Drug Abuse Prevention

BUREAU OF NARCOTICS & DANGEROUS DRUGS / U.S. DEPARTMENT OF JUSTICE / WASHINGTON, D.C. 20537

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## THE WHITE HOUSE

DRUG ABUSE PREVENTION WEEK, 1971

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BY THE PRESIDENT OF THE UNITED STATES OF AMERICA

### A PROCLAMATION

"What shall it profit a man," the Bible asks, "if he shall gain the whole world, and lose his own soul?" It is a question which the menace of drug abuse poses anew to all of us.

What can a nation profit from its abundant good life, if the same technology and material wealth which have yielded that abundance permits millions of its people, particularly its youth, to drift into the chemical modification of mind and mood at grave risk to their health -- to their very lives? What can a nation profit from its unparalleled individual freedom, if that liberty becomes license and that license leads to drug dependence which controls the bodies and warps the minds of men, women, children, and even the unborn?

Not so long ago it was easy enough to regard the tragedy of drug abuse as "someone else's problem." But recent years have brought that tragedy home -- often very literally -- to all Americans. We have learned that "drug abuse" refers not only to the crime-prone heroin addict -- though that is the disease at its deadliest, with over 1,000 heroin fatalities annually in New York City. The term also refers to the suburban housewife dependent on tranquilizers or diet pills; to the truck driver over-reliant on pep pills; to the student leaning on amphetamines to help him cram for exams; even to pre-teens sniffing glue.

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Analytical methods in **Microgram** do not have official status. Use of funds for printing this publication approved by the Bureau of the Budget, April 8, 1969. **CAUTION:** Use of this publication is restricted to forensic scientists serving law enforcement agencies.

It has become a problem that touches each of us. Its manifestations are many and varied, but all grow from a common root -- psychological and physical needs unmet through legitimate social channels -- and all feed on a common ignorance -- ignorance of the profound harm the abuser does to himself and society. Drug abuse is nothing less than a life and death matter for countless Americans, and for the moral fiber of this Nation. The drive to meet this threat must command from us our very best -- our attention, our energies, our resources and our prayers.

NOW, THEREFORE, I, RICHARD NIXON, President of the United States of America, do hereby designate the week beginning October 3, 1971, as the second annual Drug Abuse Prevention Week.

I call upon officials of the Federal Government under the leadership of the new Special Action Office for Drug Abuse Prevention, particularly those officials in the Departments of Health, Education and Welfare, Justice and Defense, to join with educators and the medical profession in intensifying programs to prevent and reduce drug abuse among the young and among all Americans. I urge State and local governments, as well as business and civic groups, to cooperate in such programs and to seek out new methods by which the risks and dangers of drug experimentation can be communicated to the entire Nation. The communications media can render invaluable assistance in this endeavor, and I urge them to do so.

I also encourage the clergy, and all of our moral and spiritual leaders, to make a special effort during this week to take up the problem of drug abuse and to offer those answers of the spirit which alone can fill the void where drug abuse begins.

And I appeal, above all, to those who bear the special trusts of parenthood -- that all of us may rededicate ourselves to the well-being of America's youth; and that we may so teach them, so guide them, so reach out to them in understanding and compassion, as to help them avoid the problems that arise from abuse of drugs and to attain the full promise of their maturity.

IN WITNESS THEREOF, I have hereunto set my hand this 17th day of September, in the year of our Lord nineteen hundred seventy-one and of the Independence of the United States of America the one hundred ninety-sixth.

RICHARD NIXON

Counterfeit McNeil Syndrox Tablets, each containing 5 milligrams of methamphetamine hydrochloride, have been identified. These tablets are unlike any previously encountered by BNDD Special Testing and Research Laboratory. We would appreciate any facts on any encounters you may have or have had with these tablets.

Heroin samples containing magnesium sulfate (Epsom salts) were recently analyzed by BNDD's New York Laboratory. Although this salt frequently is seen in combination with cocaine, this is the first report of its occurrence with heroin. Lactose and traces of quinine were also present.

Cocaine with acetanilid. Analysis of a white powder in a plastic vial revealed that it consisted of cocaine hydrochloride 30%, acetanilid 2.5% and boric acid. Acetanilid was first detected by gas chromatography, quantitated by U.V. and confirmed by I.R.

This exhibit from outside the U.S.A. is the first encounter with acetanilid as a cutting material.

Sugar water is reported by the Northern Illinois Police Crime Laboratory as being used to spray drying marijuana plants to entrap the resin content.

A field test plus an initial laboratory test on a white powder collected by an East Coast law enforcement agency indicated the presence of cocaine. As a result, nine young people were arrested. After spending from five to nine days in jail, the young people were released. Laboratory examination showed the "cocaine" to be quinine.

Methylphenidate is also known as "West Coast" according to a letter to the editor in the New England Journal of Medicine. It is becoming an increasing factor in the drug abuse problem, particularly in connection with drug treatment programs.

"Diacetyl Morfina 0.02" ampules in Marlboro cigarette "hard paks" have been encountered by the BNDD New York Laboratory. The ampules were made of yellow glass and contained approximately 2 milliliters of a yellow brown solution. Analysis revealed 8.1 milligrams of morphine per milliliter.

#### SELECTED REFERENCE

Journal of the Association of Official Analytical Chemists, 54, No. 4 (July, 1971). Contains following papers presented at Symposium on Analytical Methods for Forensic Science, October, 1970.

Starrs, James E., "The Ethical Obligations of the Forensic Scientist in the Criminal Justice System"

McCrone, Walter C., "Use of the Microscope in Criminalistics"

Snow, K. B. and W. D. Washington, "Comparison of Paints by Neutron Activation Analysis II-Colored Paints"

Brunelle, R. L., W. D. Washington, C. M. Hoffman and M. J. Pro, "Use of Neutron Activation Analysis for the Characterization of Paper"

DeZan, Paul, Roger F. Canaff and Robert Bianchi, "Fluorimetric Characteristics of Some Narcotic and Dangerous Drugs"

Harrison, W. W., G. G. Clemens and C. W. Magee, "Forensic Applications of Spark Source Spectrometry"

Getz, Melvin E, "An Automatic Spotter for Quantitative Thin Layer and Paper Chromatographic Analysis by Optical Scanning"

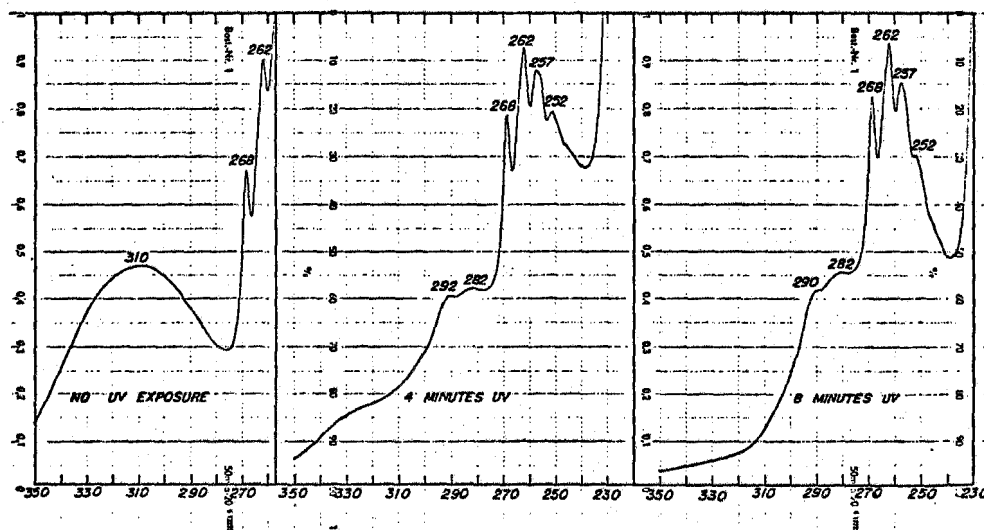
AN OBSERVATION ON THE ULTRAVIOLET ABSORPTION CURVE OF MIXTURES  
OF LSD AND PCP

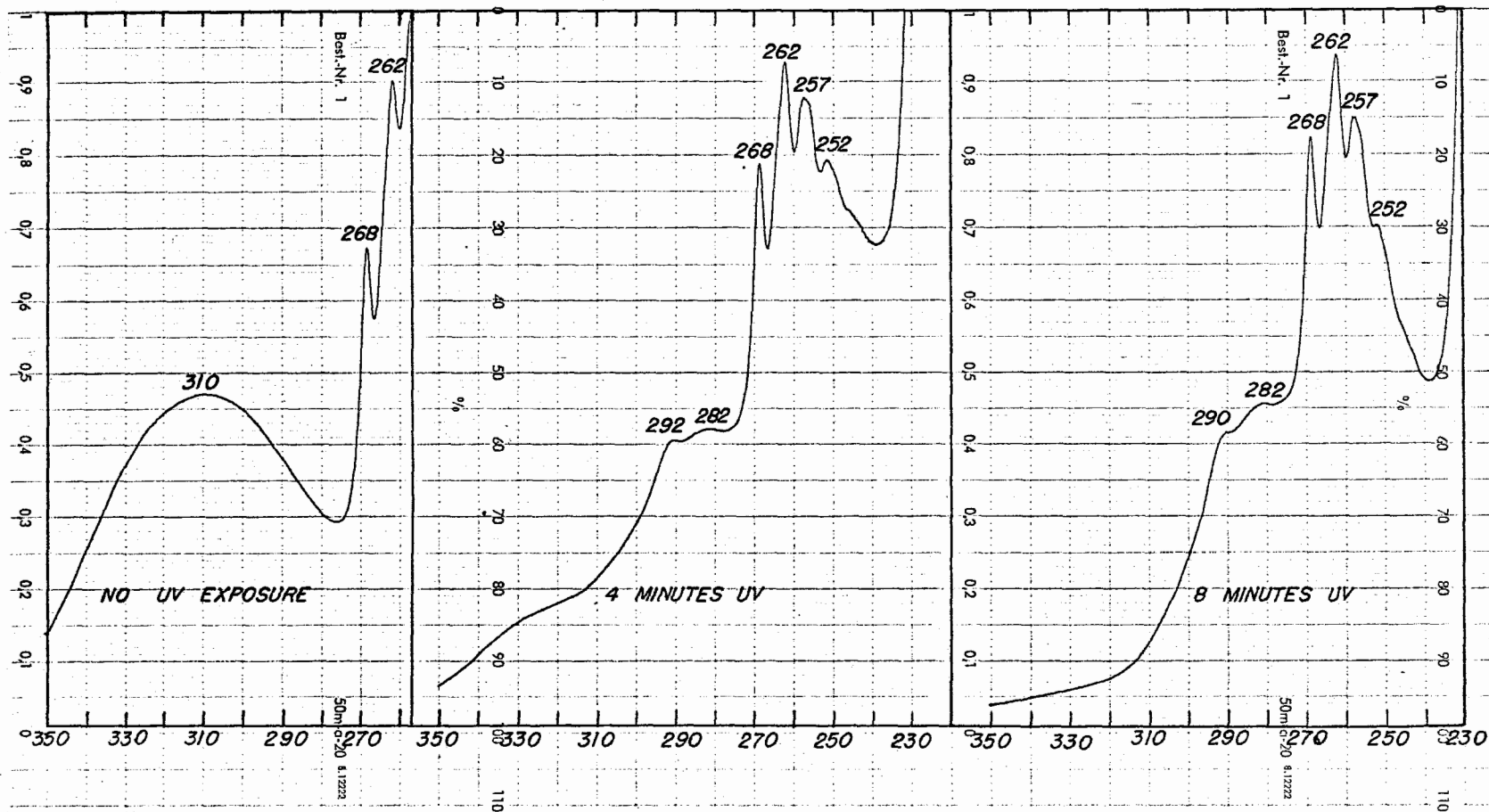
Otto Schales  
Elyria Memorial Hospital  
Elyria, Ohio 44035

Submitted for examination were several tablets, light tan-pink in color, biconvex, diameter 6.4 mm, thickness 3.2 mm at center, average weight 160 mg.

One of the tablets was powdered and extracted three times with 10 ml chloroform each. The combined extracts were filtered and evaporated to dryness at 25° C. by blowing air against the surface of the liquid in a porcelain dish. The residue was taken up in 3 ml 0.1 N sulfuric acid and the UV spectrum was recorded with a Zeiss DMR 21. In addition to the LSD maximum at 310 nm, there were two peaks at 268 and 262 nm. The solution was exposed to long wave UV light for 4 min. and the UV scan was repeated. As expected, there was a lowering of the LSD maximum and a shift toward 292 nm. Unexpectedly, however, there occurred also a marked decrease in the LSD absorbance in the shorter wavelength UV range, resulting in the emergence of a complete PCP absorbance curve. This curve was brought out even better after an additional 4 min. UV exposure.

The spectral behavior of LSD after UV radiation offers a simple means of demonstrating the presence of PCP in preparations containing LSD.





## SPECTROSCOPIC IDENTIFICATION OF DIMETHOXYAMPHETAMINES

K. Bailey, A.W. By, K.C. Graham, and D. Verner,

Food and Drug Laboratories,  
OTTAWA

In Canada, the dimethoxyamphetamines and their salts are Restricted Drugs and subject to the same legislative controls as LSD, STP, MDA and others. The 2,5-dimethoxyamphetamine HBr salt has been identified in police exhibits both in Canada and the United States.

We have prepared the six possible dimethoxyamphetamines and their hydrochloride salts. Presented here are observations and spectroscopic characteristics which may assist the analyst to identify these compounds.

It is important to note that the hydrochloride salts are more or less hygroscopic, consequently their melting points may vary depending on extensive drying or exposure to humid conditions. (Table 1). For example, the 2,5-dimethoxyamphetamine hydrochloride has a m.p. 105-106°C. On contact with moist air, the m.p. increases to 110-113°C after a few days and the salt eventually deliquesces. As shown in Table 1, the literature melting points for 2,5-dimethoxyamphetamine hydrochloride are 111.5-112.5°C and 117.5°C. The infrared spectra of samples having m.p. 105-106°C and 110-113°C could not be differentiated. 3,4-Dimethoxyamphetamine hydrochloride was obtained as the monohydrate. This was determined by combustion analysis and N.M.R. Spectra.

Table 2 lists ultraviolet data on the six dimethoxyamphetamines. The data presented in Table 3 on the integrated nuclear magnetic resonance spectra are useful for recognizing an unknown as a dimethoxyamphetamine. Apart from the 2,4- and 2,6-isomers which give readily recognizable aromatic substitution pattern signals at 60 MHz, the aromatic protons give complex or degenerate signals.

The mass spectra are very weak, consequently it is important to know that the mass spectrometer does not show extraneous signals from residual substances. Our results (figures 1-6) were obtained with a A.E.I. M.S. 12 with probe at 70eV and within the temperature range 120-140°C. The parent ion ( $m/e$  195) generally amounts to about 1% of the base peak ( $m/e$  44) and only two or three signals are greater than 5%;  $m/e$  152 (effectively protonated dimethoxytropylium) is the second strongest and the characteristic peak of all the spectra, and a metastable ion at  $m/e$  118.5 accompanying the production of 152 from 195 is observed in every case.

The attached infrared spectra serve better to identify the isomers. Spectra of the free bases obtained in a crude state by reducing the corresponding nitrostyrenes with lithium aluminum hydride, were the same as those of the bases regenerated from the recrystallised hydrochlorides. Note that although the spectra of different salts of any given dimethoxyamphetamine differ in mull phases, in KBr discs anionic exchange may render the spectra (e.g., of the hydrobromide and hydrochloride salts at least) identical. Also the degree of hydration may somewhat affect the spectra from 3500-2000  $\text{cm}^{-1}$ , but the fingerprint region should remain characteristic.

We are grateful to Mr. J.C. Ethier of this Division for his care in recording these infrared spectra.

Table 1

Analytical<sup>1</sup> and m.p.<sup>2</sup> data for Dimethoxyamphetamine Hydrochlorides

	Found %			<u>mp</u> <sup>o</sup> C	<u>Lit.</u> mp <sup>o</sup> C	
	C	H	N			
2,3-	56.8	7.8	6.0	154-5	154-6 <sup>3</sup>	
2,4-	56.9	7.9	6.0	149-50		
2,5-	56.95	7.9	6.1	105-6	111.5-2.5 <sup>3</sup>	117.5 <sup>4</sup>
2,6-	56.8	7.8	6.25	185-6 (Subl.)	185-6 <sup>5</sup>	
3,4-H <sub>2</sub> O	53.2	7.8	5.95	145-6	147.5-8 <sup>3</sup>	144 <sup>6</sup>
3,5-	57.2	7.75	6.2	161-2	160-1 <sup>3</sup>	147 <sup>7</sup>

<sup>1</sup> Calculated for C<sub>11</sub> H<sub>18</sub> Cl N O<sub>2</sub>: C, 57.0; H, 7.8; N, 6.05%  
 Calculated for C<sub>11</sub> H<sub>18</sub> Cl N O<sub>3</sub>: C, 52.9; H, 8.1; N, 5.6%

<sup>2</sup> Corrected, samples were recrystallised from isopropanol/hexane.

<sup>3</sup> Beng T. Ho et al, J. Med. Chem., 13, 26(1970).

<sup>4</sup> R. Baltzly and J.S. Buck, J. Amer. Chem. Soc., 62, 161 (1940).

<sup>5</sup> A.A. Shamshurin and Yu.M. Revenko, Izv. Akad. Nauk. Moldavsk SSR., 10, 86 (1962).

<sup>6</sup> L.G. Dring et al., Biochem. J., 116, 425 (1970).

<sup>7</sup> T.A. Gorindachari and M.V. Lakshmikantham, Proc. Indian Acad. Sci., 46A, 406 (1957).



Table 2

UV data<sup>1</sup> for Dimethoxyamphetamine hydrochlorides

2,3-	274-278 (1660),	218 (8,040)
2,4-	278-283 (300-2680),	227 (9,000)
2,5-	291 (3,930),	228 (8,130)
2,6-	272-279 (1440-1440)	221 (7,820)
3,4- <sup>2</sup>	280 (3,230)	232 (9,430)
3,5-	272-282 (1260-1330)	224 (8,210)

<sup>1</sup> Solutions in ethanol,  $\lambda_{\max}$  m $\mu$  ( $\epsilon$ ) given

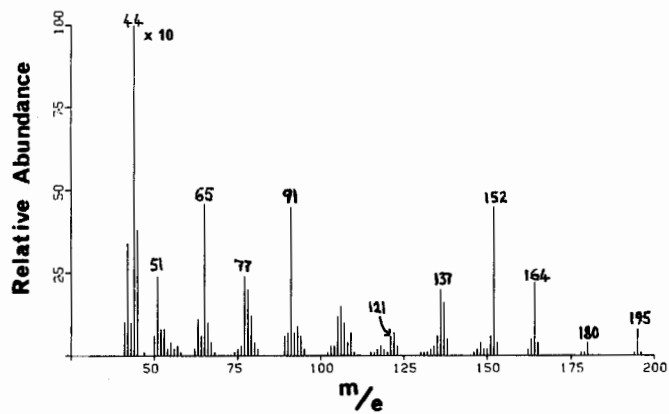
<sup>2</sup> Calculated as monohydrate

Table 3

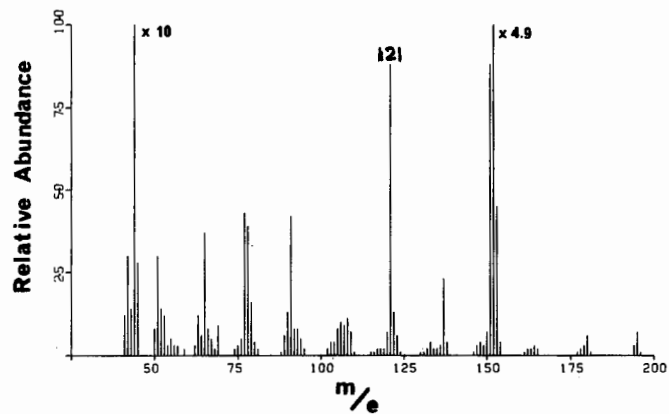
N.M.R. Spectral Data<sup>1</sup> for Dimethoxyamphetamines

Compound	$\beta\text{CH}_3$ (d)	$\text{NH}_2$	$2\alpha\text{H}$ (2 dd)	$\beta\text{H}$ (m)	$\text{ArOCH}_3$	Aromatic Protons
2,3-	8.88 (6.0)	8.12	7.44 (-12.7, 8.7) 7.30 (-12.7, 4.1)	6.81	6.18, 6.16	2.87-3.36 m
2,4-	8.92 (6.0)	8.35	7.54 (-13.0, 8.2) 7.36 (-13.0, 4.6)	6.84	6.22, 6.22	3.55 d, C-3; 3.58 dd, C-5; 2.99 d, C-6
2,5-	8.91 (5.8)	8.08	7.51 (-12.5, 8.4) 7.35 (-12.5, 4.4)	6.83	6.29, 6.29	2.32
2,6-	8.90 (6.0)	7.30	7.31 (degenerate) 7.31	6.85	6.21, 6.21	3.45 "d", C-3 and C-5; 2.84 "dd", C-4
3,4-	8.89 (6.0)	7.90	7.53 (-13.0, 8.4) 7.35 (-13.0, 4.5)	6.85	6.15, 6.15	3.07-3.40 m
3,5-	8.88 (6.0)	8.09	7.57 (-13.0, 8.5) 7.37 (-13.0, 4.3)	6.83	6.25, 6.25	3.66

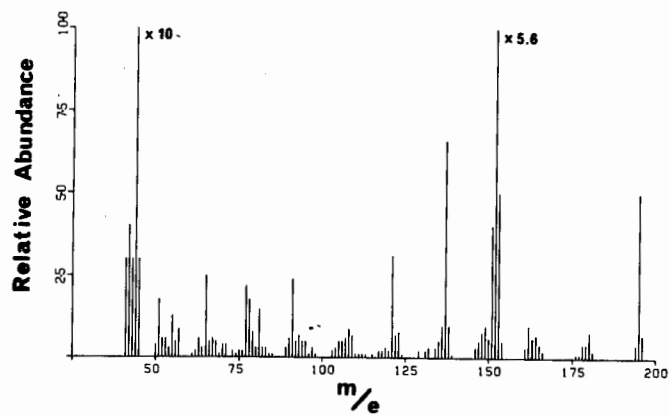
<sup>1</sup> $\tau$ -Values, measured by Mr. H.W. Avdovitch of this Division with a Varian A-60A spectrometer, solutions ca 15% in  $\text{CDCl}_3$  at  $40^\circ$  containing TMS as internal standard. Coupling constants of the  $\alpha$  protons (in Hz, calculated by the ABX method) are thought accurate  $\pm 0.1$  Hz. The  $\text{NH}_2$  protons ( $\tau$  - concentration dependent) exchange with  $\text{D}_2\text{O}$ . Appropriate integration ratios were observed. The signals were singlets except where d = doublet, dd = double-doublet, and m = multiplet.



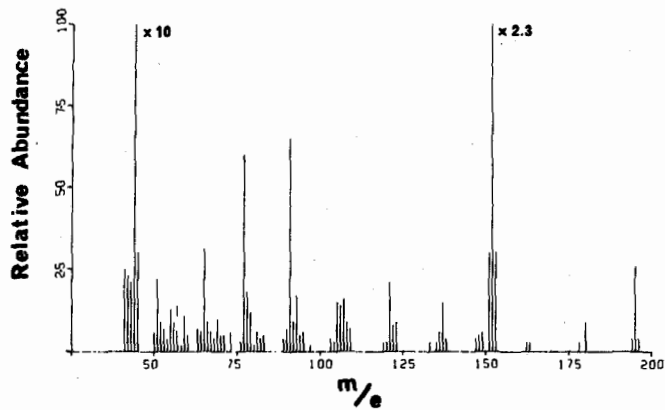
**Fig.1 2,3- Dimethoxyamphetamine .HCl**



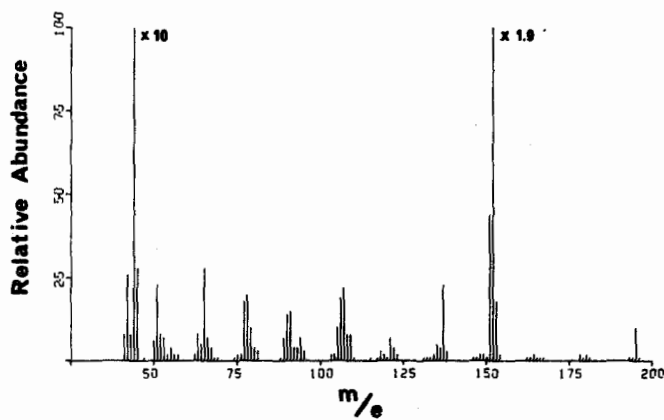
**Fig. 2 2,4- Dimethoxyamphetamine .HCl**



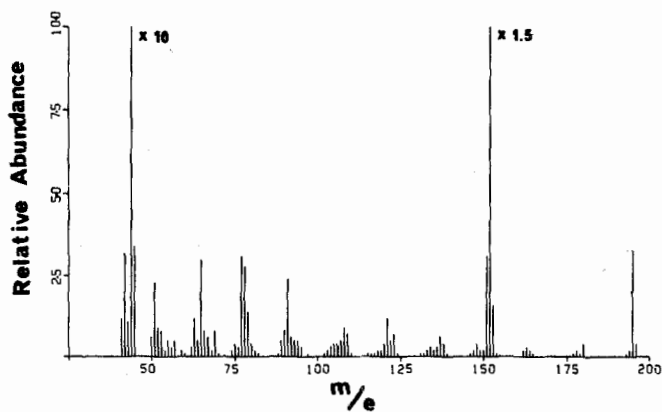
**Fig. 3 2,5- Dimethoxyamphetamine .HCl**



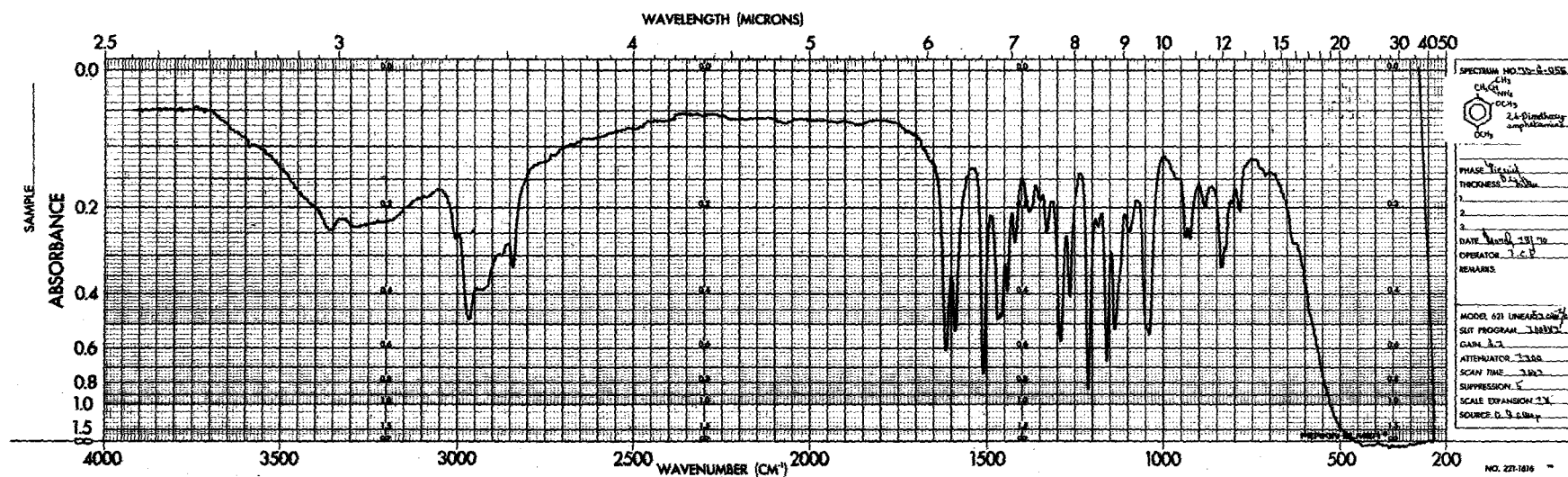
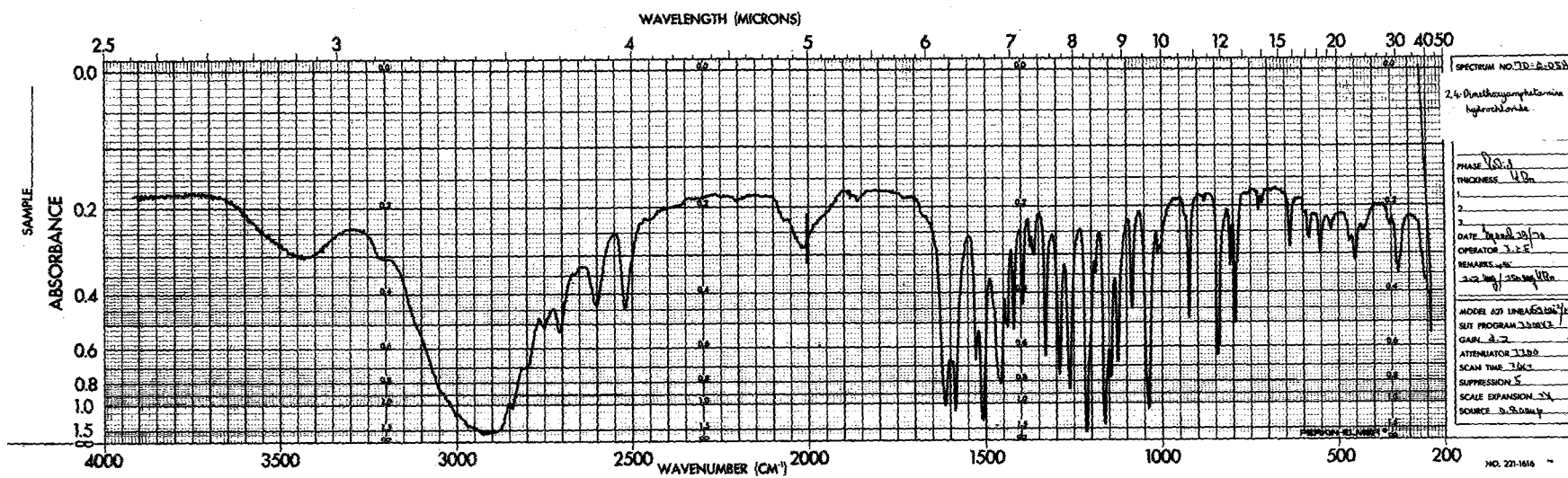
**Fig. 4** 2,6-Dimethoxyamphetamine.HCl

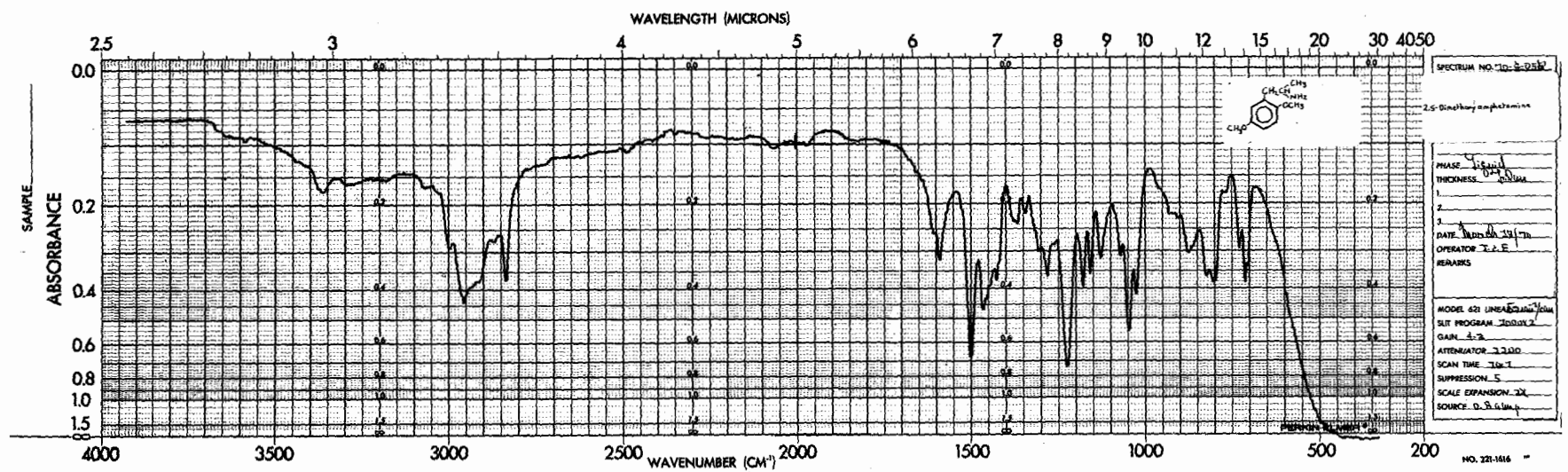
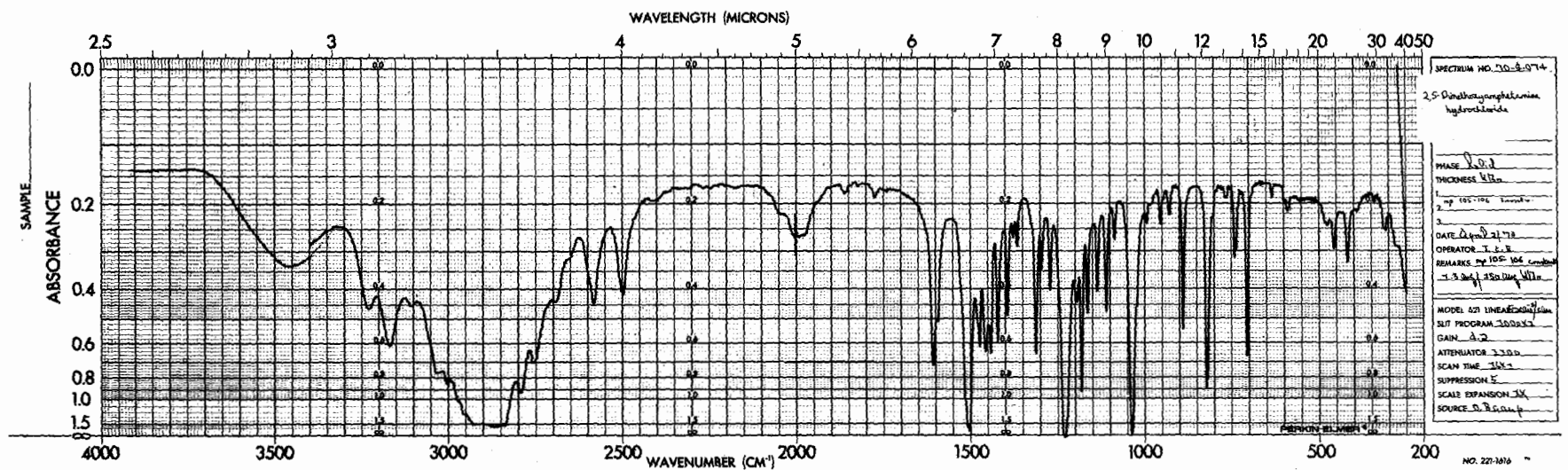


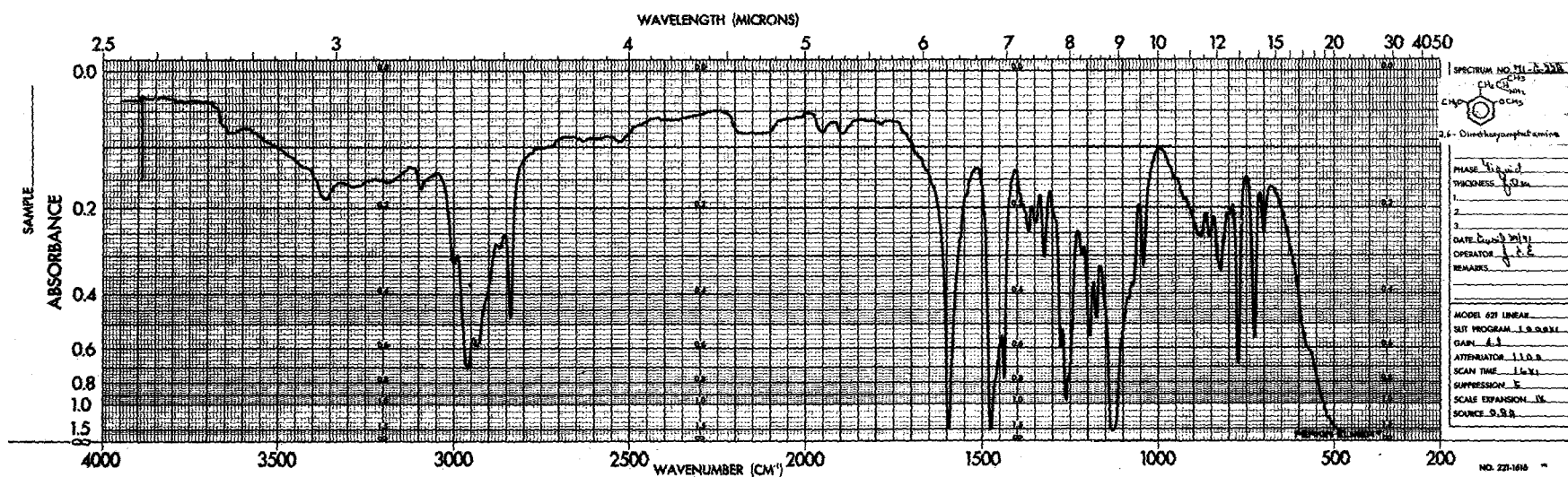
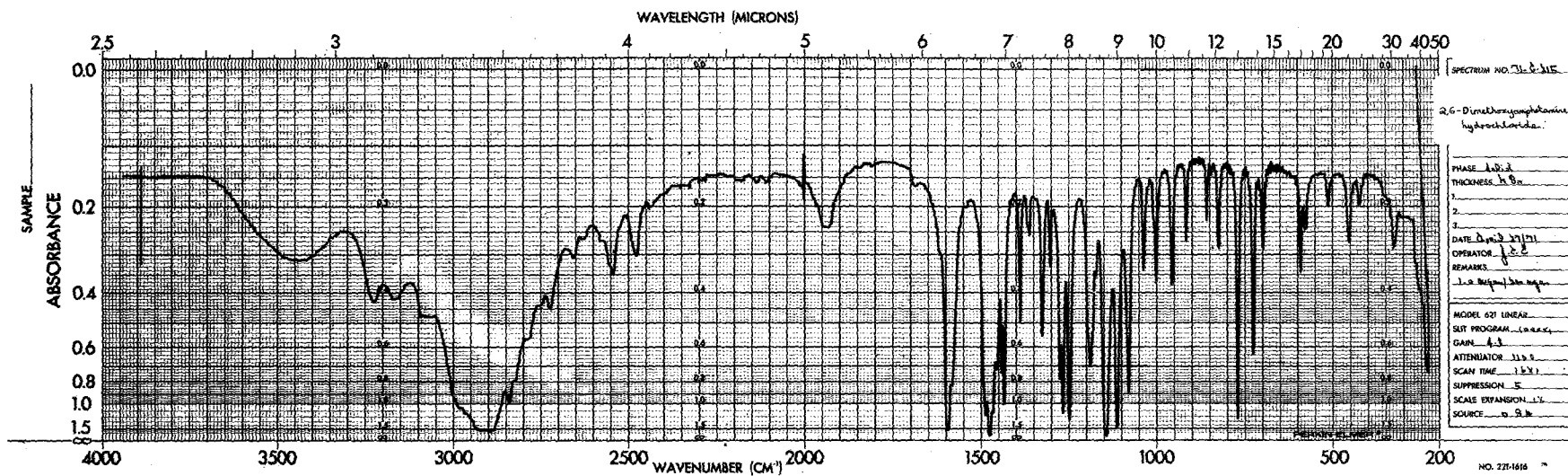
**Fig. 5** 3,4-Dimethoxyamphetamine.HCl

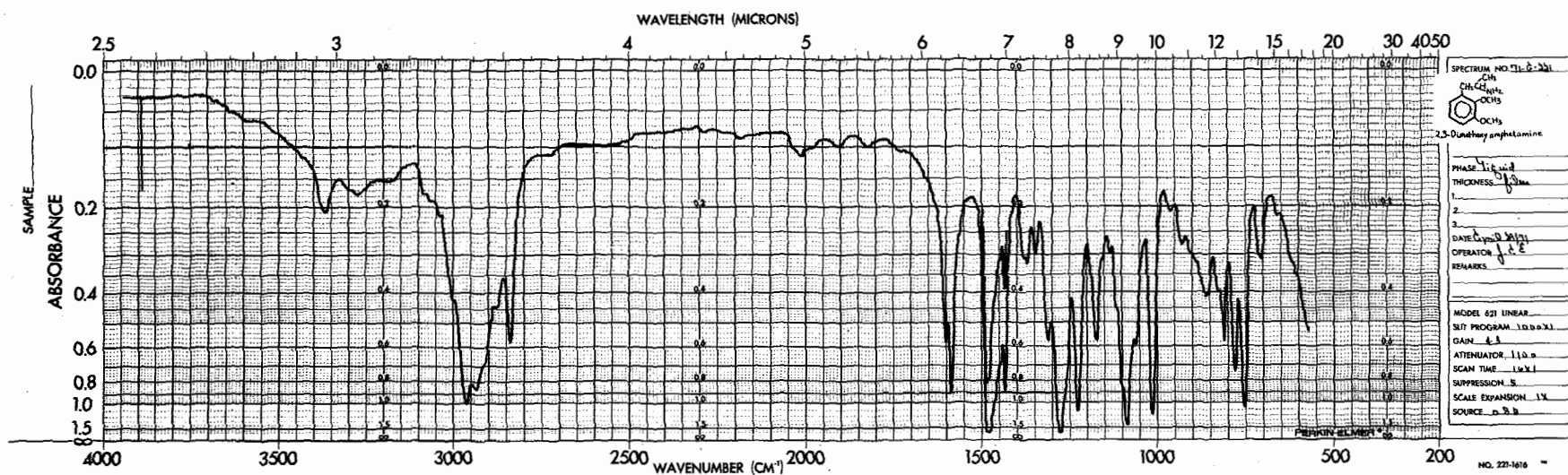
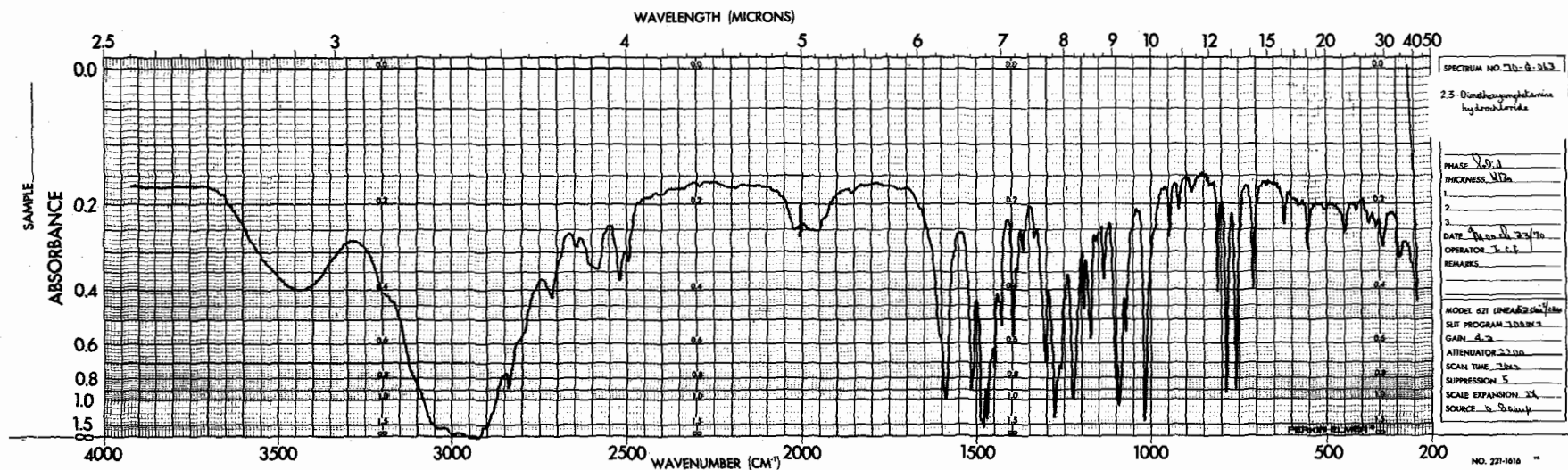


**Fig. 6** 3,5-Dimethoxyamphetamine.HCl

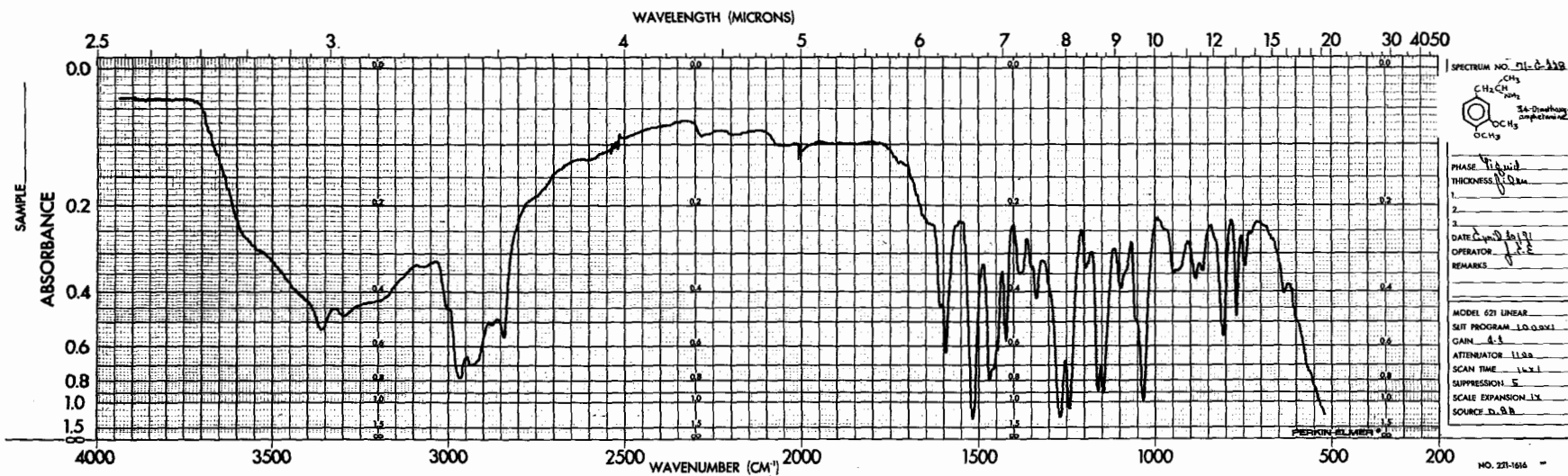
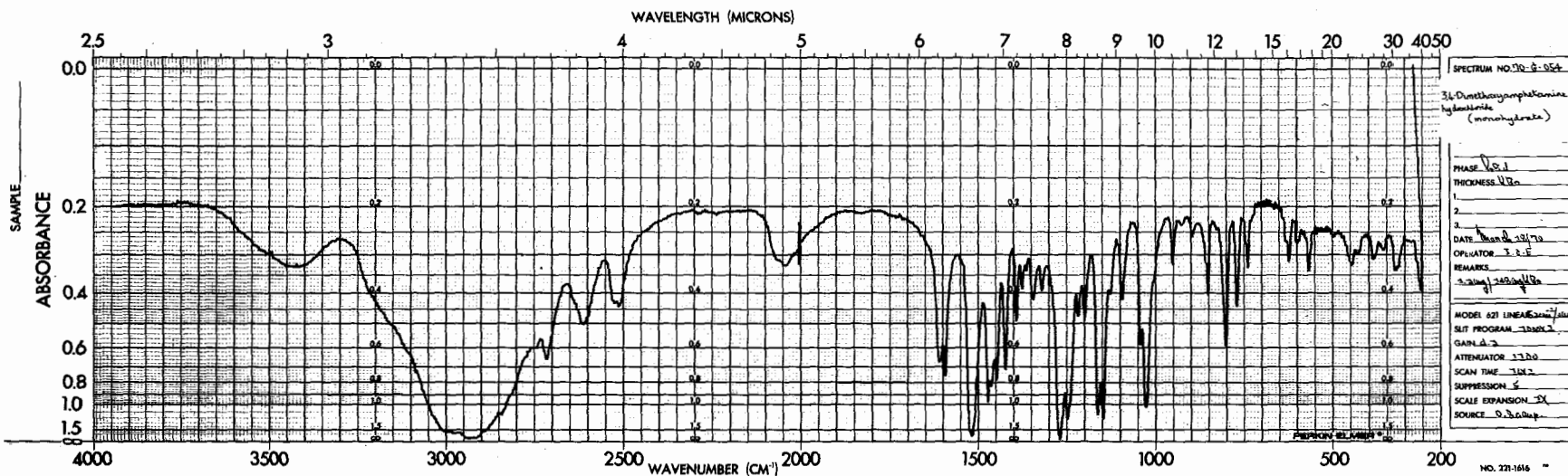


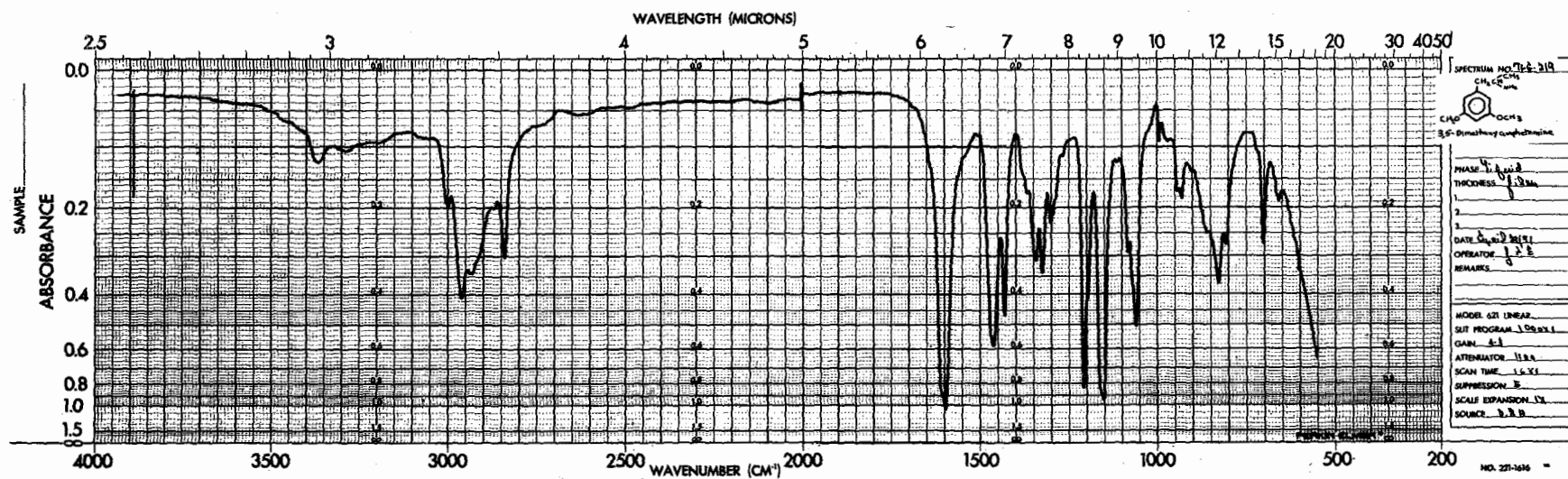
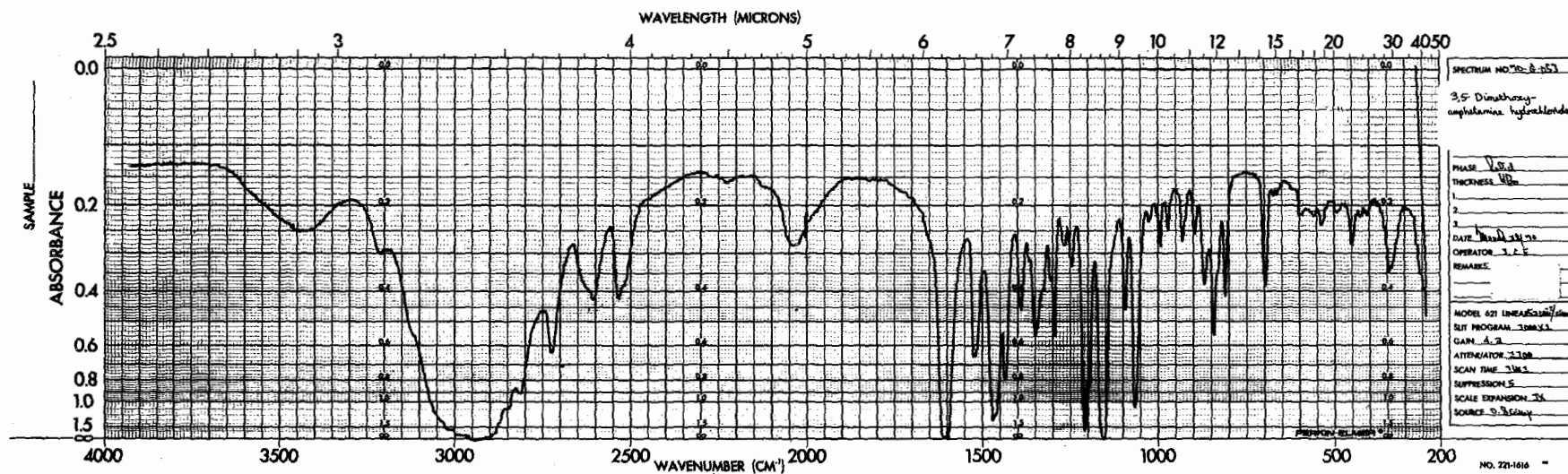














# BNDD LABORATORY NOTES

DATE June 9, 1971

NO. 18

DRUG TYPE

METHODOLOGY

## The Determination of Opium Alkaloids in Anti-Diarrheal Preparations

Stanley Koch\* and Joseph Levine\*\*

### Introduction

Powdered opium as such, or as the camphorated tincture, is frequently formulated with kaolin and/or other adsorbents and protectives in anti-diarrheal preparations. We have encountered problems in this laboratory attempting to analyze these opium alkaloids, as they are difficult to isolate from such a mixture. This is apparently due both to the adsorptive nature of kaolin, and probably to a lesser degree, to the occlusion brought about by bismuth salts. Both of these effects are more pronounced in alkaline solutions.

We have found that the following extractive procedure effectively removes from these mixtures the alkaloids of interest, permitting routine identification. The method is applicable to both tablets and suspensions. It may well be capable of providing adequate quantitative analyses, if not as written, with some modification, depending on the preparation. We have not investigated the method from this standpoint.

### Experimental

Grind tablets thoroughly before sampling. Heat suspension on a steam bath to drive off any alcohol present. Take an amount of tablet triturate or suspension to provide the equivalent of 10-25mg. powdered opium; this amount is dependent upon the analyses to be performed on the isolate. Add approximately 2ml. of dimethyl sulfoxide (DMSO) and mix to a smooth consistency. Slowly add about 5ml. pH<sup>4</sup> citrate buffer (M/2) followed by an amount of acid-washed Celite 545 to provide, on thorough mixing, a fluffy consistency suitable for packing in a chromatographic column. This usually requires as much Celite as the combined weights of the non-support constituents. Transfer to a standard, 25 x 250mm glass column containing a pledget of glass wool, tamp to a uniform mass, and cover with a mat of glass wool. Use two or more columns should the quantity of Celite require it (about 5-6gms. Celite per column maximum).

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Present Address: U.S. Food & Drug Administration, Rockville, Maryland

\*\*U.S. Food & Drug Administration, Washington, D.C.

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BND-115 (9/69)

Pass 100ml. water-washed ether through the column and discard. Follow ether with 100-150ml. water-washed chloroform; this fraction should contain the major portion of papaverine and narcotine; thebaine is also to be found here. Then pass 150ml. of 1:25 di-(ethylhexyl) phosphoric acid (DEHP) in water-washed ether through column followed by 50ml. 1:100 DEHP. Concentrate the eluate to about 50ml. and extract with three 10ml. portions of N/2 sulfuric acid; add 2 grams sodium chloride to the extract, make basic with ammonium hydroxide, and extract with 3-4 small portions of 3:1 chloroform-isopropanol. Evaporate this extract to a small volume and proceed with analysis for morphine and codeine.

Identification of the major opium alkaloids in this laboratory was accomplished by TLC and GLC. The TLC systems included: [chloroform: dioxane:ethyl acetate:ammonium hydroxide (25:60:10:5)]; and [ethyl acetate:benzene:ammonium hydroxide (60:35:5)] using iodoplatinate spray for visualization. The GLC column used was 3% OV-17 at 264°C, using a flame detector.

#### Discussion

The method as described effectively permits the separation and identification of the primary opium alkaloids when in combination with certain adsorbents and/or protectives. The success of the procedure is dependent on proper sample preparation and relies on the ability of DEHP to extract morphine and certain other alkaloids, conditions permitting, from acidic solution. The DEHP anion forms an ion pair with morphine. Because of the large bulk of the organic moiety in the molecule, the charge, in effect, is occluded and the salt becomes soluble in organic solvents.

DMSO provides an excellent solvent for the opium alkaloids and its use is suggested to enhance their release (1). It may prove beneficial, in efforts at quantitation, to increase the exposure time of the alkaloids to DMSO immediately prior to column packing. Heating the alkaloids in DMSO on a steam bath has been found to expedite dissolution. (2)

Attempts at quantitation might be more successful if the following points are kept in mind:

1. The use of a pH5 buffer on the column will facilitate morphine elution with DEHP. However, a more acid column will retain morphine and codeine to a greater extent during the  $\text{CHCl}_3$  wash.

2. All the alkaloids can be eluted together in the DEHP eluate by eliminating the  $\text{CHCl}_3$  wash. However, the practicality of such a move is dependent on the impurities, excipients, etc. found in this eluate. The  $\text{CHCl}_3$  wash, in addition, may prove desirable as a means of separating and isolating certain of the alkaloids; i.e., noscapine, papaverine, and narcoteine.
3. The volume of the  $\text{CHCl}_3$  wash may have to be increased to quantitatively remove papaverine and narcoteine.
4. The volume of the DEHP in ether may necessitate an increase in order to remove all the morphine.

References

- (1) Levine, J., and Doyle, T.D., J. Pharm. Sci. 56, 619-622 (1967)
- (2) Smith, E., JAOAC 53, 603-608 (1970)



# BNDD LABORATORY NOTES

DATE June 10, 1971

NO. 20

DRUG TYPE Barbiturates

METHODOLOGY Infrared Spectrophotometry

## BARBITURATE IDENTIFICATION BY FAR INFRARED SPECTROSCOPY

by

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Dallas Regional Laboratory  
Bureau of Narcotics & Dangerous Drugs

### INTRODUCTION

Barbiturates show changes in infrared spectrum due to changes in crystal form relating to the method of alkali halide disk preparation. This was demonstrated by Cleverley and Williams (1) for the regions 1800-1600 and 900-700  $\text{cm}^{-1}$ . The infrared spectra of a barbiturate is also characterized by the nature of the substitution groups and whether it is the acid or salt form. (2) The barbiturates sampled in the KBr disk form also exhibit infrared spectra between 700  $\text{cm}^{-1}$  and 250  $\text{cm}^{-1}$ . These bands are characteristic of barbiturate functional groups and can be used as an aid in the identification of the drugs. (3)

After isolation of an unknown barbiturate, the analyst will find it advantageous to obtain an infrared spectra of the drug between 700 and 250  $\text{cm}^{-1}$ . This region does not show spectral variation due to the change of crystal form when the barbiturate is prepared for sampling in a KBr disk.

Barbiturates are encountered in the form of tablets, capsules, or in solutions. For the purpose of identification, it is usually necessary to separate it from other drugs or from its own decomposition products.

- (1) Cleverley, B. and Williams, P. P. (1959) *Chem. Ind.* 78, 49
- (2) Clarke, E. G. C. Isolation and Identification of Drugs (1969) The Pharmaceutical Press, London.
- (3) Freeman, S. K., Interpretive Spectroscopy, P. 148, Reinhold Publishing Corporation New York, 1965.

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BND-115 (9/69)

The barbiturates are isolated from other drugs and material by extraction from an aqueous acidic solution with an organic solvent (4). A solvent of choice is ethyl ether since the free barbituric acids are very soluble, whereas other organic salts, acids, or excipients are usually less soluble in ether.

#### APPARATUS

Perkin-Elmer 457 Infrared Spectrophotometer; Centrifuge, Centrifuge tubes.

#### REAGENTS

Spectrograde KBr; Anhydrous Ethyl Ether; Anhydrous Sodium Sulfate; 6M H<sub>2</sub>SO<sub>4</sub>; and 1M NaOH.

#### METHOD

A representative portion of the sample is transferred to a centrifuge tube with water and made alkaline with 1M NaOH. The aqueous solution is extracted several times with CHCl<sub>3</sub> and the CHCl<sub>3</sub> discarded through a narrow tube with the aid of suction. Add 6M H<sub>2</sub>SO<sub>4</sub> to the aqueous solution until acidic then extract with ether. Filter the ether through anhydrous sodium sulfate and evaporate the filtrate. Make a KBr disk of the dry residue and obtain an infrared spectra from 4000 cm<sup>-1</sup> to 250 cm<sup>-1</sup>. For screening identity, make a comparison of the sample spectra to a standard spectra between 700 cm<sup>-1</sup> and 250 cm<sup>-1</sup>.

#### RESULTS AND DISCUSSION

The isolation procedures aids in reducing or eliminating interfering compounds found in combination with barbiturate drugs. Interfering organic neutral compounds and organic bases are removed by CHCl<sub>3</sub> from the alkaline media or reduced to a concentration where they will not contribute significantly to the barbiturate infrared spectra. Most excipient compounds remain in the aqueous media as sulfate salts and do not partition into the ether extract. To remove light particulate matter from the ether extract, and to remove excess water from the solvent resulting in reduced drying time of the extracted barbiturate residue, the solvent is passed through a sodium sulfate column.

- (4) Higuchi, T., Hanssen, E.B., Pharmaceutical Analysis, Interscience, New York, 1961.

Of the 20 barbiturates tested, all show two strongly absorbing bands near 500 and 400  $\text{cm}^{-1}$  with the exception of the Thiobarbiturate, Thiopentobarbital. This drug has a single strongly absorbing band at 500  $\text{cm}^{-1}$ . Caffeine, Diphenylhydantoin, Mesantoin, Theophylline,

each having a functional group  $\begin{array}{c} \text{O} \quad \cdot \quad \text{O} \\ | \quad | \\ -\text{N}-\text{C}-\text{N}-\text{C}- \\ | \quad | \end{array}$  occurring in a hetrocycle show strong bands at 500  $\text{cm}^{-1}$  and 400  $\text{cm}^{-1}$ . Bemegrade

Glutethimide have a group  $\begin{array}{c} \text{O} \quad \text{O} \\ | \quad | \\ -\text{C}-\text{C}-\text{N}-\text{C}- \\ | \quad | \end{array}$  occurring in a hetrocycle show a single strong band at 400  $\text{cm}^{-1}$ .

Low frequency molecular vibrations found in the far infrared are said to be sensitive to changes in overall structure of the molecule involved (5). This is an advantage in that the type of substitution at the number (5) position on the barbiturate ring would cause each barbiturate to have a characteristic spectra in the infrared region of 700  $\text{cm}^{-1}$  to 250  $\text{cm}^{-1}$ . Of the 20 barbiturates tested similarly all exhibit characteristic spectra between 700  $\text{cm}^{-1}$  and 250  $\text{cm}^{-1}$ . In addition to disimilar spectra, the effect of polymorphism is less in the far infrared region than it is in the regions of 1800-1600 and 900-700  $\text{cm}^{-1}$ .

To determine if polymorphism caused an effect in the 700-250  $\text{cm}^{-1}$  region, various methods of KBr disk preparation and sample recrystallization procedures were tried. In addition, other cooperating analysts obtained spectra using their own techniques of sample and KBr disk preparation. The methods that were tried included mechanical grinding, hand grinding, obtaining crystals from fast solvent evaporation and slow recrystallization of barbiturates from a solvent. Of the 20 different spectra obtained in Amobarbital, Secobarbital, Phenobarbital, Pentobarbital, Barbital, and Barbituric acid, only slight changes between spectra were noted and in no case as dramatic as in other regions of the normal infrared spectrum.

The existence of several well defined characteristic barbiturate spectra is demonstrated. The bands near 500 and 400  $\text{cm}^{-1}$  are strong and are useful for identification of this important class of compounds.

- (5) Freeman, S. K., Interpretive Spectroscopy, p. 165  
Reinhold Publishing Corporation, New York, 1965



ACKNOWLEDGEMENTS

Buddy R. Goldston  
Michael D. Miller  
John D. Wittwer, Jr.

B A R B I T U R A T E S

KBr Disks

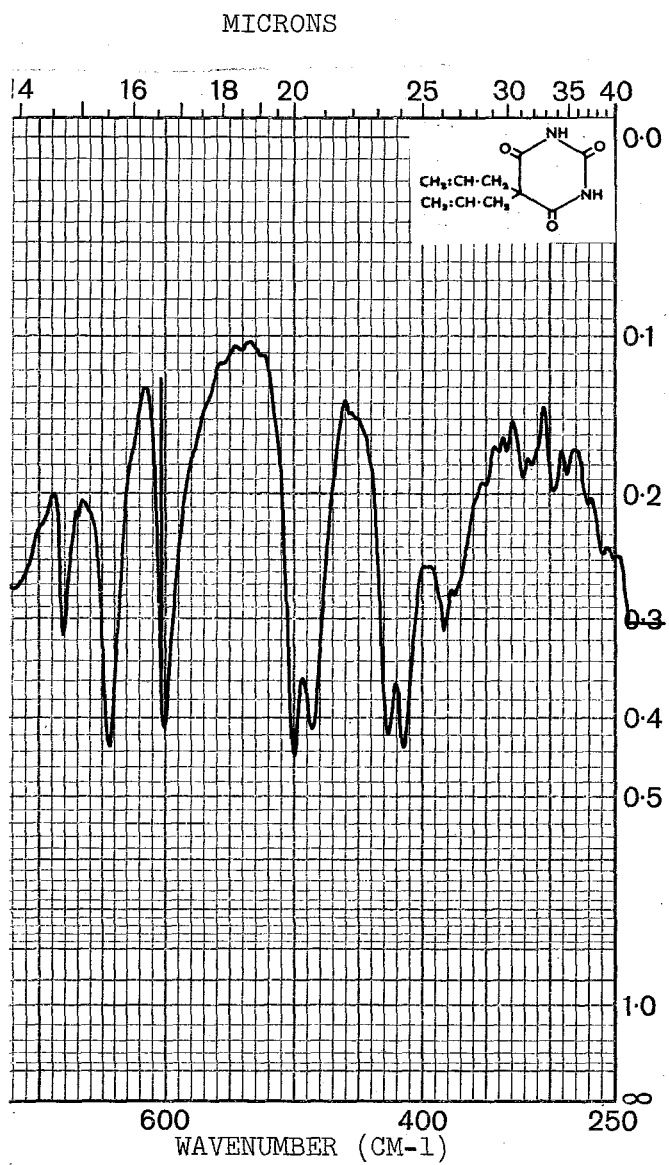
Concentration-- $\frac{1}{2}$  to 1%

Reference--Air

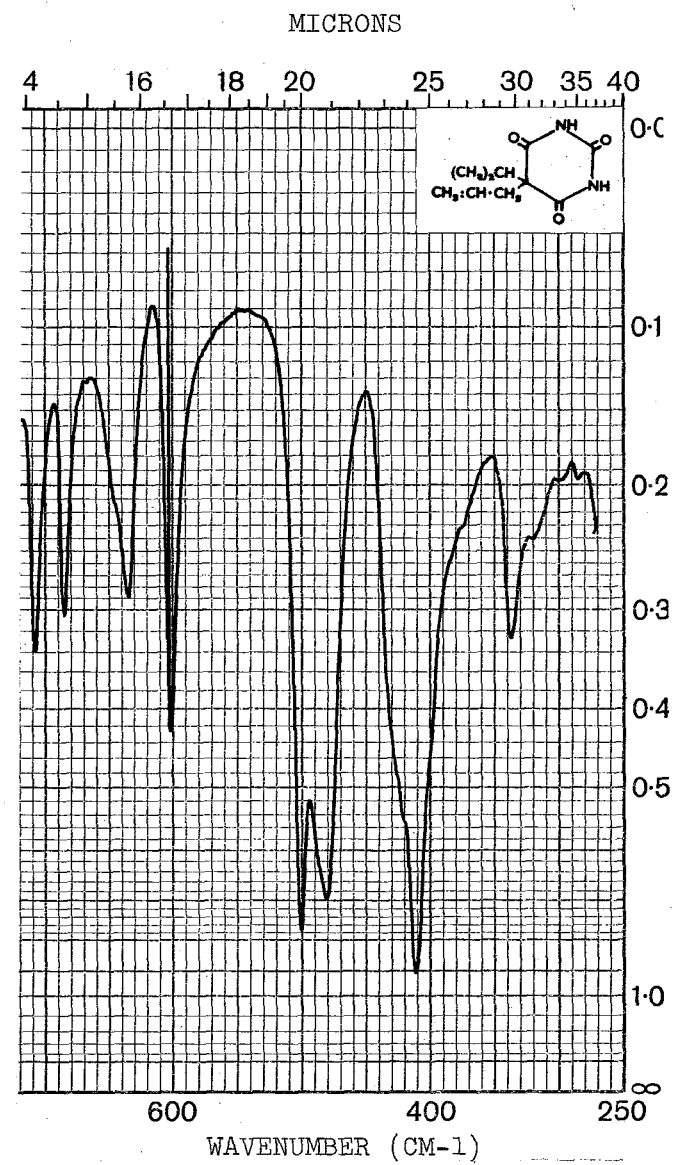
Scan Speed--Fast

Slit--N

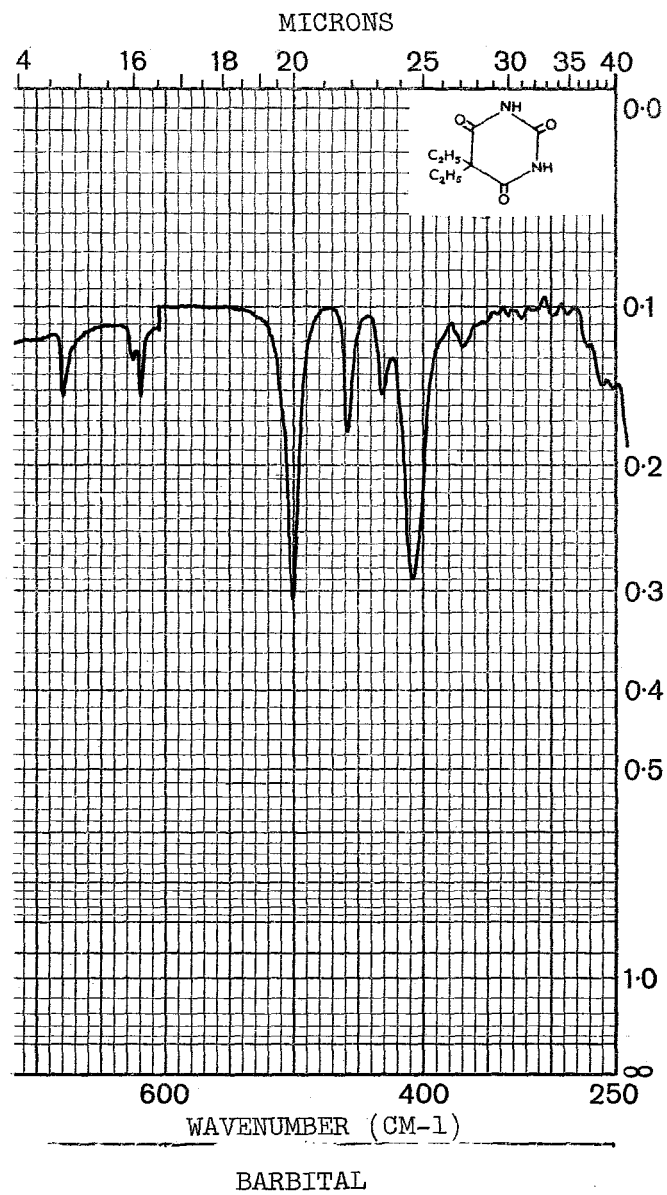
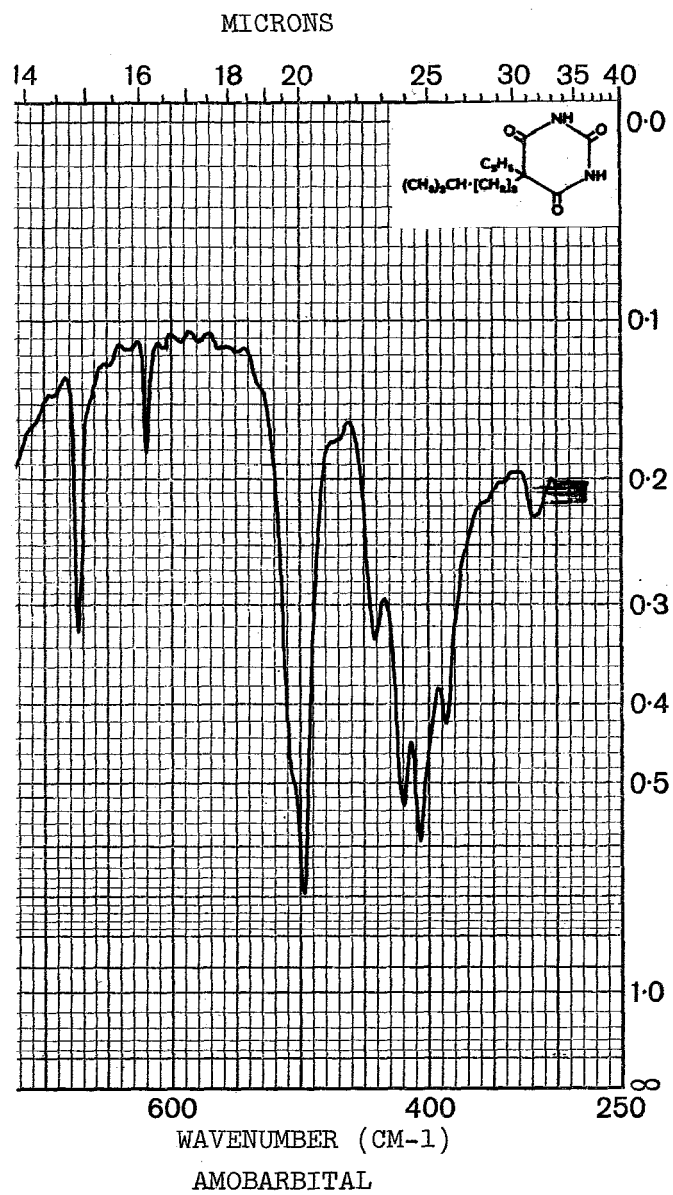
Perkin-Elmer 457 Infrared Spectrophotometer

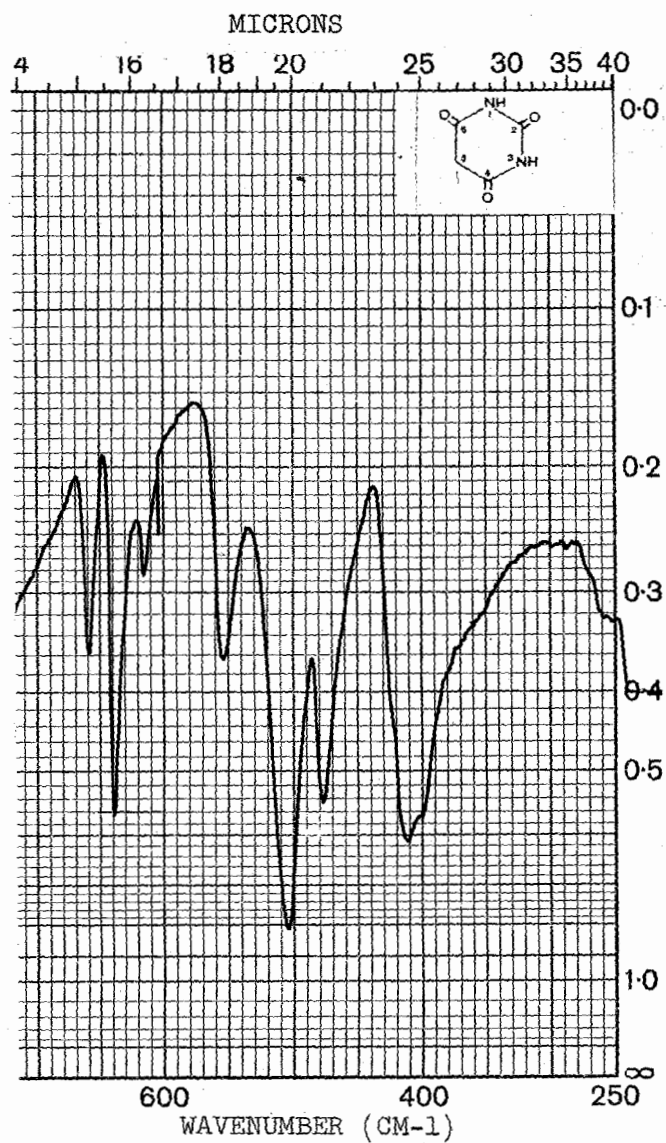


ALLOBARBITAL

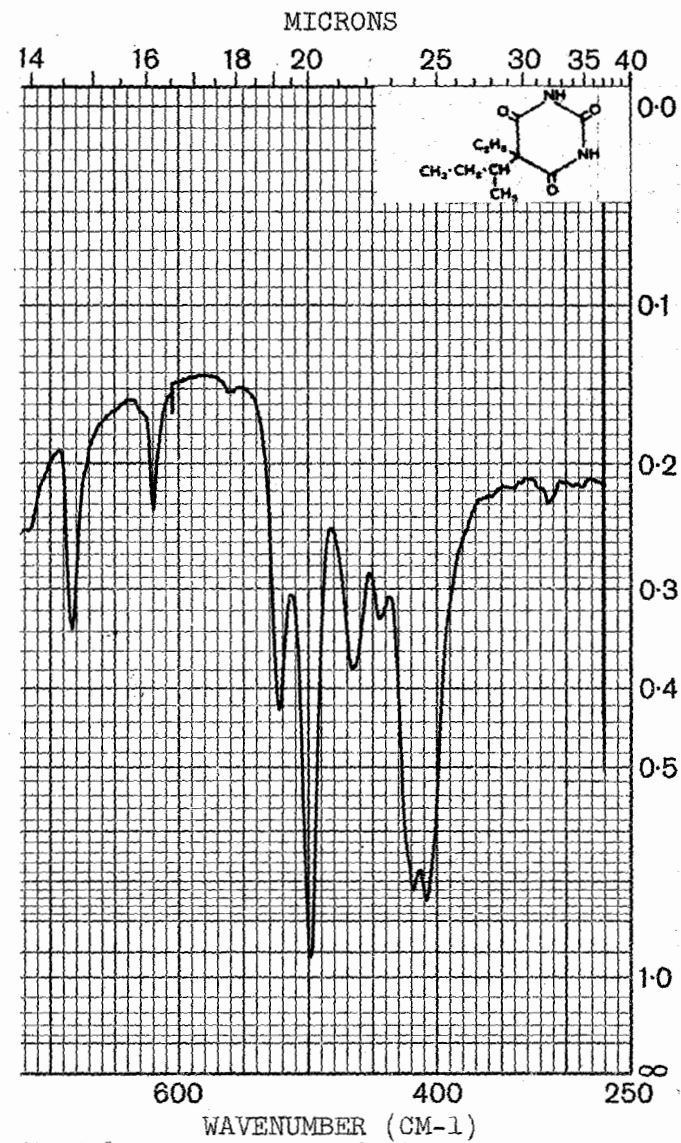


APROBARBITAL

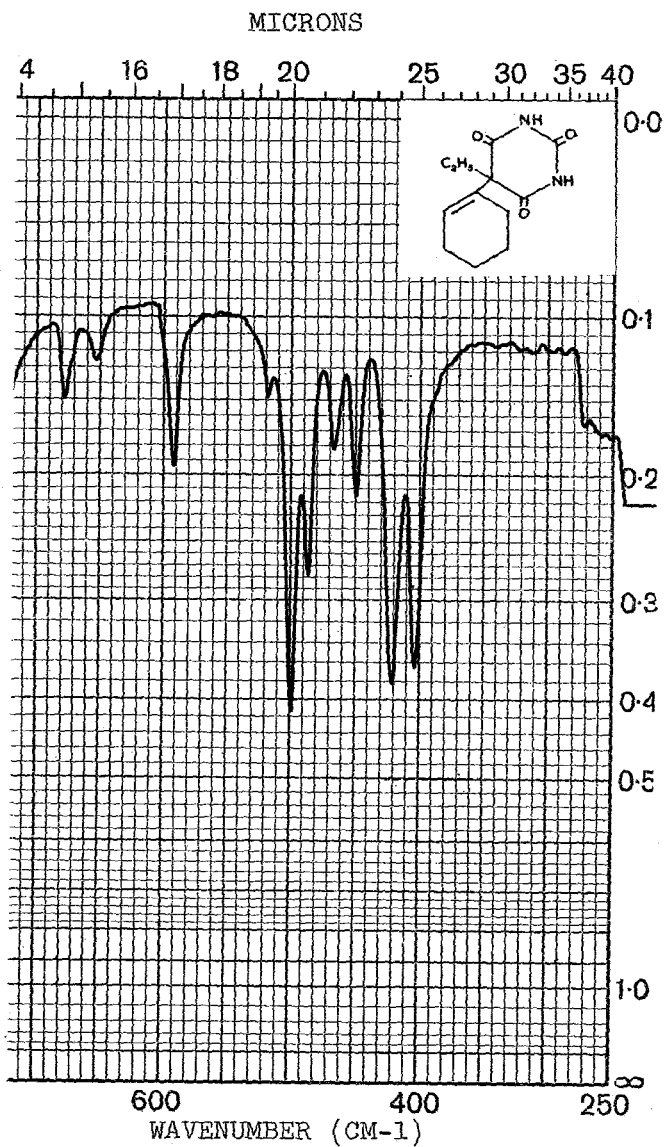




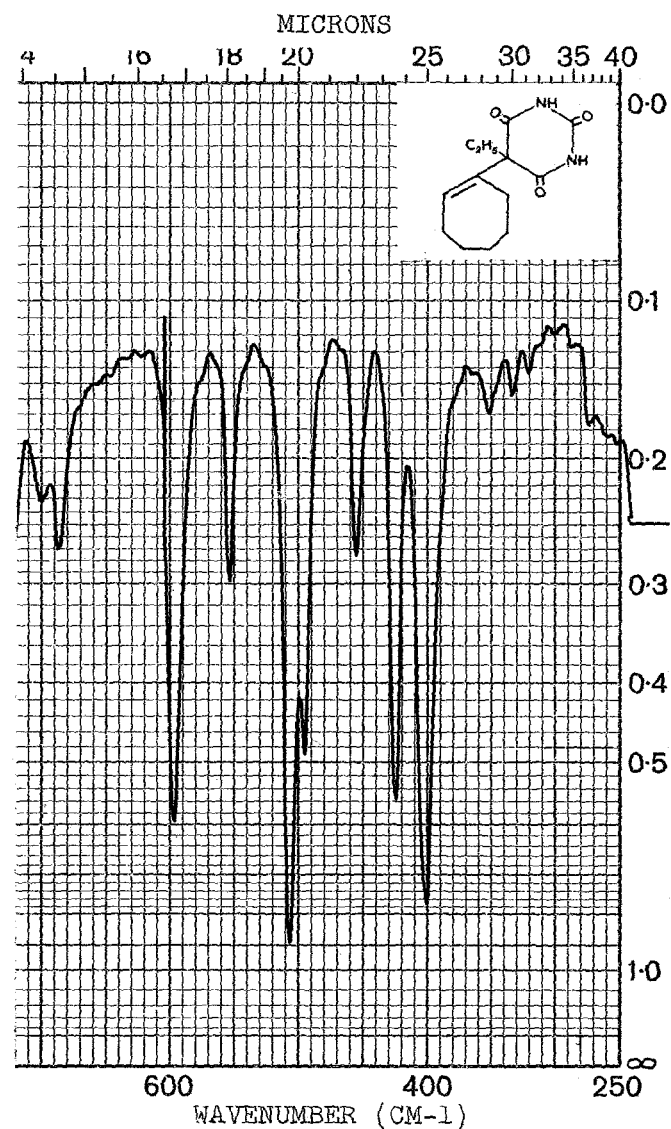
BARBITURIC ACID



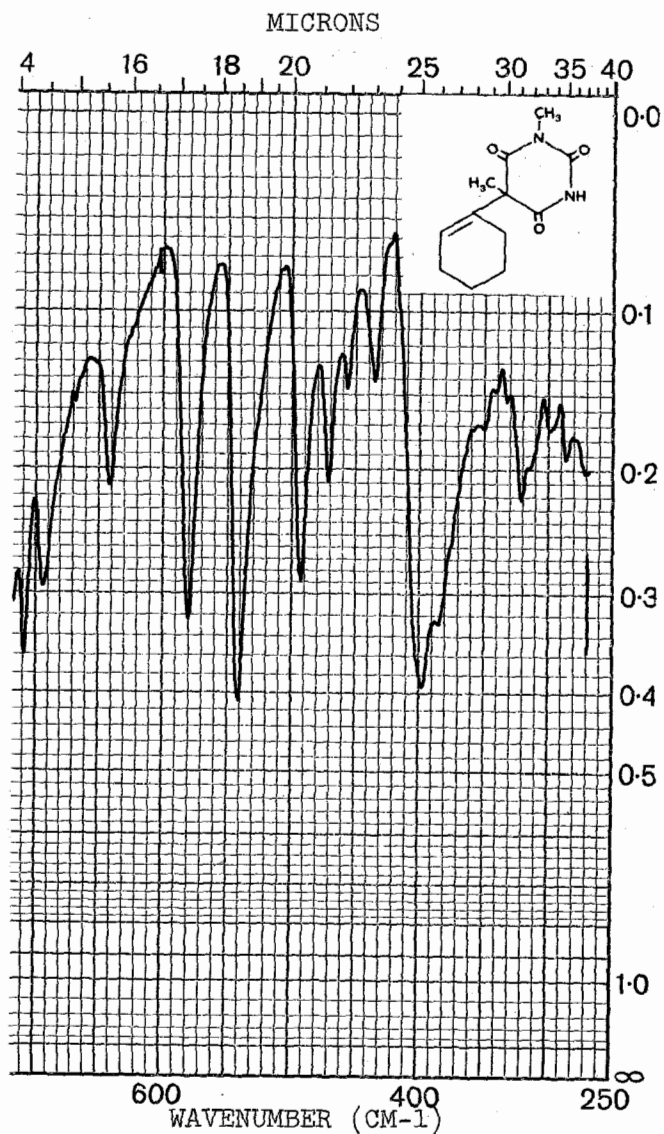
BUTABARBITAL



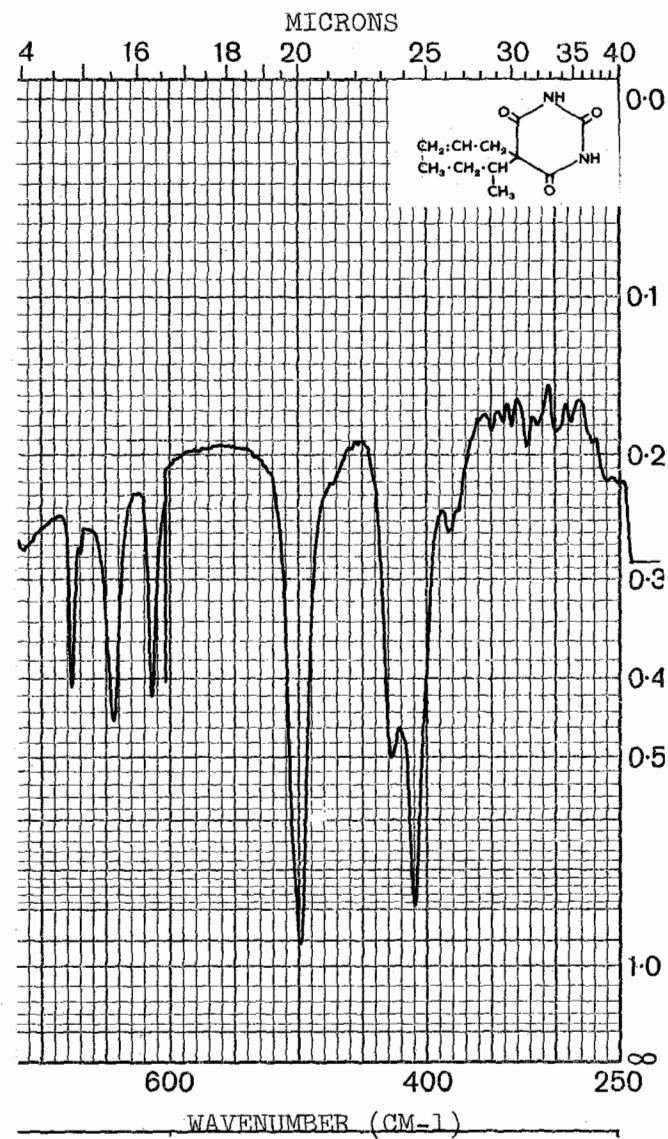
CYCLOBARBITAL



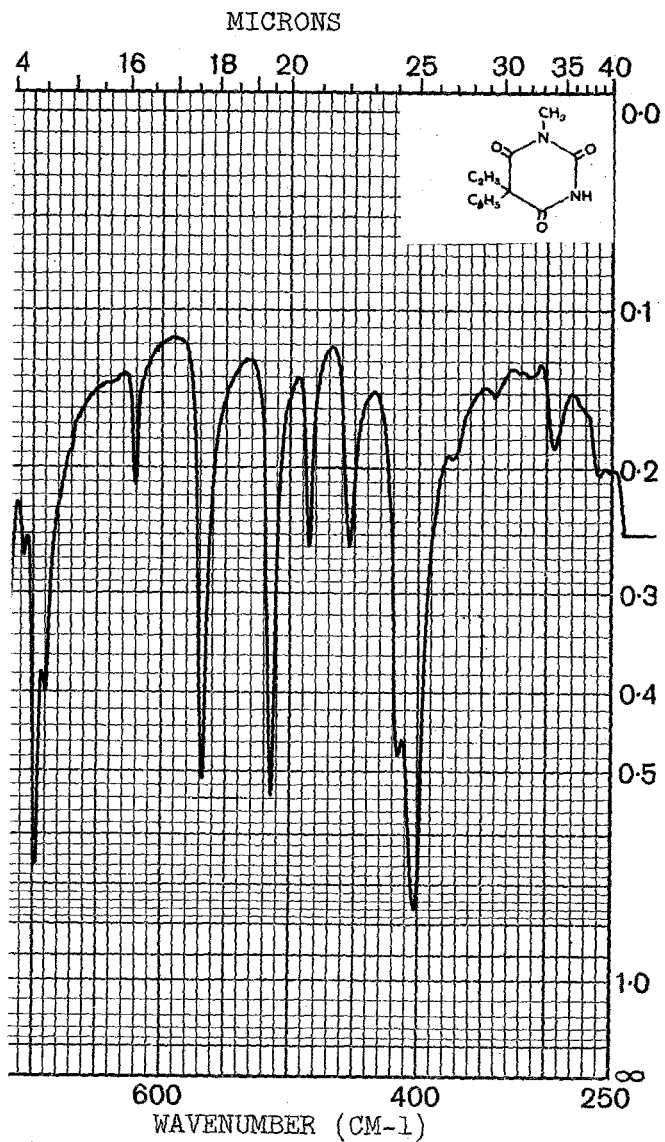
HEPTABARBITAL



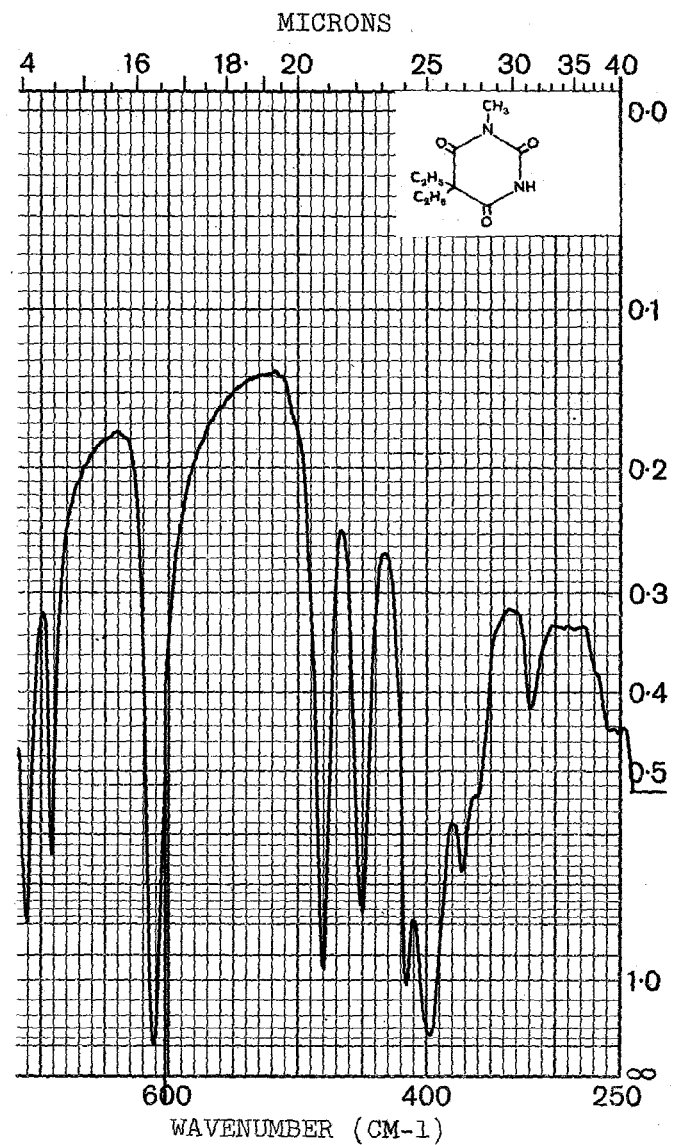
HEXOBARBITAL



ITOBARBITAL

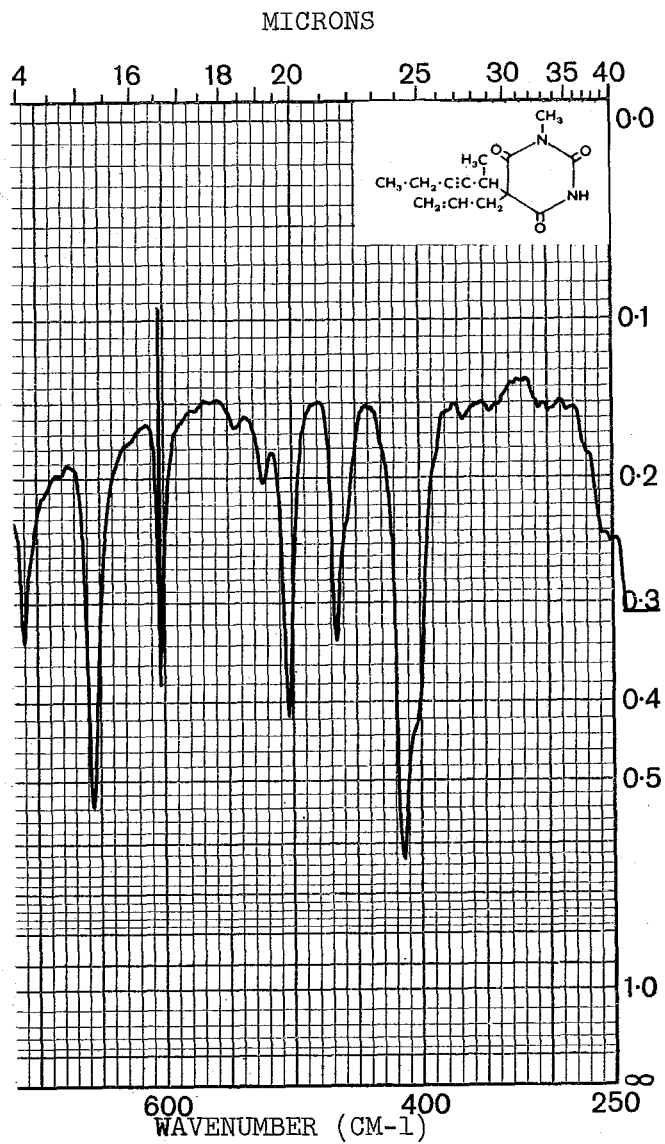


MEPHOBARBITAL

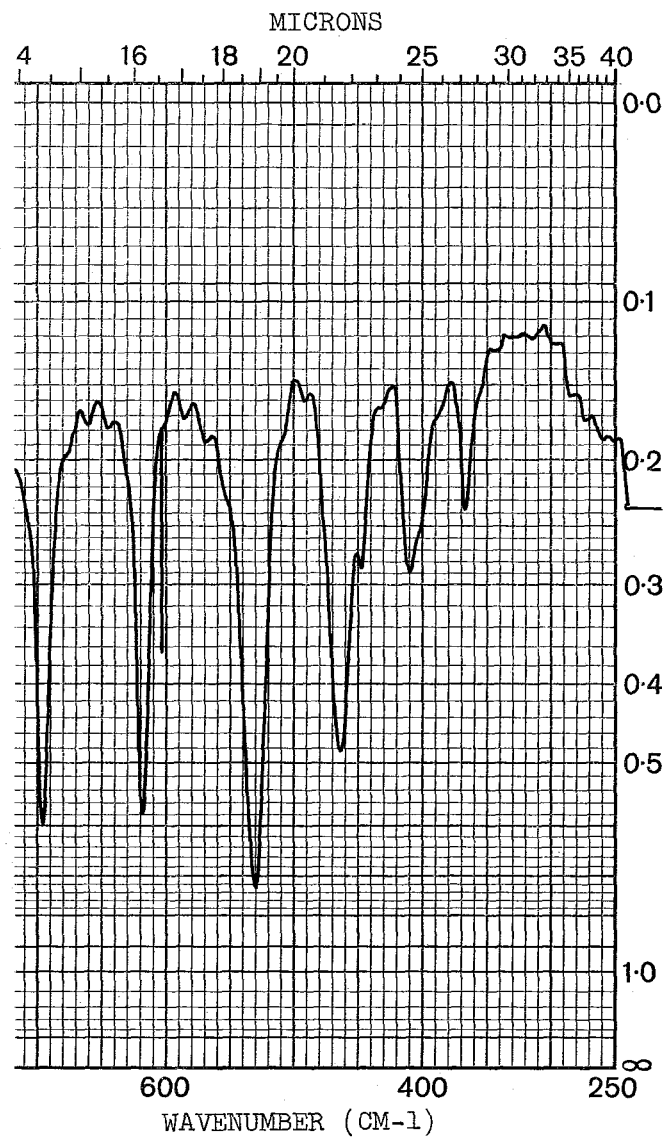


METHARBITAL

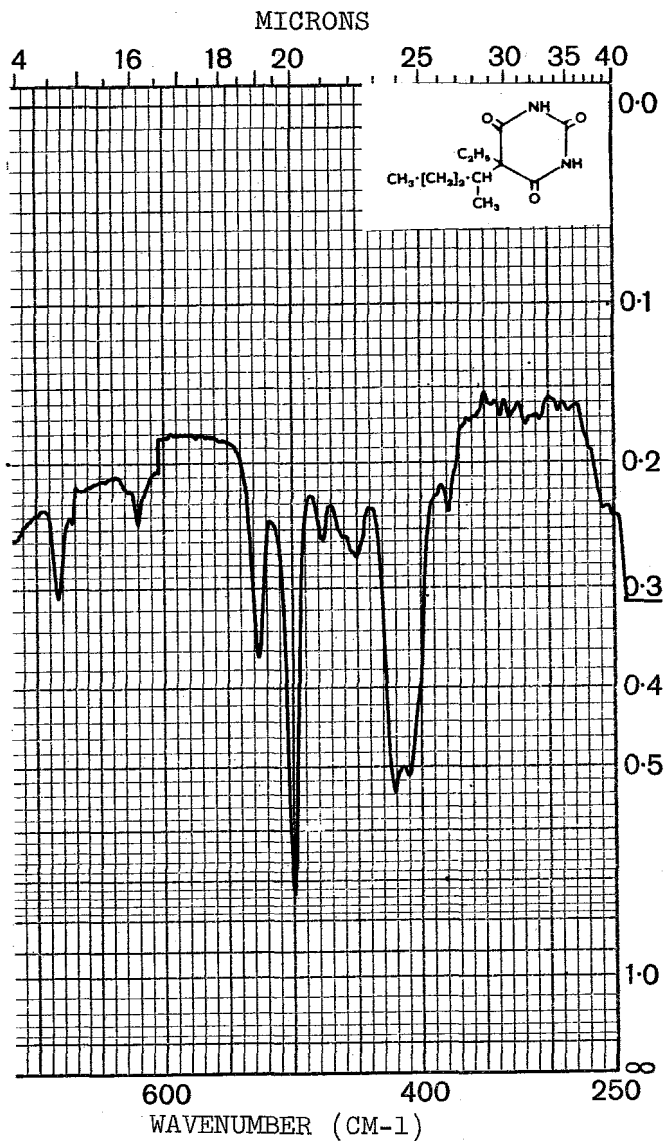




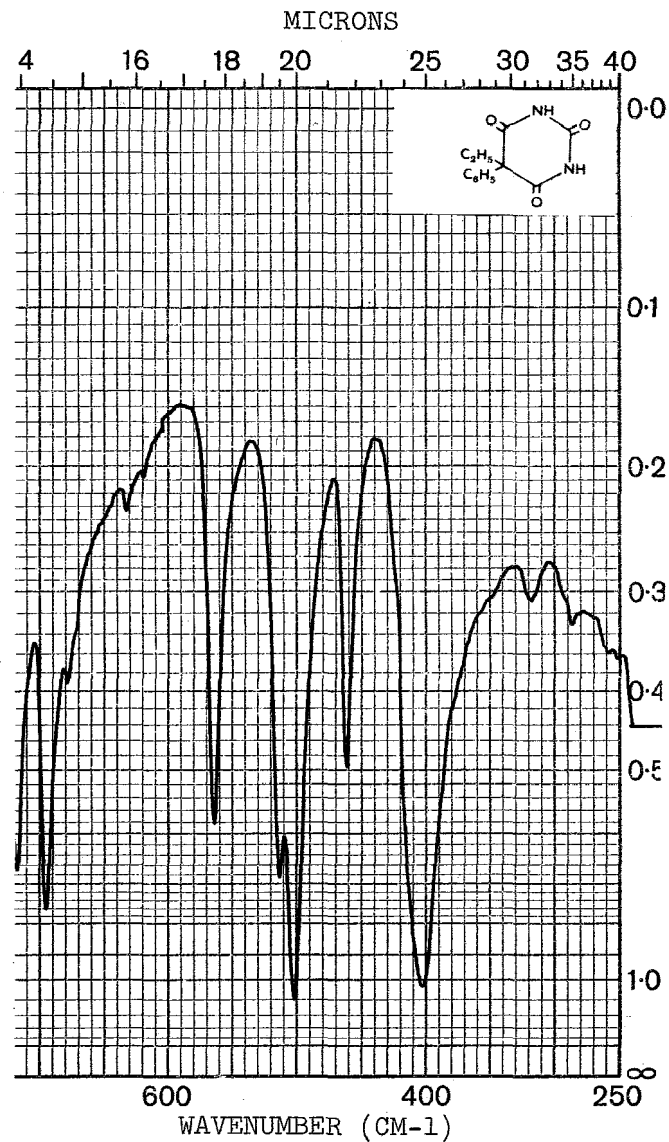
METHOHEXITAL



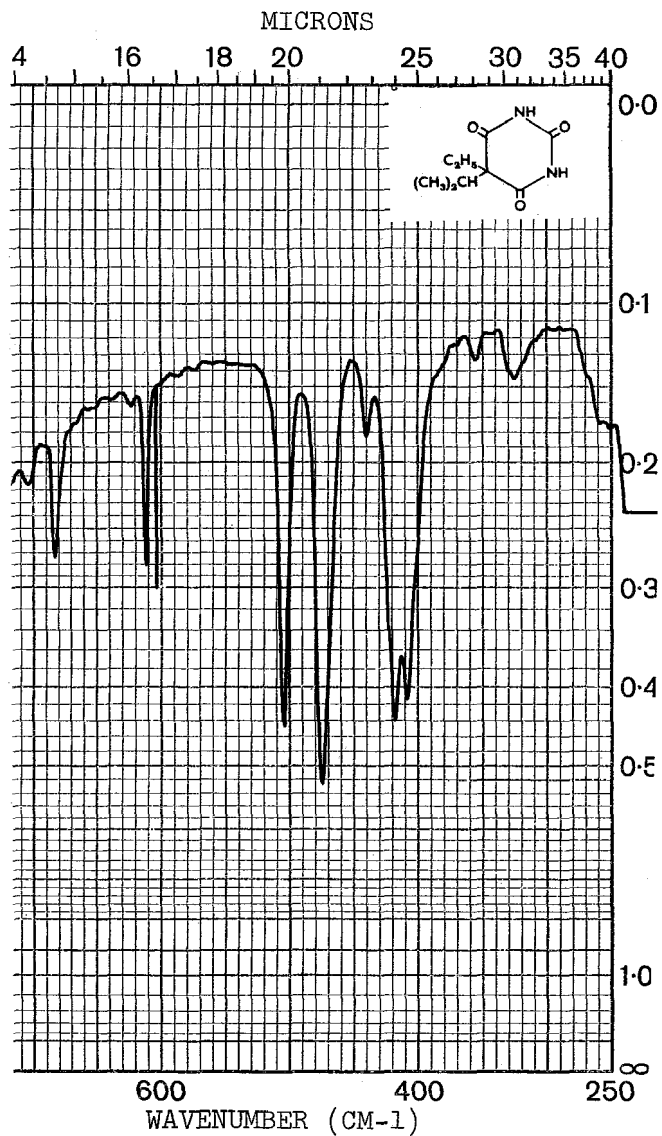
5-NITRO BARBITURIC ACID



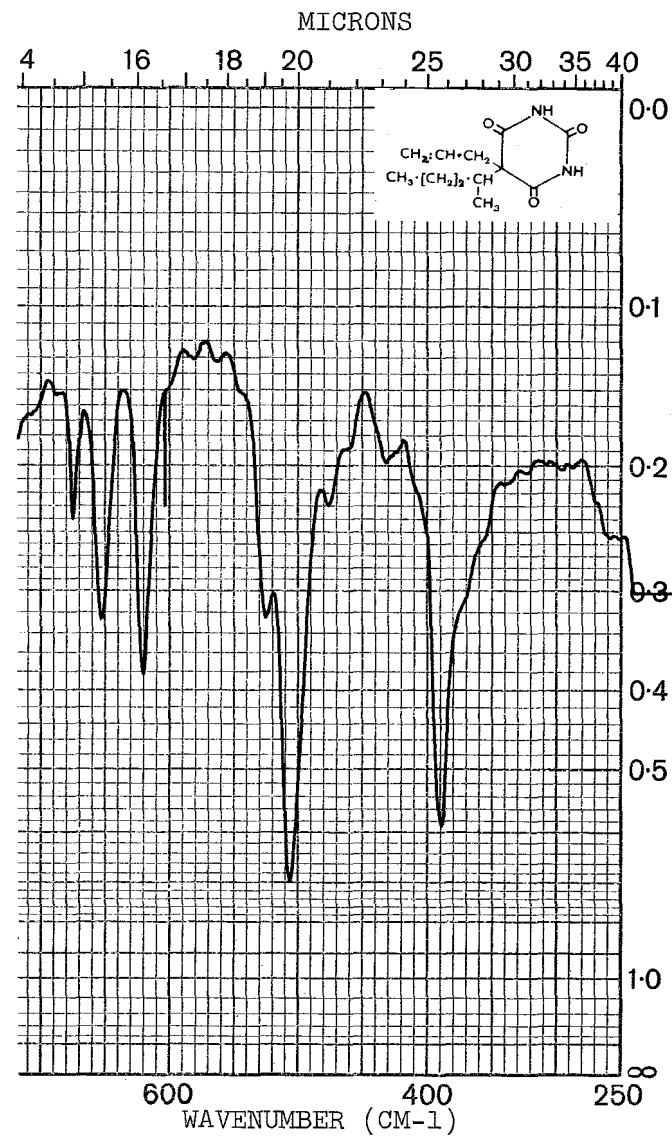
PENTOBARBITAL



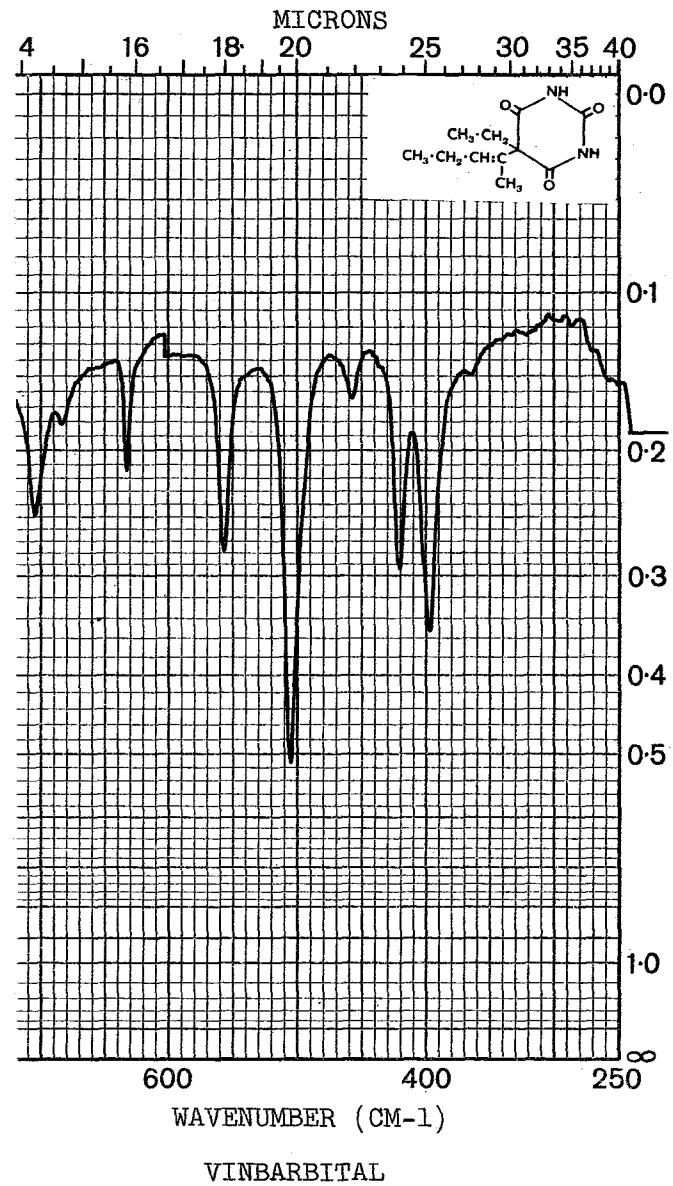
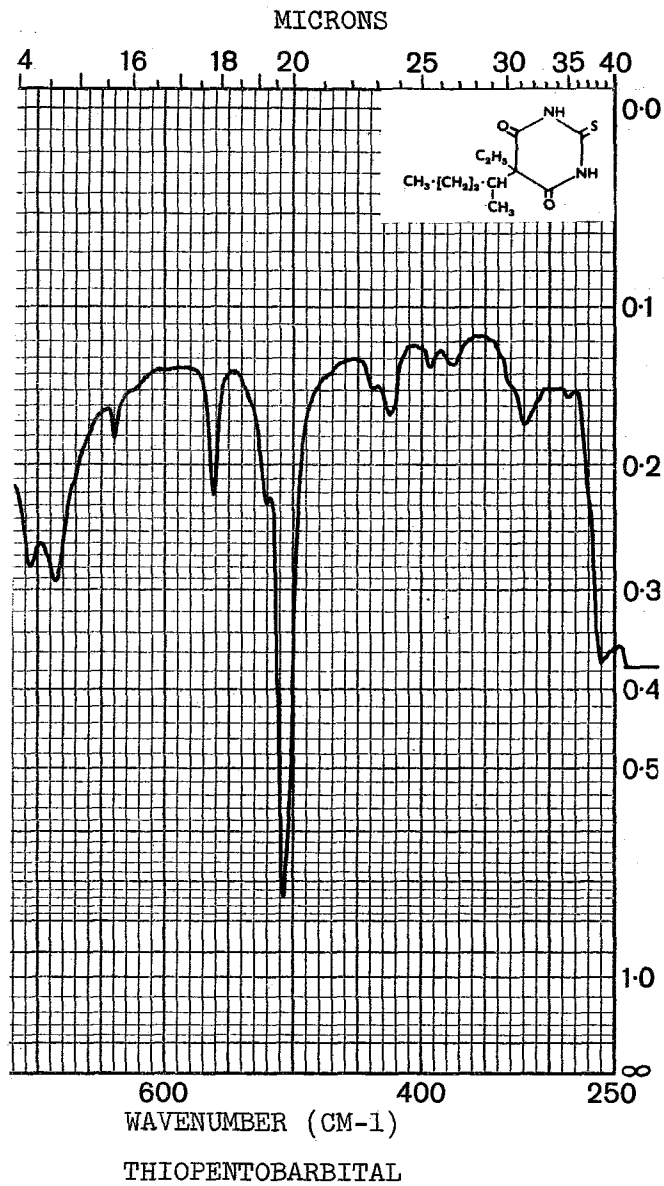
PHENOBARBITAL

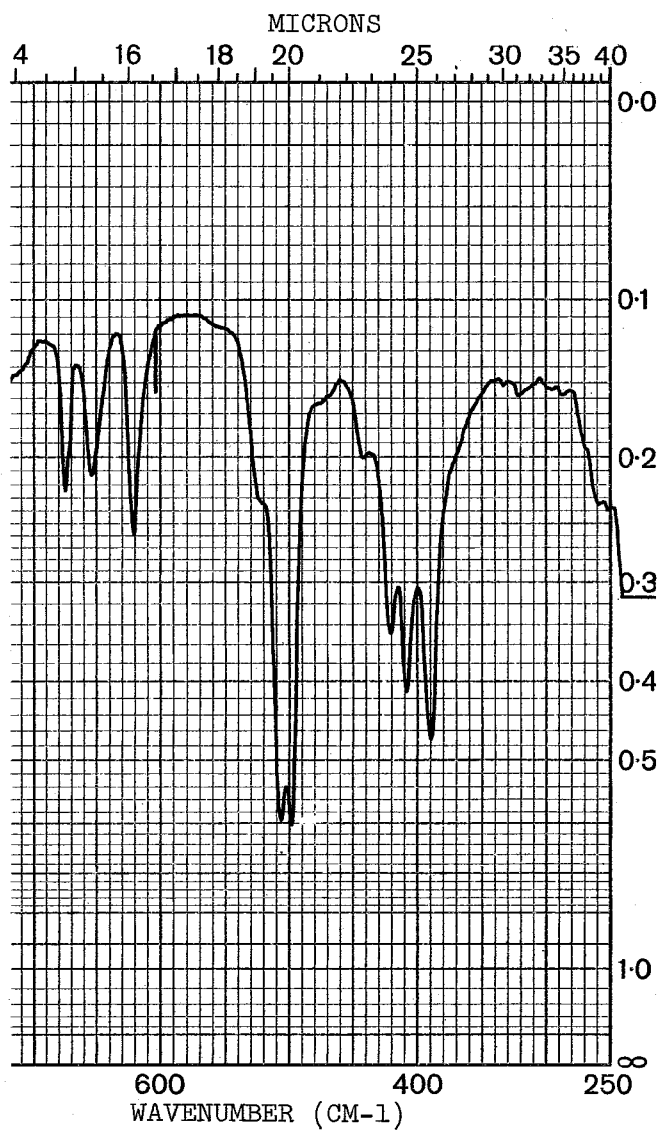


PROBARBITAL

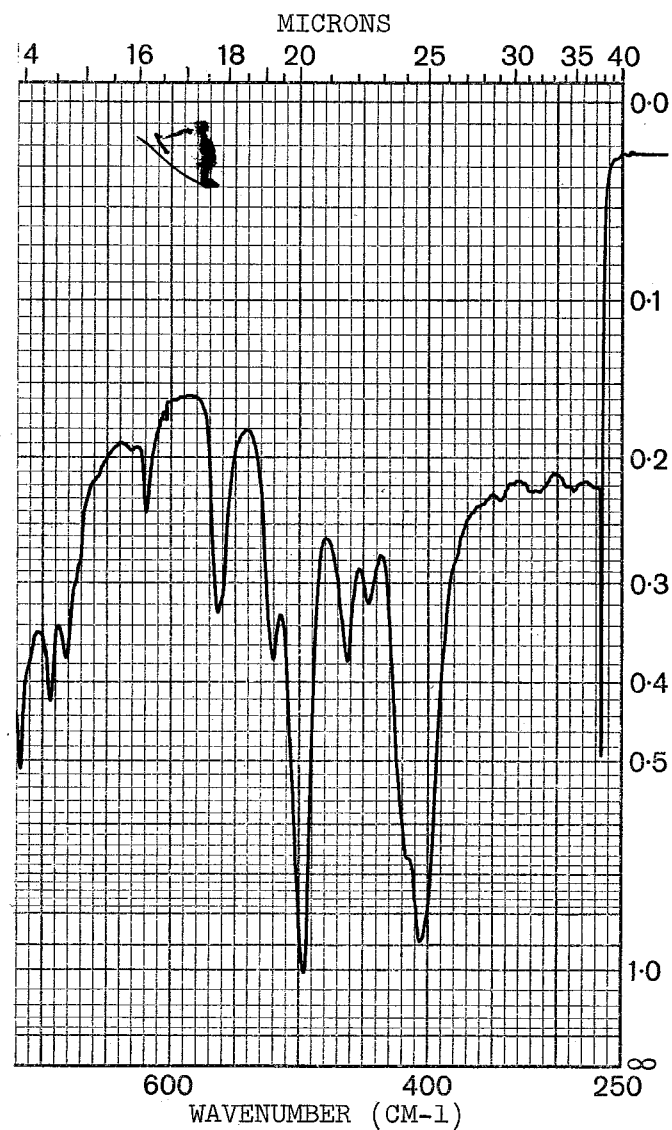


SECOBARBITAL

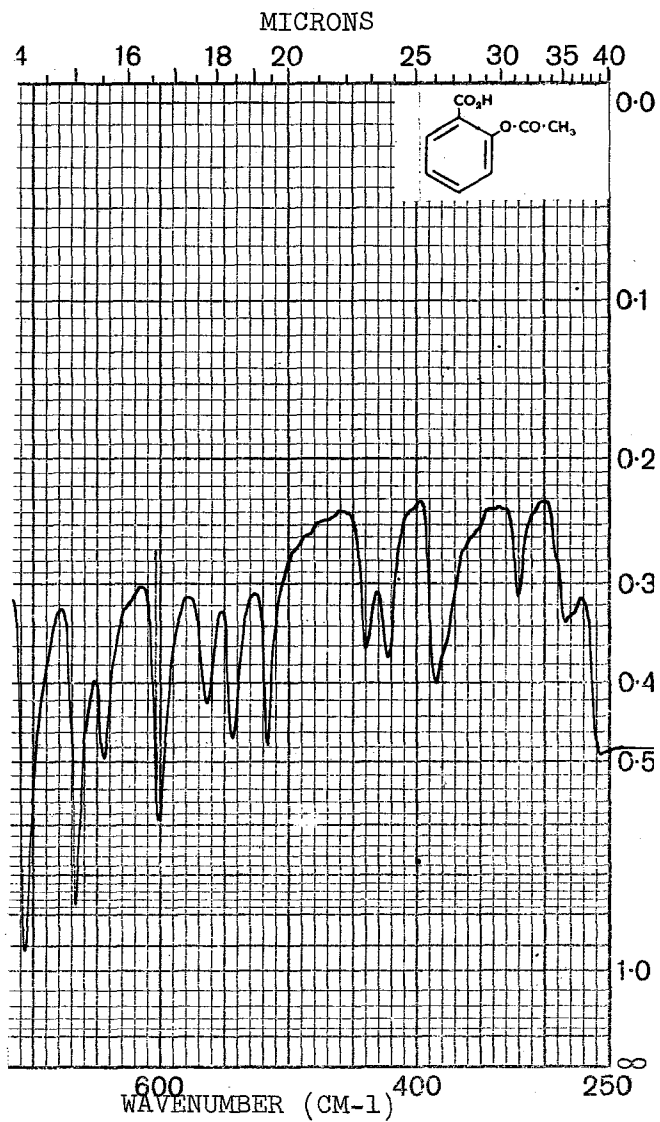




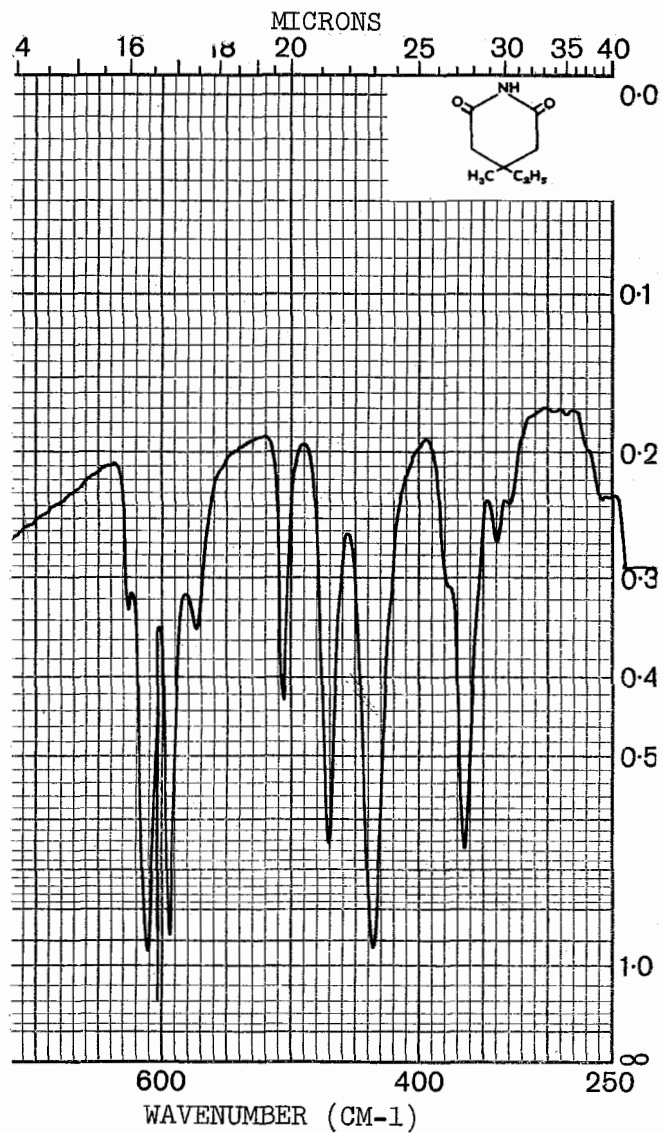
AMOBARBITAL/SECOBARBITAL COMBINATION  
(1+1)



PHENOBARBITAL /BATABARBITAL COMBINATION  
(1+1)



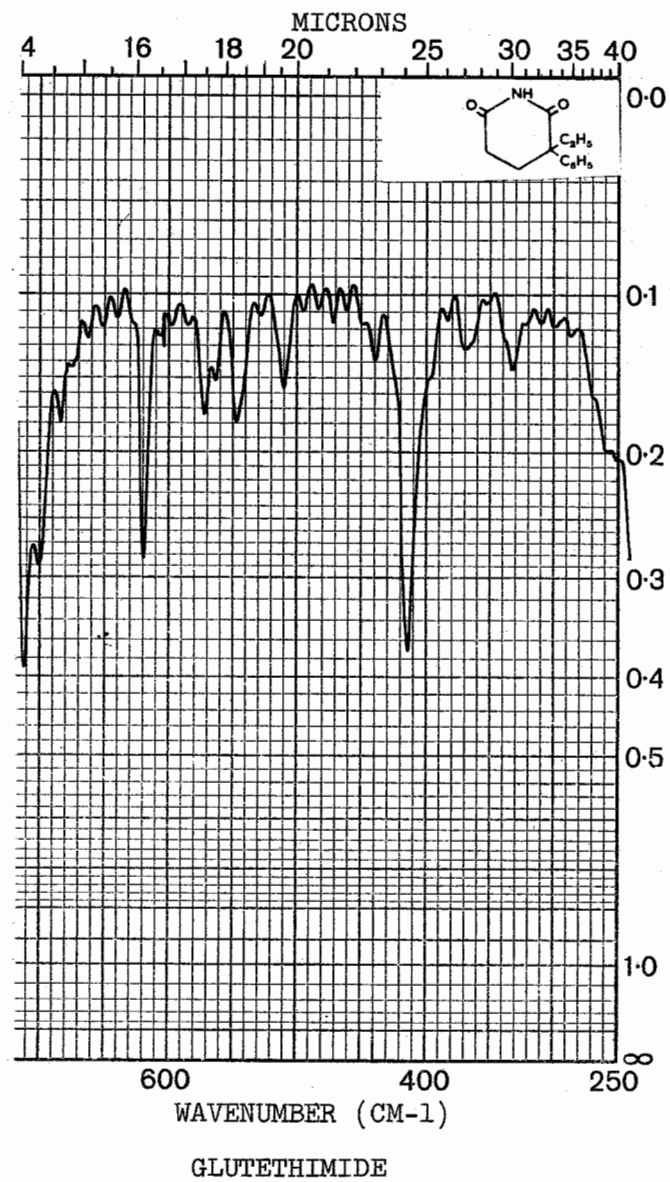
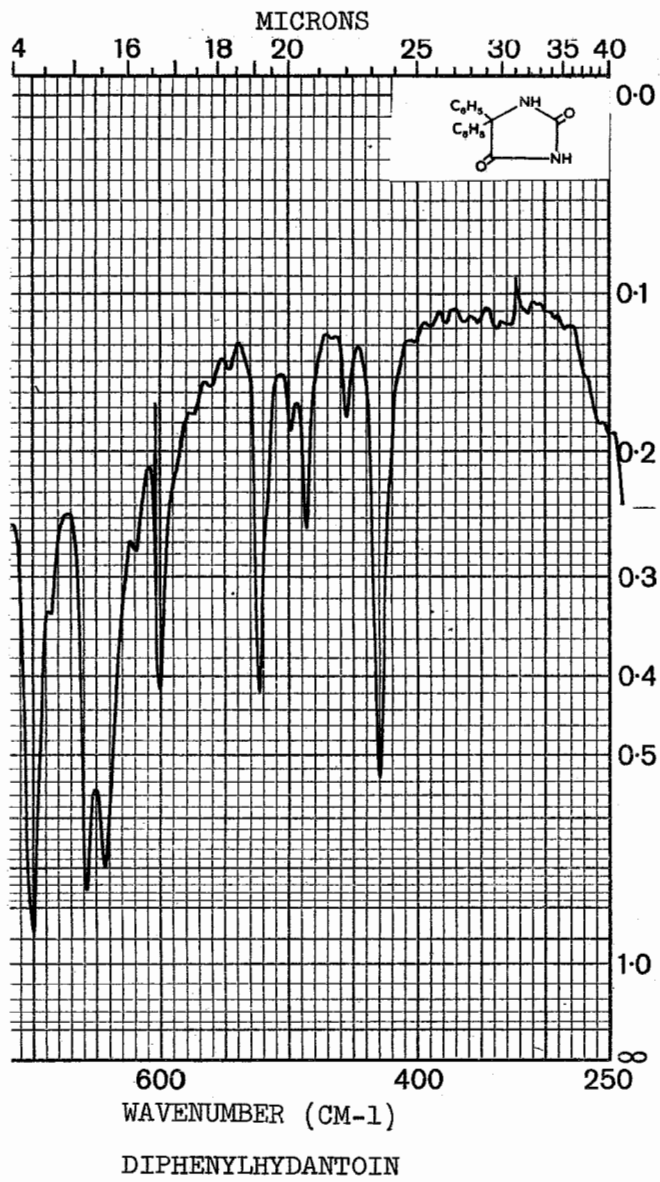
ASPIRIN



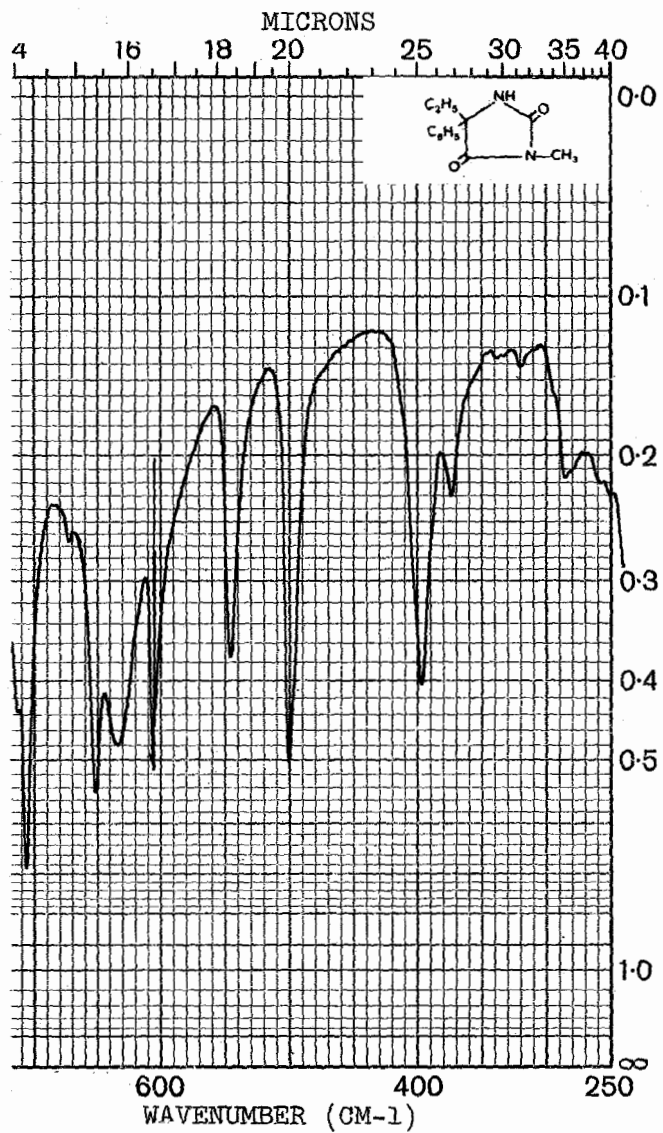
BEMEGRIDE



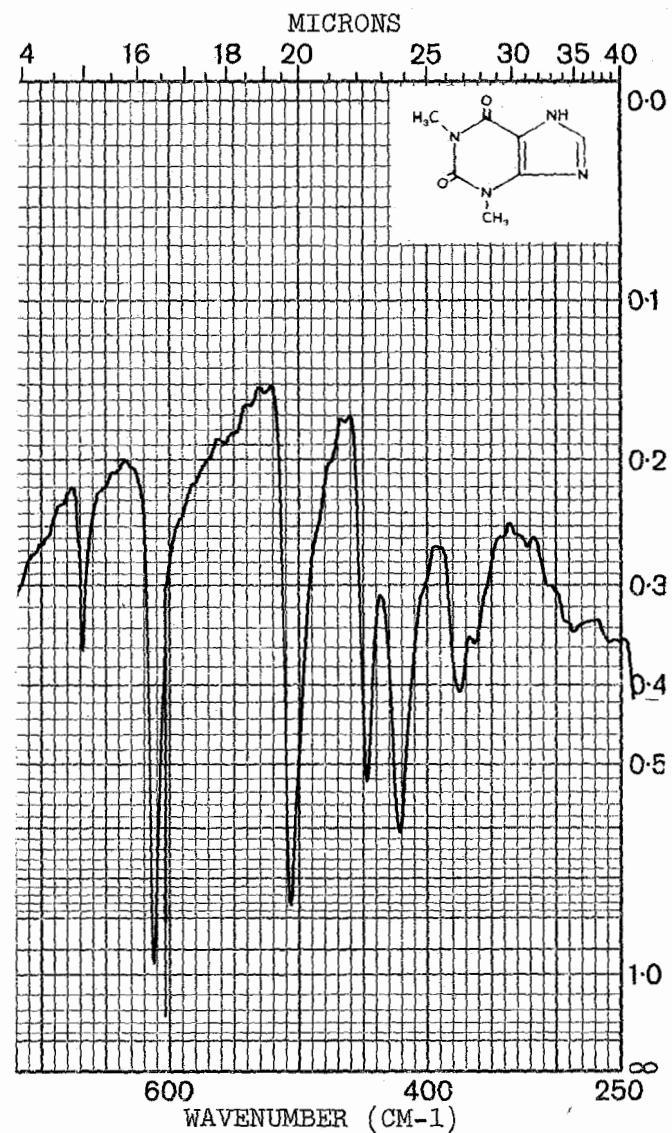
CAFFEINE



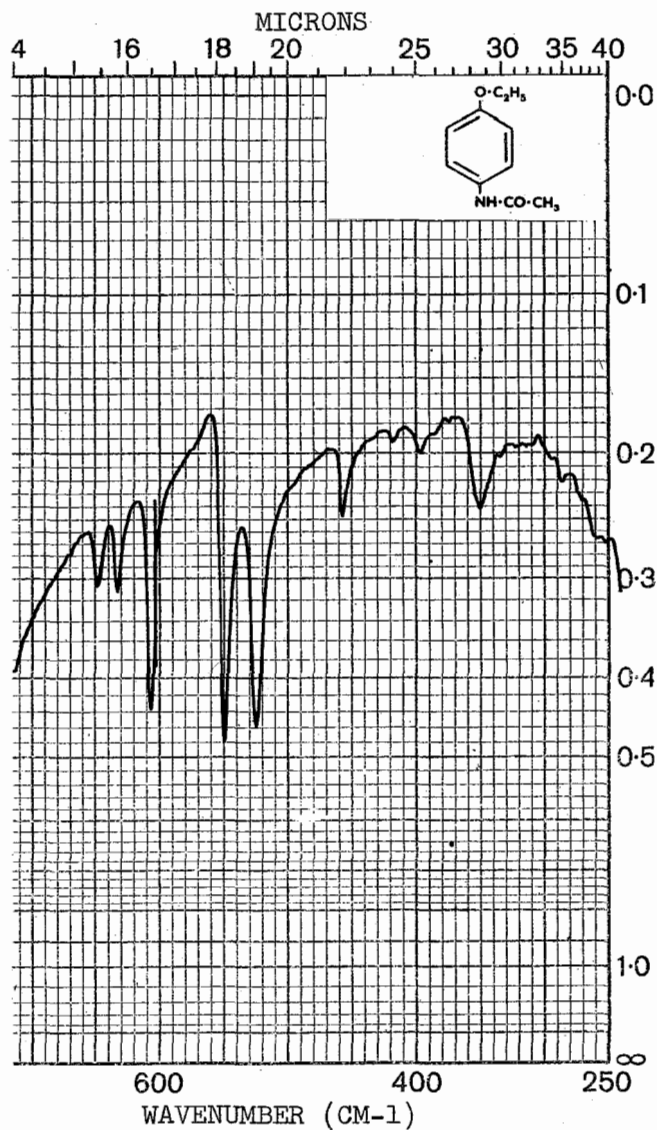




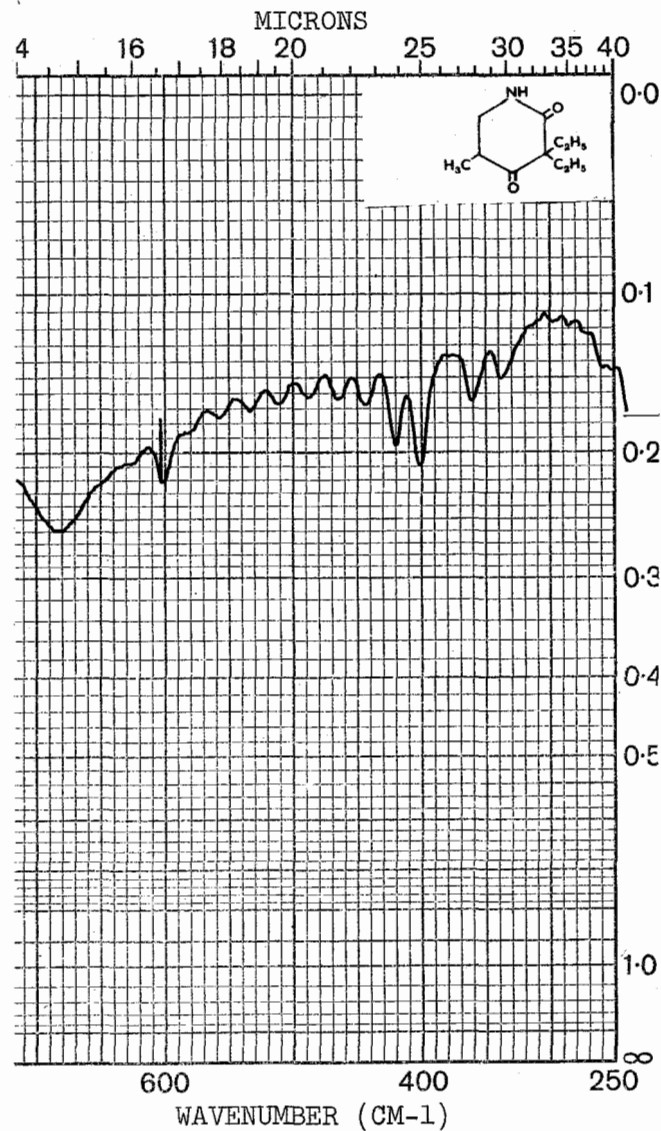
MESANTOIN



THEOPHYLLINE



PHENACETIN



METHYPRYLONE