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THE PREPARATION AND CHARACTERIZATION OF THE PALLADIUM(II) AND PLATINUM(II) CHELATES OF THREE CYCLIC TERTIARY AMINO ACIDS

A Dissertation

Presented to

the Faculty of the Graduate School

University of the Pacific

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

---

by

Floyd M. Hogue

September, 1973

This dissertation, written and submitted by

FLOYD MICHAEL HOGUE

is approved for recommendation to the Committee on Graduate Studies, University of the Pacific

Dean of the School or Department Chairman:

Dissertation Committee:

Chairman

Dated

THE PREPARATION AND CHARACTERIZATION OF THE PALLADIUM (II) AND PLATINUM (II) CHELATES OF THREE CYCLIC TERTIARY AMINO ACIDS

Abstract of the Dissertation

The purpose of this study was to prepare and characterize the palladium (II) and platinum (II) chelates of 1-pyrrolidineacetic acid, 1-piperidineacetic acid, and hexahydro-1-azepineacetic acid.

The ligands were prepared by reacting the cyclic secondary amines (pyrrolidine, piperidine, and hexahydroazepine) with sodium chloroacetate. The resulting cyclic tertiary amino acids were saponified and, finally, converted to the hydrochloride salts by neutralization with hydrochloric acid.

The chelates were prepared by adding 1.0 millimole of K_2PdCl_4 or K_2PtCl_4 to a solution made by dissolving 2.0 millimoles of amino acid hydrochloride in 25 ml. of water. The pH was adjusted to 7.4 and the solution was steam heated for an hour. The volume was reduced to 25 ml. by evaporation. Crystals began to form in one to three days and crystallization was complete in seven days. The products were not recrystallized since no appropriate solvents could be found. The six coordination compounds prepared are unreported in the literature.

Elemental analyses, UV - visible spectra, and IR spectra were utilized to elucidate the structure of the coordination compounds. The amino acids form chelates between the carboxyl and amine groups with the form: $M(\text{amino acid})_2$. The three amino acids are believed to form square planar complexes with palladium and platinum. It is proposed that the six new compounds are:

cis bis 1-pyrrolidineacetato palladium (II),
cis bis 1-pyrrolidineacetato platinum (II),
cis bis 1-piperidineacetato palladium (II),
cis bis 1-piperidineacetato platinum (II),
trans bis hexahydro-1-azepineacetato palladium (II),
trans bis hexahydro-1-azepineacetato platinum (II).

The ionization constants of the three amino acids were determined using the poteniometric method of Albert and Sergeant. The ionization constants of 1-pyrrolidineacetic acid and hexahydro-1-azepineacetic acid are unreported in the literature.

The stability constants of all six of the coordination compounds were determined using the method of Albert and Sergeant. This method involved the potentiometric titration of a solution 0.005 molar in K_2PdCl_4 or K_2PtCl_4 and 0.01 molar in amino acid hydrochloride with 0.1N potassium hydroxide at 25°C. The stability constants of the chelates differ only slightly with the ring structure of the amino acids under investigation. The stability constants of the palladium chelates are about 10^2 greater than the corresponding platinum chelates.

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CHAPTER I

INTRODUCTION

Coordination compounds are formed by the interaction of a metal (called the central atom or ion) with various anions, cations, or molecules (called ligands) containing an unshared pair of electrons. A coordination, or complex, compound is distinguished from other types of chemical compounds by the fact that complex compounds use preformed compounds as building blocks whereas other compounds use elements. The central atom and the ligands are, also, both capable of independent existence as stable chemical species.

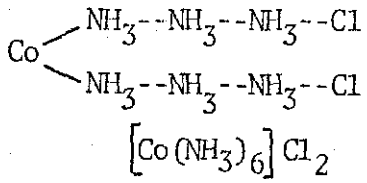
Historically the application of complex compounds is much older than the development of its theory. In the first century A.D., Pliny described an analytical method based on the formation of complex compounds. He tested for iron, which is an impurity of copper sulfate, by dipping a strip of moistened papyrus paper in an extract of gall nuts, and then into the solution of the sample. (14) The appearance of a black color indicated the presence of iron as an impurity. Pliny's test was still being used in the sixteenth century to study water.

In 1597, Libavius, knowing about the blue complex that copper forms with ammonia, used this complex as a test for the detection of ammonia in water. Prussian blue, discovered at the beginning of the eighteenth century, was used for the detection of very small amounts of iron in water and several other materials. Potassium hexacyanoferrate (II) soon became one of the most popular and versatile reagents.

In 1779, Wiegleb precipitated calcium with oxalic acid. The study of oxalic acid and similar acids led to the discovery of masking, which is the addition of a complexing agent so that the metal will complex and become unreactive. In the presence of oxalic, tartaric or succinic acid, iron would not precipitate with alkali. Osterreicher, in 1781, used tartaric acid to keep iron in solution during precipitation of magnesium hydroxide. Svanberg suggested the use of ammonium molybdate for detection of phosphate. (14) This was probably the first analytical application of the heteropoly acids.

The introduction of synthetic organic reagents opened a new era in the history of analytical chemistry. The complex-forming properties of these compounds was first used as a way of characterizing them. Later on these reagents were extensively used for qualitative and quantitative analysis of metals. The fact that these organic reagents were found to be selective, made them quite valuable in eliminating tedious preliminary processes of separation.

From 1870 to 1890 Jorgensen was the recognized master of the field. He prepared and carefully characterized large numbers of complexes but used and extended Blomstrand's chain formulations. His painstaking work and meticulous observations laid the groundwork for Werner's theory. (31) Typical of some of these earlier formulas was:



As an outgrowth of the studies of ammine complexes the very important synthesis of ethylenediamine complexes was achieved just prior to the end of the nineteenth century. 1,2-diaminoethane (ethylenediamine) and other diamines were reacted with various metals, by Werner, and were used to disprove the linear chain structures of the ammine coordination compounds that had been proposed by Jorgensen. (38)

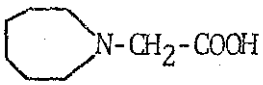
When the ligand, such as ethylenediamine, consists of two or more donor groups on the same molecule, the ligand is called a chelate or chelating agent. The name chelate was taken from the Greek word chela, meaning claw, and was first applied by Morgan and Drew in 1920. (21) Chelates attach themselves in a clawlike fashion to a central metal atom.

Shortly after Werner made the first ethylenediamine compounds it was discovered that glycine had the properties of a chelate. Ley, in investigating the glycine complexes of cooper, chromium, and platinum was the first to recognize the special significance of the cyclic structure of these chelate compounds. (19) Ley's work began metal-amino acid chemistry because he showed metal-glycine complexes were electrically neutral, did not add ammonia, and were not addition products.

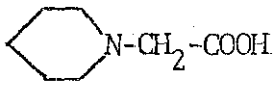
Extensive work has been done in preparing and studying the naturally occurring amino acid complexes. (5) (20) (29) (30) (39) Very little work, on the other hand, has been done on the complexes of cyclic secondary and tertiary alpha amino acids. Proline (pyrrolidine-2-carboxylic acid) complexes have been reported for

copper, zinc, nickel, palladium, and platinum in the literature. (8) (10) (15) (16) (35) (36) Pipecolinic acid (piperidine-2-carboxylic acid) has been complexed with Pd(II). (15)

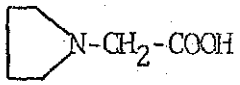
The nature of this study involves the preparation of coordination compounds of palladium(II), platinum(II), and three amino acids, namely hexahydro-1-azepineacetic acid, 1-piperidineacetic acid, and 1-pyrrolidineacetic acid. Shown below are the structures of the acids along with their names and the abbreviations that will be used subsequently in this report:



hexahydro-1-azepineacetic acid (HexAA)



1-piperidineacetic acid (PipAA)



1-pyrrolidineacetic acid (PyrAA)

The cyclic tertiary amino acids, above, have two different electron pair donors. These are the carboxylate radical of the acid and the nitrogen of the amine group. With its extra electron from hydrogen, the carboxylate radical is a fairly strong electron donor and combines with metals to form ionic bonds. The extra pair of electrons on the nitrogen of the amine group exhibits only coordinate bonding. These amino acids are obviously, then, potential chelating agents. No complexes of these amino acids have been reported in the literature.

The outline of the investigation in this report is as follows:

1. To prepare the hydrochloride salts of the cyclic amino acids: HexAA, PipAA, and PyrAA.

2. To prepare the palladium(II) and platinum(II) chelates of the three amino acids.
3. To determine the ionization constants of the ligands by potentiometric titration.
4. To determine the stability constants of the chelates by potentiometric titration.
5. To elucidate the structure of the chelates by:
   a. Elemental analysis
   b. Infrared, visible, and ultraviolet spectral studies

CHAPTER II

PREPARATION OF COMPOUNDS

Preparation of 1-piperidineacetic Acid

The first report of the synthesis of 1-piperidineacetic acid, PipAA, was made by Ursey and Paty in 1961. (32) They reacted piperidine and methyl monochloroacetate at room temperature. No data were reported on the yield.

After many trials the following method was found to give the best yield:

One mole of sodium chloroacetate was added to a 1 liter round bottom flask and the flask was fitted with a condensing column. 200 ml. of ethanol and 50 ml. of water was poured over the sodium salt and the flask was placed in ice bath. Two moles of piperidine (Eastman, reagent) were added to the flask. The reaction evolved a tremendous amount of heat initially. The reaction was allowed to proceed, with occasional stirring, for twelve hours. The reaction vessel was then heated on a steam bath for an additional hour. The reaction products were treated with 1.0 mole of sodium hydroxide dissolved in 50 ml. of water, followed by 100 ml. of ethanol. The resulting mass was cooled and filtered to produce the crude sodium salt of PipAA. The sodium salt of PipAA was recrystallized in absolute ethanol (prisms, M. P. 280°C.) with a yield of 74% calculated from sodium chloroacetate.

The sodium salt of PipAA was neutralized (pH=6.2) with hydrochloric acid using a pH meter, evaporated to dryness, and the

resulting PipAA was extracted with dry chloroform and recrystallized in dry chloroform (needles, M. P. 214-16°C.). The melting point coincides with the literature value. (32)

The hydrochloride, PIPAAHCl, was formed by dissolving the sodium salt of PipAA in water, adding hydrochloric acid until the pH was 2, evaporating in vacuo to dryness, and extracting with hot absolute ethanol. The hot ethanol extract was filtered with Norite to remove oily impurities. The ethanol extract was cooled and the crude hydrochloride was then filtered off. The PipAAHCl was recrystallized in 2-propanol (prisms, M. P. 192-5°C.) with a yield of 81%. Ursy and Paty reported crystals of fine needles with a M. P. of 217°C. (32)

Preparation of Hexahydro-1-azepineacetic Acid Hydrochloride

Hexahydro-1-azepineacetic acid hydrochloride, HexAAHCl, was synthesized in 1963 by Cheng and Chi. They reacted hexahydroazepine with ethyl chloroacetate to form the ethyl ester of HexAA. The ester was then hydrolyzed with aqueous hydrochloric acid to form HexAAHCl. No yields were reported. (9)

This investigator used exactly the same synthesis for HexAAHCl as he used for PipAAHCl: One mole of sodium chloroacetate was reacted with two moles of hexahydroazepine to form crude HexAA. The reaction solution was saponified with sodium hydroxide and filtered. The crude sodium salt of HexAA was recrystallized in absolute ethanol (prisms, M. P. 292°C.) with a yield of 72%.

The sodium salt of HexAA was acidified with hydrochloric acid to a pH of 2, evaporated in vacuo to dryness, and extracted with hot, absolute ethanol. The ethanol extract was cooled, the HexAAHCl was filtered off, and then recrystallized in 2-propanol (prisms, M. P. 184-8°C.) with a yield of 78%. All attempts to isolate the free amino acid, HexAA, failed.

Preparation of 1-pyrrolidineacetic Acid Hydrochloride

Although 1-pyrrolidineacetic acid hydrochloride, PyrAAHCl, has not been reported in the literature, it became commercially available, in research quantities, in January of 1973 by Aldrich Chemical Company.

The compound was found to be easily synthesized: One mole of sodium monochloroacetate was added to a 1 l. flask fitted with a condensing column. 200 ml. of ethanol and 50 ml. of water was mixed with two moles of pyrrolidine (Eastman, reagent) and the entire mixture was added to the reaction flask. The flask was placed in an ice bath to absorb the initial heat of reaction. The reaction was allowed to proceed, with occasional shaking, for twelve hours. The reaction vessel was then heated on a steam bath for an additional hour. The reaction products were saponified with one mole of sodium hydroxide dissolved in 50 ml. of water and 100 ml. of ethanol. The resulting mass was cooled and filtered to produce the crude sodium salt of PyrAA. The sodium salt of PyrAA was recrystallized in absolute ethanol (prisms, M. P. 272°C.) with a yield of 68% calculated from sodium chloroacetate.

PyrAAHCl was prepared by dissolving the sodium salt of PyrAA in water, adding hydrochloric acid until the pH was 2, evaporating in vacuo to dryness, and extracting with hot absolute ethanol. The ethanol extract was filtered hot, with Norite, to remove orange colored impurities. The ethanol extract was then cooled in order to filter off the crude PyrAAHCl. The pure PyrAAHCl was recrystallized in 2-propanol (prisms, M. P. 179-81°C.) with a yield of 79% calculated from the sodium salt of PyrAA.

The carbon, hydrogen, and nitrogen elemental analyses for all the ligands prepared are given in Table I. Analyses were made by Schwarzkopf Microanalytical Laboratory, Woodside, New York.

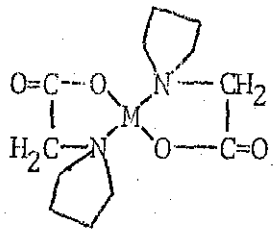
Preparation of Chelates

The method used in the preparation of the chelates was to add 1.0 millimole of K_2PdCl_4 or K_2PtCl_4 to a solution made by dissolving 2.0 millimoles of amino acid hydrochloride in 25 ml. of water. The pH of the resulting solution was adjusted, by means of a pH meter, with 0.1 N potassium hydroxide to a pH of 7.4. The solution was heated on a steam bath for an hour and the pH was maintained. Colloidal metal oxide, if any, was removed by filtering with Norite. The volume was reduced to about 25 ml. by evaporation and the solutions were transferred to covered beakers to crystallize. Crystals began to form in one to three days and crystallization was complete in seven days. The crystals were collected on a filter, washed with a few milliliters of cold water, followed by a rinse with ethanol, and finally, rinsed with ether. The product was not recrystallized

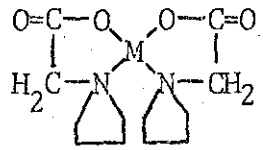
since no appropriate solvent could be found. Hot solvents attempted included: water, ethanol, methanol, and 2-propanol. The crystals were dried in a vacuum desiccator at 4 mm. Hg in the presence of sulfuric acid.

The crystal structure, the decomposition points and the best yields are summarized in Table II.

Since palladium(II) and platinum(II) ions always form complexes with square planar configurations, two geometric chelate isomers are possible. The trans isomer has the two nitrogen atoms opposite each other across the metal ion, while the cis isomer has the two nitrogen atoms adjacent on the metal ion. The following diagram clearly shows the difference between the two isomers:



TRANS



CIS

Pinkard and coworkers, in their study of amino acid chelates with palladium(II) and platinum(II), found that the cis structure always crystallized first in the form of needles and that the supernatent liquid slowly formed a second crop of crystals which were less soluble, were in the form of plates, and were of the trans configuration. (27) All but two of the compounds synthesized in this study were found to be in the form of needles, and the exceptions, $Pt(HexAA)_2$ and $Pd(HexAA)_2$, were in the form of plates.

TABLE I

ELEMENTAL ANALYSES FOR LIGANDS

	Amino Acid			
	PyrAAHCl	PipAA	PipAAHCl	HexAAHCl
Carbon				
found	43.38%	58.67%	46.71%	49.53%
calculated from formula	43.51	58.70	46.80	49.61
Hydrogen				
found	7.21%	9.23%	7.81%	8.28%
calculated from formula	7.30	9.14	7.85	8.32
Nitrogen				
found	8.44%	9.65%	7.74%	7.02%
calculated from formula	8.46	9.80	7.80	7.23
Empirical Formula	$C_6H_{12}O_2NCl$	$C_7H_{13}O_2N$	$C_7H_{14}O_2NCl$	$C_8H_{16}O_2NCl$

Infrared spectroscopy was utilized in an attempt to determine the isomer structure of these compounds.

TABLE II

CRYSTAL STRUCTURE, BEST YIELDS, AND DECOMPOSITION POINTS

Compound	Yield	Decomposition Point	Crystal Structure
$Pd(PyrAA)_2$	42.8%	198°C.	yellow needles
$Pt(PyrAA)_2$	7	265	colorless needles
$Pd(PipAA)_2$	49.5	210	yellow needles
$Pt(PipAA)_2$	51.2	270	colorless needles
$Pd(HexAA)_2$	39.3	217	yellow plates
$Pt(HexAA)_2$	48.5	274	colorless plates

CHAPTER III

PROOF OF CHELATE STRUCTURE

When an amino acid hydrochloride is neutralized, as was done in the preparation of the complexes, the resulting neutral molecule exists as a zwitter ion. If a chelate is formed the carboxyl group and the nitrogen are attached to the central metal atom and the hydrogen ion attached to the quaternary amine is lost.

It is proposed that each of the six compounds that has been prepared is the bis amino acid metal(II) compound with square planar structure. The compounds of PyrAA and PipAA are probably cis isomers, while the HexAA compounds are most likely trans isomers.

Elemental Analyses

Since the coordination compounds all contained organic ligands, the samples were analyzed for carbon, hydrogen, and nitrogen. Tables III and IV show the reported elemental analyses and the calculated values assumed from the proposed structures of the compounds. In each of the palladium compounds the reported values were very close to the theoretical values. The platinum compounds also had reported values that were quite close to the theoretical values.

The agreement between the reported elemental analyses and the theoretical values is close enough to justify the empirical formulas that have been proposed for the compounds.

TABLE III

ELEMENTAL ANALYSES OF
PALLADIUM COMPOUNDS

	Amino Acid		
	PyrAA	PipAA	HexAA
Found			
carbon	39.62%	43.06%	45.88%
hydrogen	5.57	6.28	6.86
nitrogen	7.69	7.10	6.46
Calculated from $Pd(Ligand)_2$			
carbon	39.70%	43.10%	45.80%
hydrogen	5.55	6.20	6.75
nitrogen	7.71	7.18	6.69

TABLE IV

ELEMENTAL ANALYSES OF
PLATINUM COMPOUNDS

	Amino Acid		
	PyrAA	PipAA	HexAA
Found			
carbon	31.87%	35.12%	37.81%
hydrogen	4.66	5.07	5.58
nitrogen	6.15	5.97	5.53
Calculated from $Pt(Ligand)_2$			
carbon	31.90%	35.20%	37.80%
hydrogen	4.47	5.05	5.57
nitrogen	6.19	5.85	5.52

Ultraviolet-Visible Spectra

Spectra of each reaction solution made in the preparation of the complexes were taken using a Beckman DB spectrophotometer. This method was used because of the poor solubility of the compexes in all solvents tried. It was found that all the palladium compounds showed an absorption peak in the 320 to 323 millimicron region. This absorption does not occur with either the pure amino acid solutions or with the K_2PtCl_4 or K_2PdCl_4 solutions. It is assumed, therefore, that the absorption at 320 millimicrons is due to the formation of the palladium complexes.

The observed energy transition at 320 millimicrons also helps substantiate the formation of a chelate instead of a purely ionic palladium salt. If the compounds had been ionic the palladium would have existed as a diaquo complex in solution. The absorption of an aquo palladium complex would have been at about 420 millimicrons. (39)

Spectra of the platinum reaction solutions did not show an absorption peak in the region measurable by the instrument (200 - 800 mμ).

The spectra for the palladium compounds are included in Appendix A.

Infrared Spectra

Infrared spectra were determined for all six of the prepared chelates and for the three amino acid hydrochlorides by using potassium bromide discs. The discs were prepared by pressing 3 mg. of compound in 300 mg. of I. R. grade potassium bromide. All discs

were analyzed on a Perkin-Elmer Model 137B spectrophotometer and some were analyzed on a Perkin-Elmer 337 infrared spectrophotometer.

Bellamy has stated, "Tertiary amines are extremely difficult to identify spectroscopically." (6) This is so because the only nitrogen-hydrogen bond available is the NH^+, if present, and many of the normally easily recognized bands are shifted. The unionized carboxyl group (COOH) absorbs at 1700 to 1750 cm^{-1} in the amino acid hydrochlorides. The complexes absorb at or near 1680 cm^{-1}, indicating that the carboxyl group has formed an ionic bond with the metal. The absorption of the ionized carboxyl group has been shifted to a much higher frequency than it is commonly found, however.

Bellanato, in 1956, found that the NH^+ stretching band is located at 2735 cm^{-1}. (7) The spectra of the three amino acid hydrochlorides all had a strong absorption peak at or near 2735 cm^{-1}, while the six prepared coordination compounds had no absorption at that frequency. This fact provides additional proof that these compounds are coordination compounds and not ionic salts. The infrared spectra for the amino acid hydrochlorides and the coordination complexes are found in Appendix B.

It is more difficult to prove that the complexes are either cis or trans isomers. The metal-nitrogen stretch for the PipAA complexes appears to absorb at 525 cm^{-1} while the two HexAA complexes have a tentative metal-nitrogen stretch assignment at 550 cm^{-1}. According to Powell, the ligand in a trans position to the M - N bond is a ligand of stronger trans effect than nitrogen if the band is shifted to a lower frequency. (28) Since the carboxyl group has a stronger trans

effect than the nitrogen, the carboxyl group should be trans to nitrogen at the lower absorption frequency in the PipAA complexes; making the complexes cis isomers. By the same reasoning, then, the HexAA complexes are trans isomers. When the structural formulas of $Pt(HexAA)_2$ and $Pd(HexAA)_2$ are drawn out it is easy to see that the bulky seven member rings of the ligand molecules may get in each other's way if they align themselves in a cis configuration. The drawings on page ten of this report show the differences between these two configurations.

The early work of Pinkard in studying glycine chelates of palladium and platinum, which are similar compounds to those in this investigation, found that the cis compound always crystallized as needles and that the trans compounds always formed plates. (27)

I propose then, from the preceding observations and conclusions, that: the six prepared compounds be named as follows:

1. Cis bis 1-pyrrolidineacetato palladium(II)
2. Cis bis 1-pyrrolidineacetato platinum(II)
3. Cis bis 1-piperidineacetato palladium(II)
4. Cis bis 1-piperidineacetato platinum(II)
5. Trans bis hexahydro-1-azepineacetato palladium(II)
6. Trans bis hexahydro-1-azepineacetato platinum(II)

CHAPTER IV

DETERMINATION OF ACID IONIZATION CONSTANTS

The ionization constants of PyrAA and HexAA are unreported in the literature. The ionization constants of PipAA have been reported as 1.98 and 10.20 @ 20°C. using the half-neutralization method. (9) Since ionization constants of the acids were required to determine the stability constants of the complexes, they were determined using the potentiometric method of Albert. (4) This method consisted of ascertaining the pH at twenty points between the start of titration and after the second equivalence point.

The titrations were all carried out using carbonate-free potassium hydroxide because it has been found to eliminate most electrode error in alkaline solutions commonly due to sodium ions. The carbonate-free potassium hydroxide is more tedious to prepare than carbonate-free sodium hydroxide, but the following technique of Albert was very straight forward. (4)

The potassium hydroxide was made up to a stronger concentration than would finally be used. Barium hydroxide was added to remove any carbonate present. The barium carbonate that formed was allowed to settle overnight in an inverted Erlenmyer flask. The mixture of potassium hydroxide and barium hydroxide solution was then passed through a potassium-loaded Amberlite resin (IR 120H) into a polyethylene container that had been flushed with nitrogen to dispel any carbon dioxide. The container was fitted with a soda-lime vent tube to prevent contamination. The concentration of

the potassium hydroxide was determined and the solution was diluted to a concentration of about 0.1 N by adding boiled water. The concentration of this diluted base was determined potentiometrically against potassium hydrogen phthalate.

All titrations were carried out at $25^{\circ} \pm 0.1^{\circ}C.$ under a nitrogen atmosphere. 42.5 ml. of boiled, distilled water was accurately measured into a 100 ml. beaker containing 0.5 millimoles of amino acid hydrochloride and 0.5 millimoles of potassium chloride. The potassium chloride was added to make the conditions for measuring the ionization constants identical to those for measuring the stability constants of the complexes. The beaker was placed in a holder and lowered into a 20 l. water bath. The beaker was covered with a rubber stopper with five holes. Two holes were used for the Beckman electrodes (calomel reference and a full range glass electrode). The three additional holes were used by the nitrogen inlet tube, the buret tip, and the stirring mechanism, respectively.

Water pumped nitrogen was used as an inert atmosphere. Tank nitrogen was bubbled through a chromium(II) sulfate solution to remove oxygen and then through a sodium hydroxide solution to remove carbon dioxide.

The actual titration was carried out by adding 0.5 ml. increments of base to the acid solution. The solution was stirred for two minutes and the pH was noted on a Beckman Expandomatic pH meter. The titration was continued until 10.00 ml of base had been added. The titration data for the amino acids are listed in Appendix C. The titration curves are also shown in Appendix C.

The ionization constants were calculated by the method of Albert and Sergeant. (4) This method allows one to measure the pK value for each pH measurement taken in the titration. The titration divides the calculations into parts: the first half of the titration yields calculations on the pK of the ionization of the carboxyl hydrogen, and the second half of the titration is used to determine the pK of the ionization of the quaternary amine hydrogen.

For the calculations used, let:

C = the total concentration (all species) of the acid being titrated.

B = the concentration of base added (assuming no reaction).

H^+ = the concentration of hydrogen ion calculated from the pH reading.

OH^- = the concentration of hydroxide ion calculated from the pH reading.

For each pH measurement in the first half of the titration a value for the pK_1 was determined from the following equation:

$$pK_1 = pH + \log \frac{(C - B - H^+)}{(B + H^+)}$$

The pK_1 values for the amino acids are summarized in Table V.

The pK_2 values were calculated for each incremental addition of potassium hydroxide after the first equivalent point, which corresponded to the last five milliliters of potassium hydroxide added. Each pK_2 value was calculated from the following equation:

$$pK_2 = pH + \log \frac{(2C - B + OH^-)}{(B - C - OH^-)}$$

TABLE V

pK VALUES FOR THE AMINO ACIDS

	Amino Acid		
	PyrAA	PipAA	HexAA
pK_1 experimental	2.41 ± .04	2.18 ± .03	2.20 ± .03
pK_1 literature value		1.98	
pK_2 experimental	10.49 ± .04	10.19 ± .03	10.61 ± .04
pK_2 literature value		10.20	

The pK_2 values for the three amino acids are summarized in Table V. The precision of the values of both pK_1 and pK_2 was found to be ± .04 or better, using from eight to ten values in each set. Each titration was duplicated and the results were reproducible.

CHAPTER V

DETERMINATION OF STABILITY CONSTANTS

The stability constants of the six chelate compounds were determined using the method of Albert and Sergeant. (4) This method involved the potentiometric titration of a solution .005 molar in K_2PdCl_4 or K_2PtCl_4 and .01 molar in amino acid hydrochloride with 0.1 N potassium hydroxide using a Beckman Expandomatic pH meter.

All titrations were carried out at 25° ± .1°C. under a nitrogen atmosphere. 45.00 ml. of boiled, distilled water was added to a 100 ml. beaker containing 0.5 millimoles of amino acid hydrochloride and 0.25 millimoles of K_2PdCl_4 or K_2PtCl_4. The titration was accomplished by adding 0.5 ml. increments of 0.1 N carbonate-free potassium hydroxide, stirring for two minutes, and recording the pH from the pH meter. The titration was completed before the pH reached seven. The titration data for the chelate compounds are listed in Appendix D.

The $PdCl_4^{-2}$ complex has a stability constant of about 10^{14} and the $PtCl_4^{-2}$ has a stability constant of 10^{16}. (40) Unless the stability constants of the chelates under investigation are higher than 10^{16}, competing equilibria should interfere with the calculations of the chelate stability constants. Fortunately, the stability constants of the palladium complexes of the amino acids were found to be 10^{19} or higher and the platinum chelates had stability constants of 10^{17} to 10^{20}. It was assumed that the greater stability of the chelates allowed calculation of stability constants without interference from the metal chloro complexes.

The potentiometric method requires the calculation of two functions, L^- and $\bar{n}$. L^- is the concentration of the free chelating species ($R_2N - CH_2 - CO_2^-$), and $\bar{n}$ is the average number of molecules of ligand bound by one atom of metal. For the 2:1 complexes under study, $\bar{n}$ must obviously be between 0 and 2. L^- and $\bar{n}$ were found from the following equations:

1. $\log L^- = \log (2C - B - H^+ + OH^-) - \log P$

   where C = the total concentration (all species) of the amino acid being titrated,

   B = the concentration of titrant if only water was present in the titration vessel;

   the factor (2) is required because the amino acid is present as the hydrochloride, which will neutralize an equivalent amount of base; and

2. $P = \frac{H^+}{K_b} + \frac{2(H^+)^2}{K_a K_b}$ where K_b and K_a are the ionization constants for the amino acid.

3. $\bar{n} = \frac{C - QL^-}{M}$ where M is the total concentration of the metal, and Q is defined by:

4. $Q = \frac{H^+}{K_b} + \frac{(H^+)^2}{K_a K_b} + 1$

Albert evaluated the constants algebraically by the method of least squares. (4) Values of $\bar{n} / (\bar{n} - 1) L^-$ are calculated for each pH reading in the titration. These values are called Y, and are added to give ΣY. (The values of Y are crude values of $-K_1$.)

Next, all values of $(2 - \bar{n}) L^- / (\bar{n} - 1)$ are calculated for each reading in the titration. These values are called X, and are added to give ΣX. (The values of X are crude values of $1/K_2$.)

Values of X^2 and XY are tabulated for each titration reading, and are added to give ΣX^2 and ΣXY, respectively. These sums are used to solve the standard simultaneous equations for least squares:

5.
$$\Sigma Y = n\,a + b\Sigma X$$
$$\Sigma XY = a\,?X + b\Sigma X^2 \qquad ? = \Sigma ?$$

where n equals the number of observations. The coefficient a is $-K_1$ and b is K_1K_2. (4)

The results of the stability constant calculations are summarized in Table VI. The stability constants of the palladium chelates are about 10^2 larger than the corresponding platinum chelate. The size of the amino acid ring does not appear to directly affect the stability constant of the chelate, since the PyrAA chelates are most stable followed by the HexAA and PipAA chelates, in that order.

Although the first stability constants (K_1) are reported in Table VI, Albert and Sergeant would state that they are not reliable because K_1 approximates K_2 and therefore the reaction behaves as if only the 2:1 complex is being formed, even at the beginning of the titration. (4) The K_1 values are unreliable in the sense that they cannot be used to calculate the concentration of the 1:1 complex. This is so because as soon as a 1:1 complex is formed, the probabilities are approximately equal that the 1:1 complex adds a ligand molecule to form the 2:1 complex as readily as a ligand molecule is attached to a metal ion to form a new 1:1 complex.

TABLE VI

STABILITY CONSTANTS

Amino Acid	Palladium		Platinum	
	K_1	K_1K_2	K_1	K_1K_2
PyrAA	1.6×10^{11}	1.7×10^{21}	2.8×10^{9}	7.5×10^{19}
PipAA	2.1×10^{10}	5.2×10^{19}	2.9×10^{8}	2.7×10^{17}
HexAA	3.0×10^{10}	2.8×10^{20}	3.3×10^{9}	5.7×10^{18}

CHAPTER VI

SUMMARY

Palladium and platinum coordination compounds have been synthesized from the three amino acids: 1-pyrrolidineacetic acid, 1-piperidineacetic acid, and hexahydro-1-azepineacetic acid. These acids form chelates between the carboxyl and amine groups with the metal in the form: M(amino acid)$_2$. The three amino acids are believed to form square planar complexes with the palladium and platinum. The chelates of HexAA formed trans isomers while PyrAA and PipAA formed cis isomers with the metal. None of the chelates have been prepared before.

The ionization constants of the five and seven membered ring amino acids, PyrAA and HexAA, are slightly higher than the six membered PipAA.

The stability constants of the chelates differ only slightly with the ring structure of the amino acids under investigation. The stability constants of the palladium chelates are about 10^2 greater than the corresponding platinum chelates.

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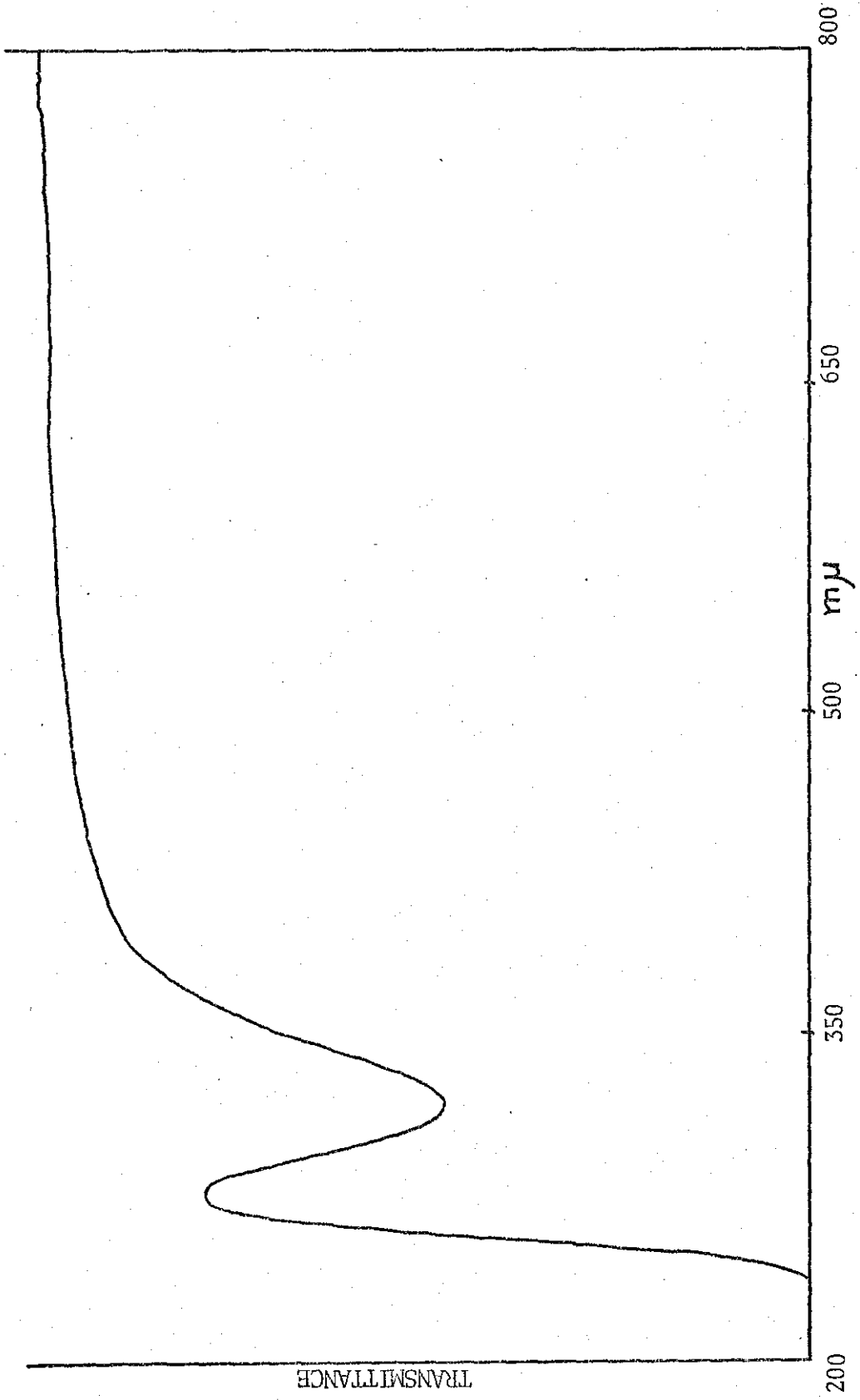
APPENDIX A

ULTRA-VIOLET AND VISIBLE SPECTRA



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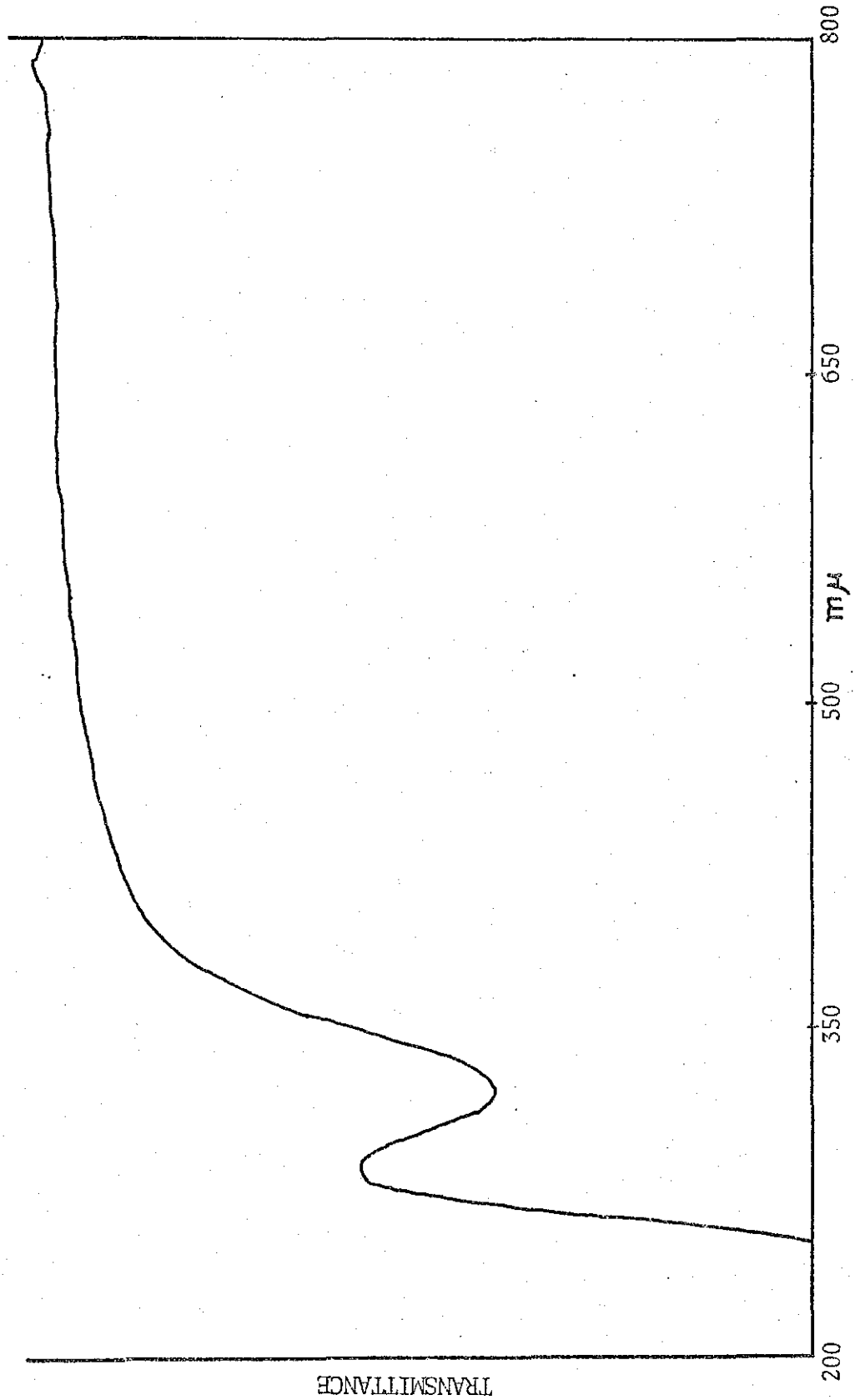

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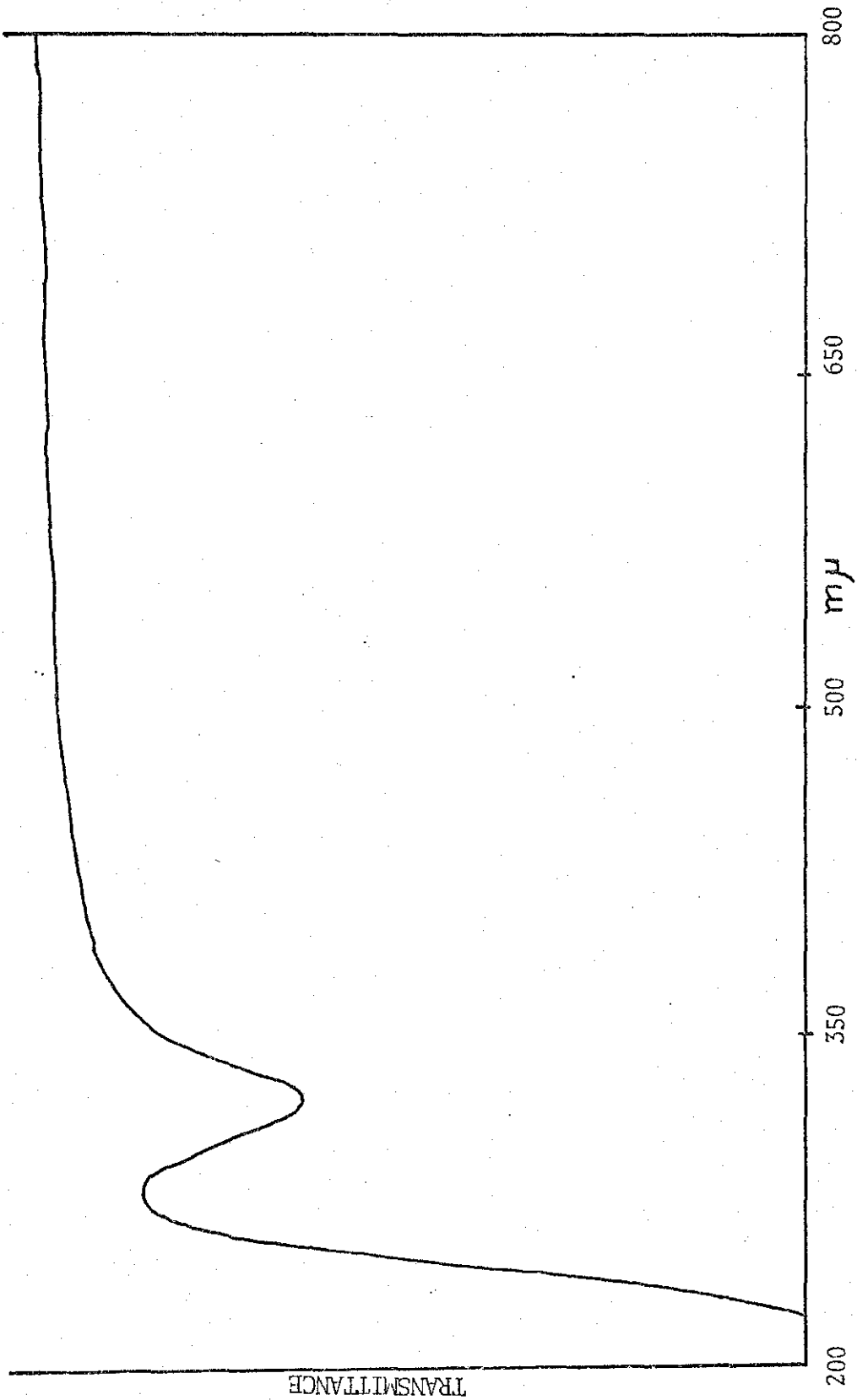
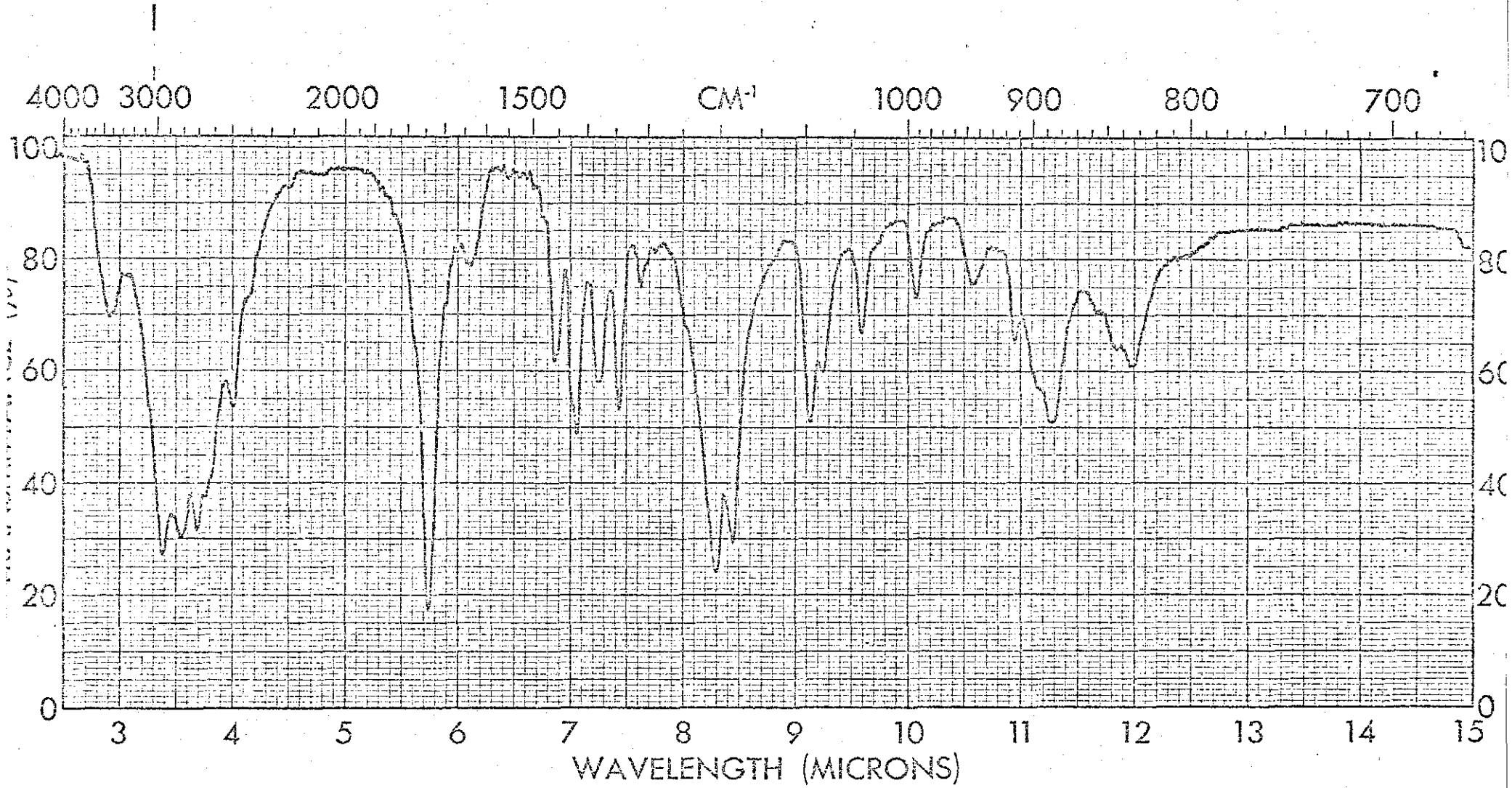


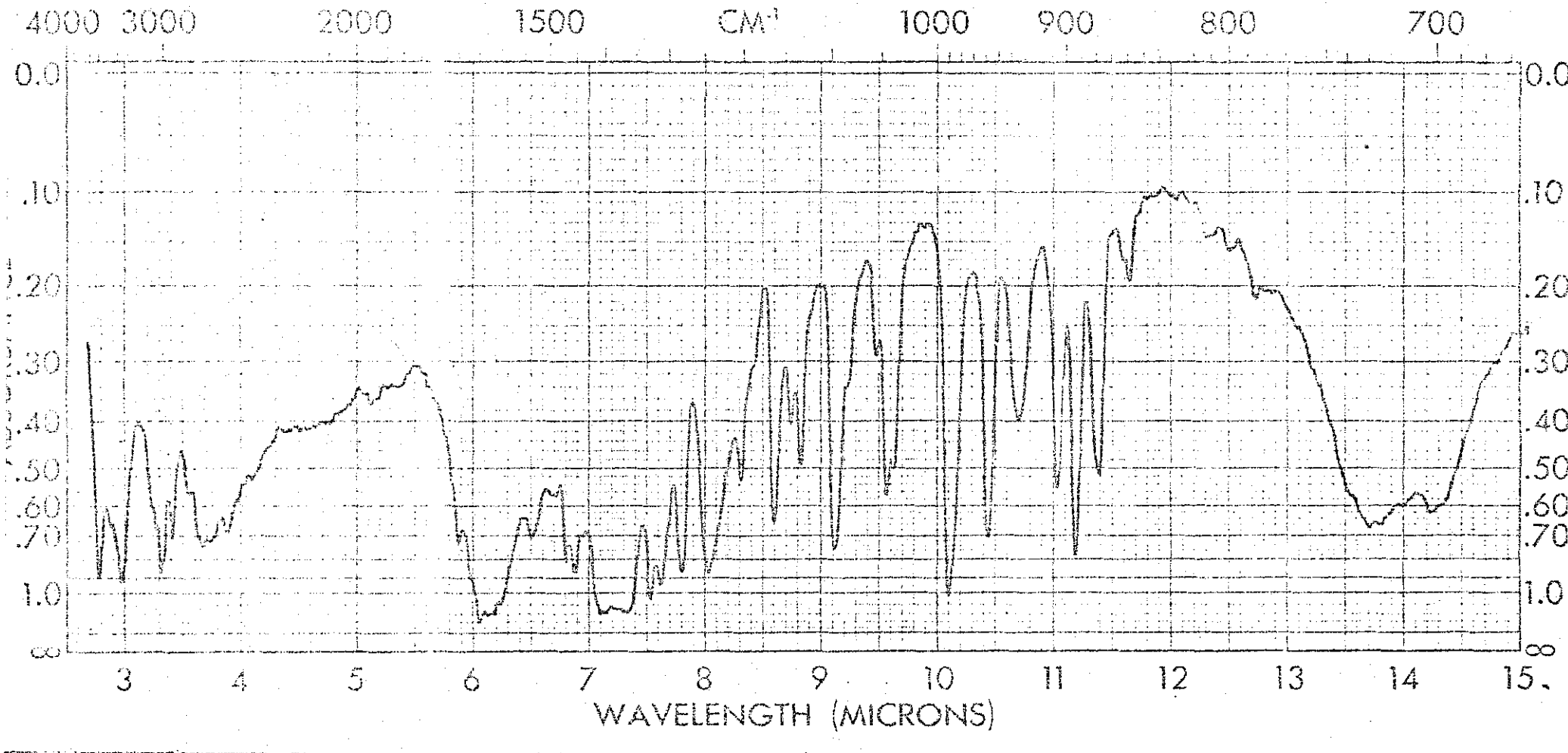
Bis 1-hexahydroazepineacetato palladium (II)

APPENDIX B

INFRA-RED SPECTRA



1-pyrrolidineacetic acid hydrochloride



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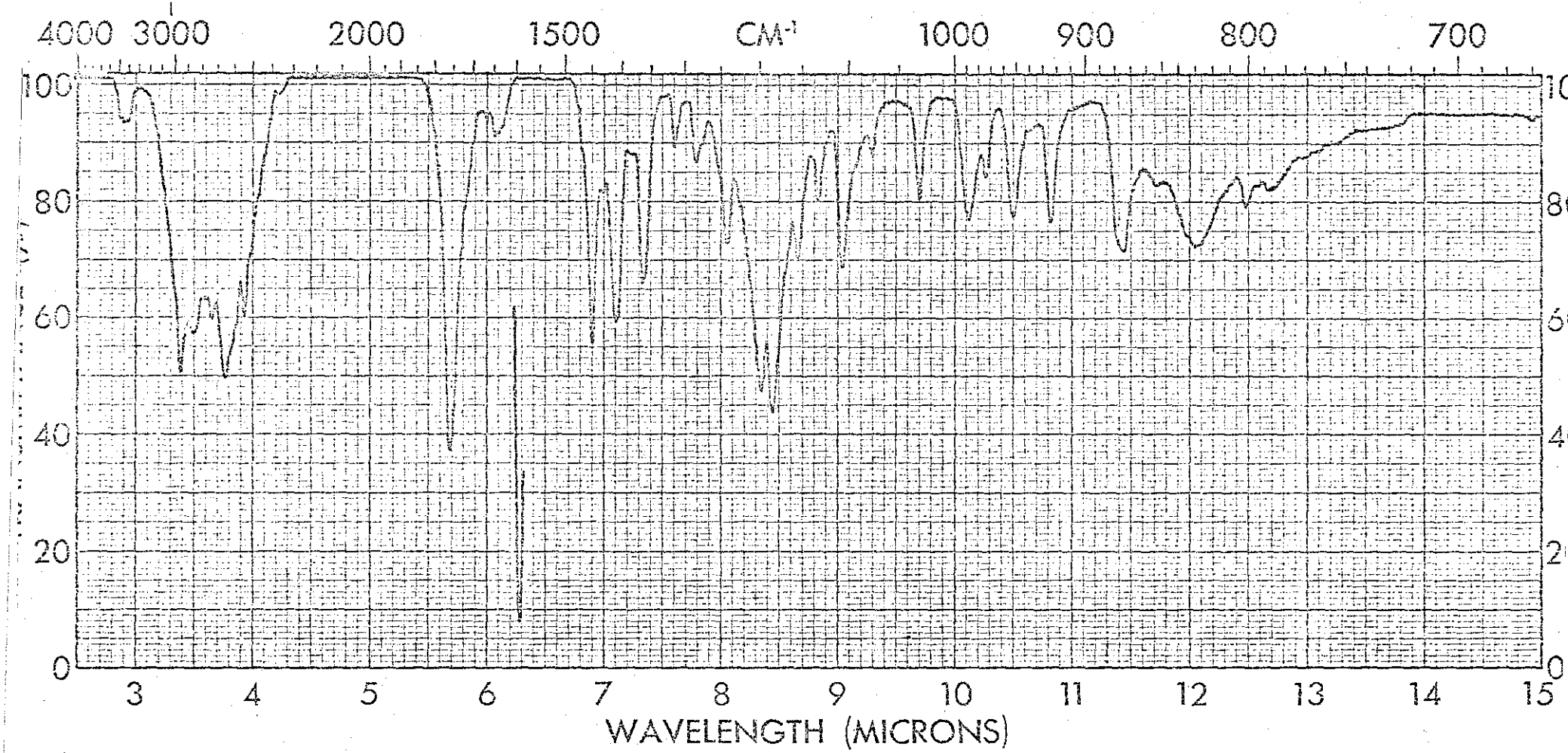

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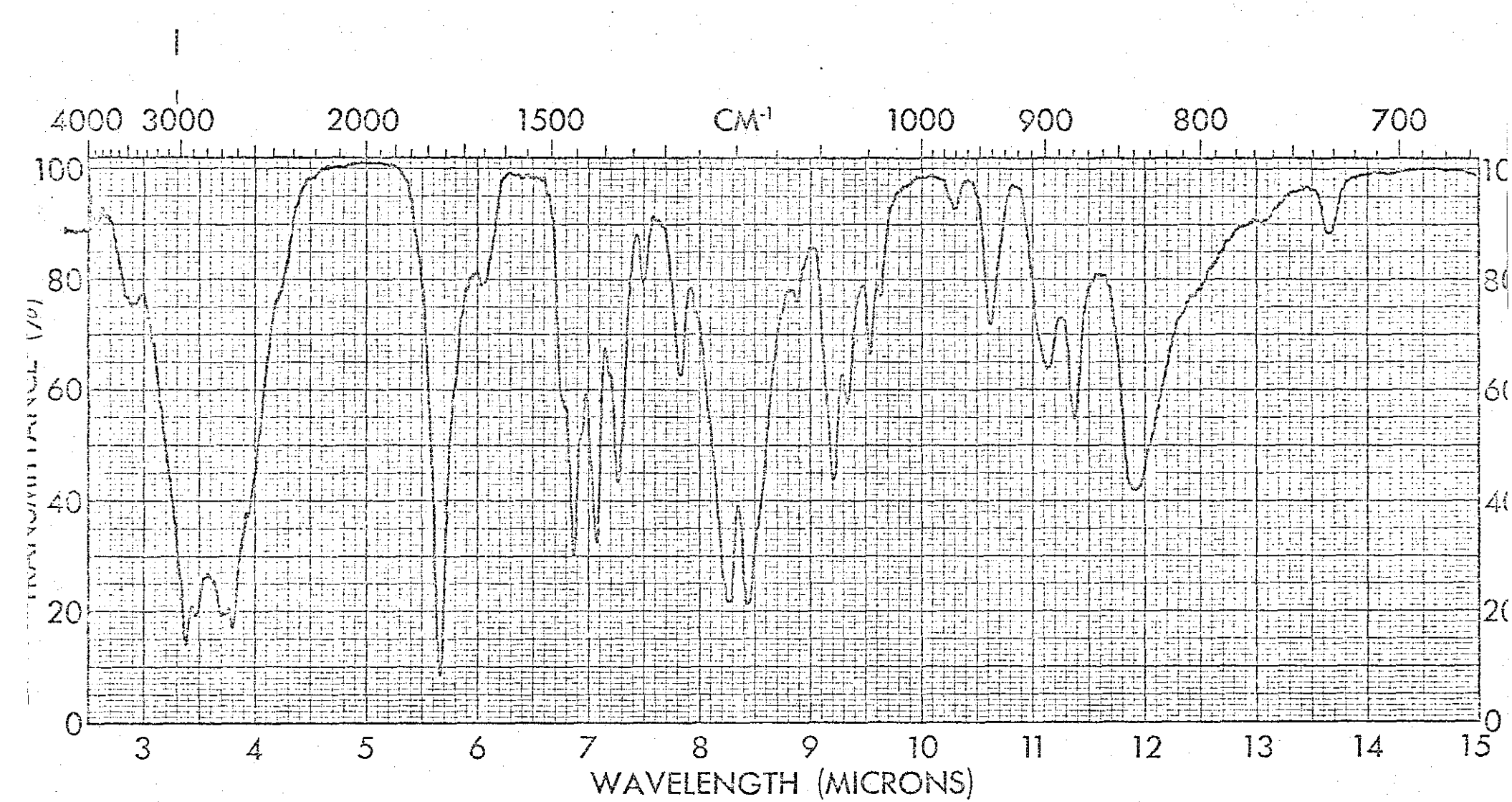

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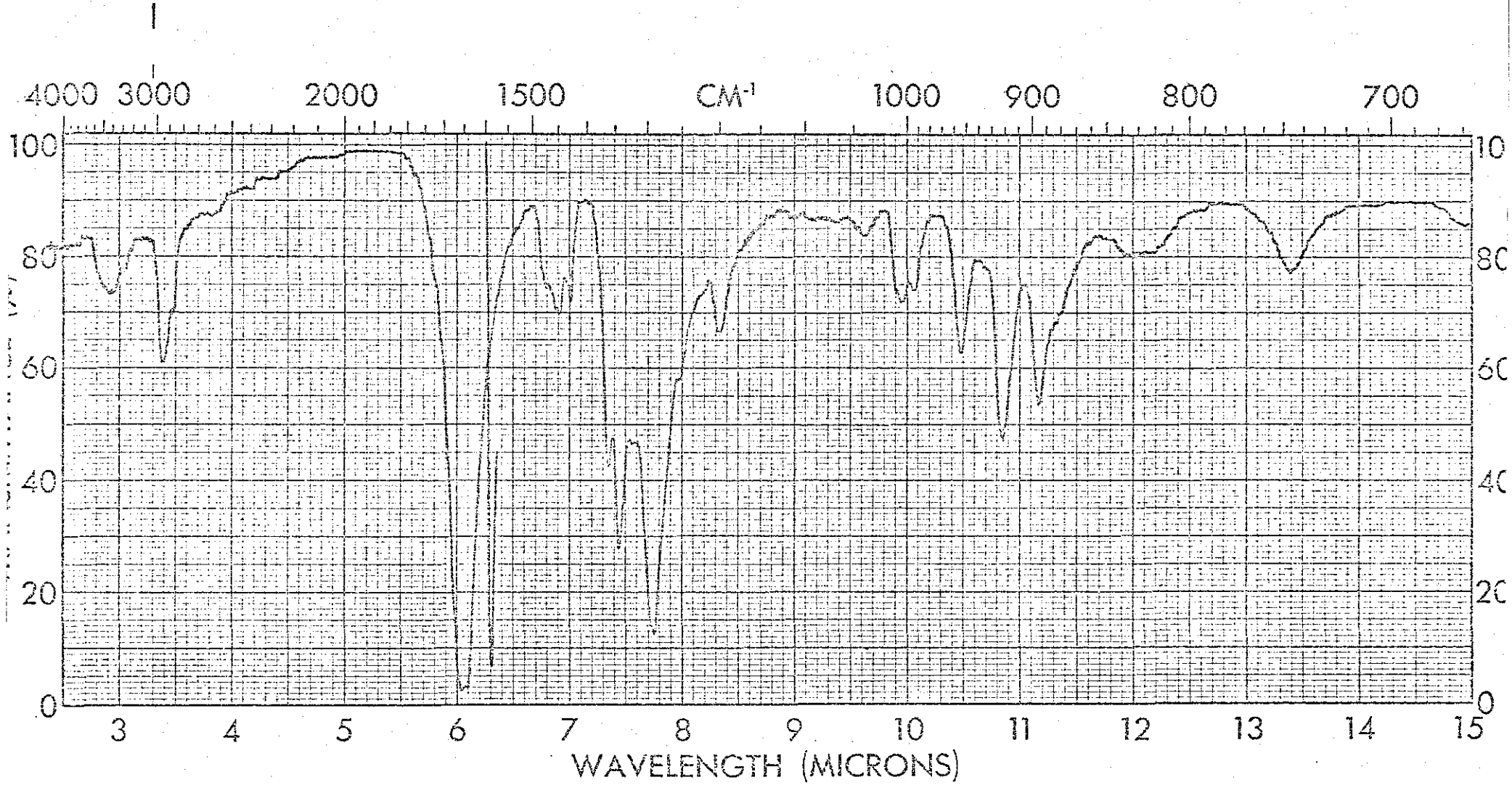

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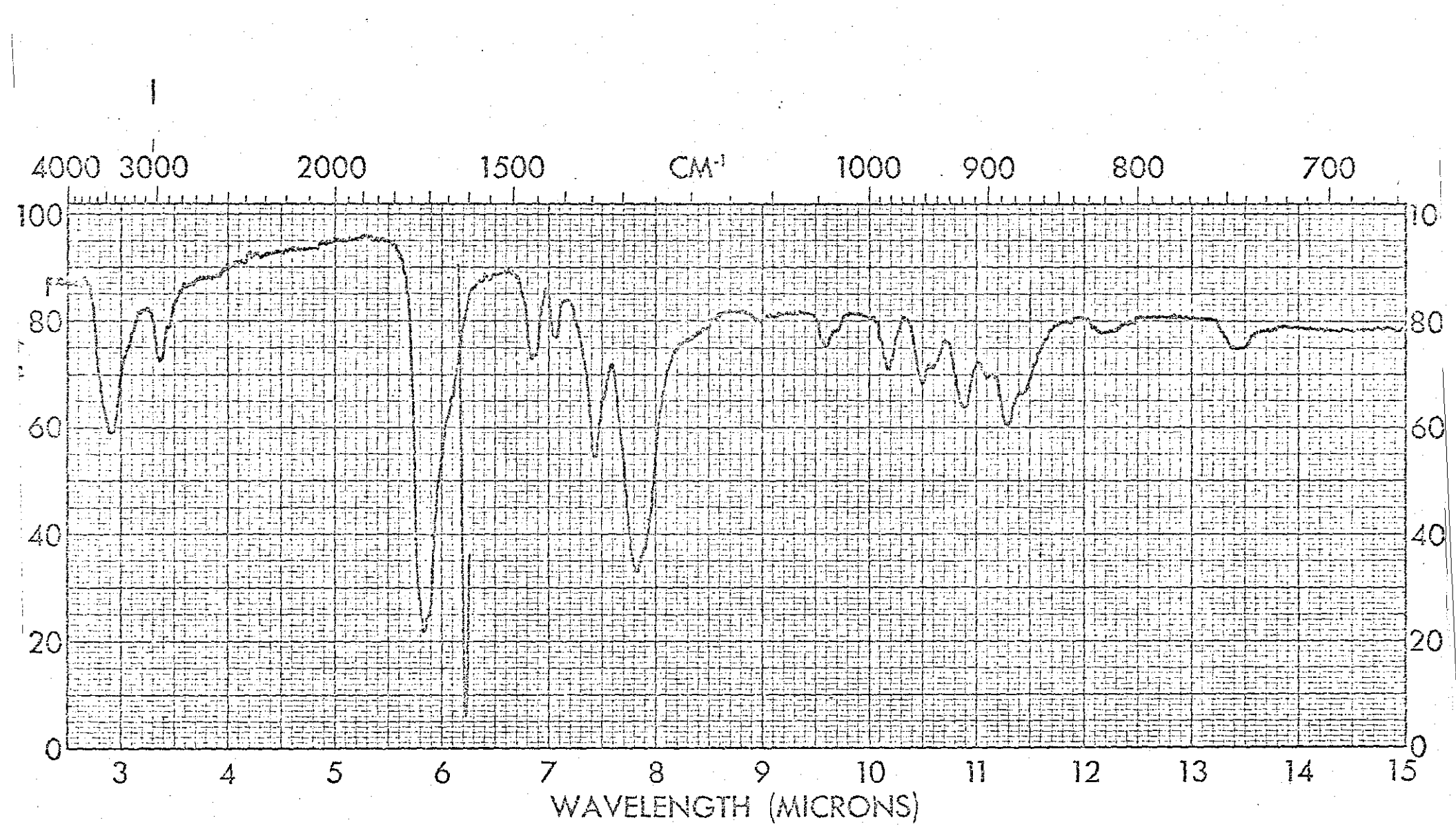

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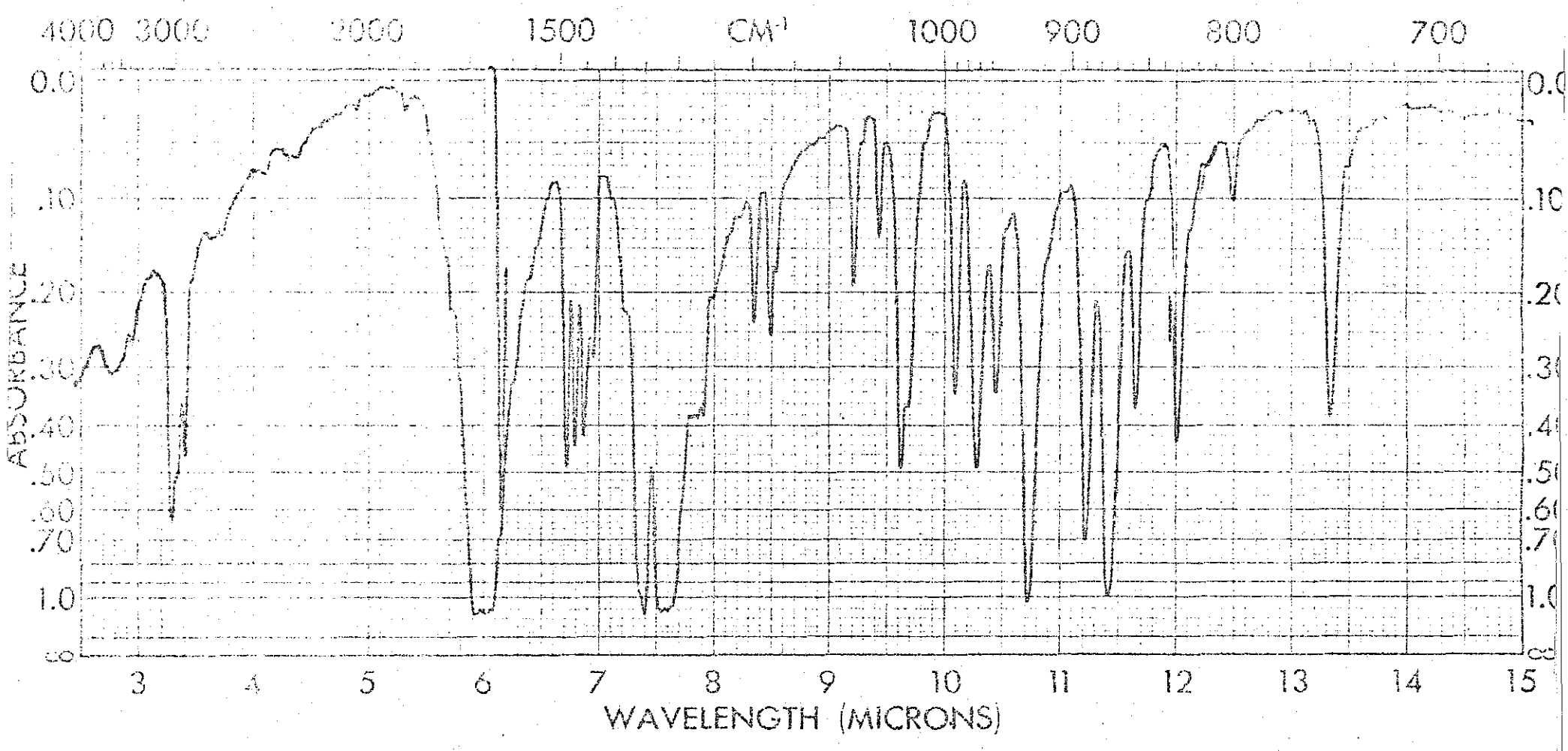

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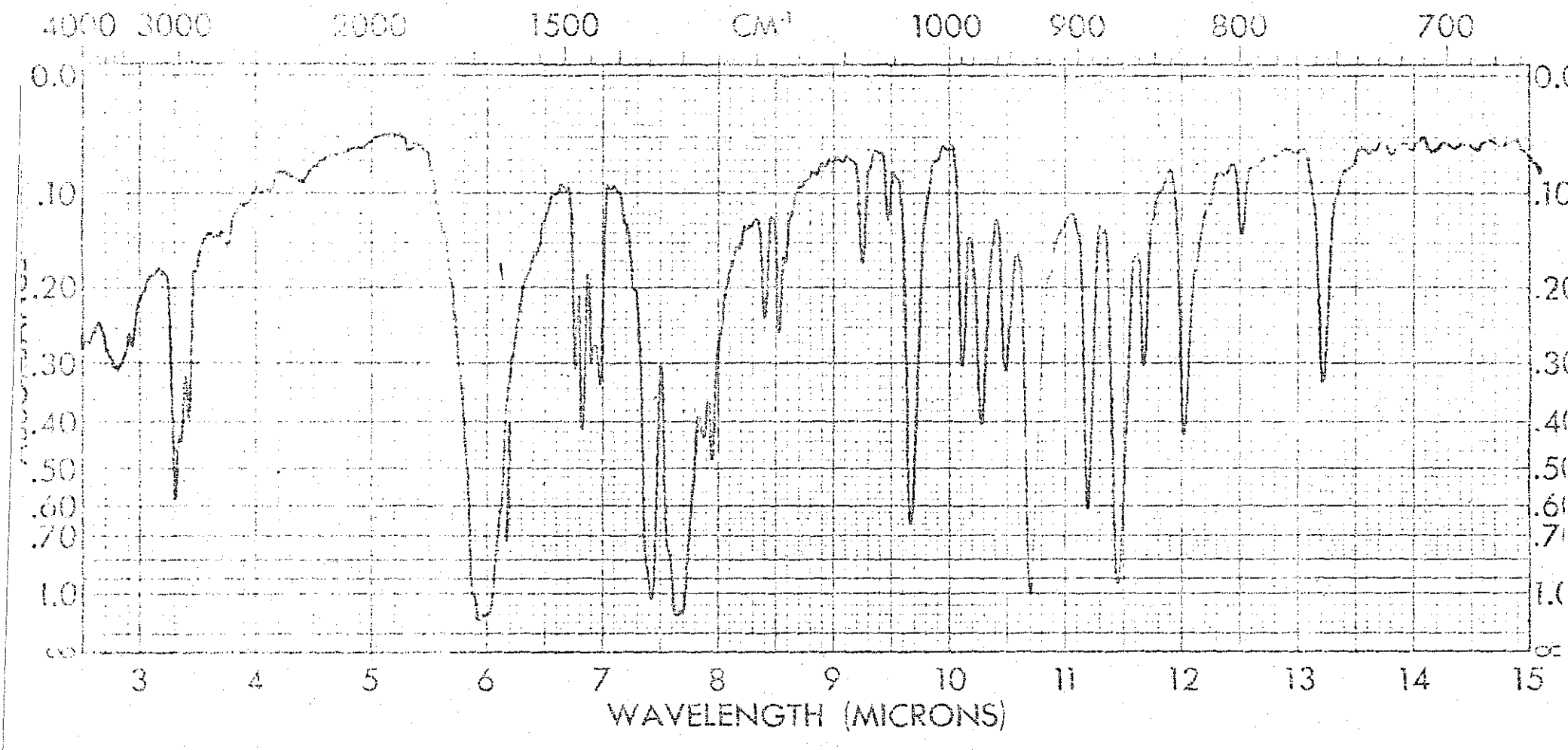

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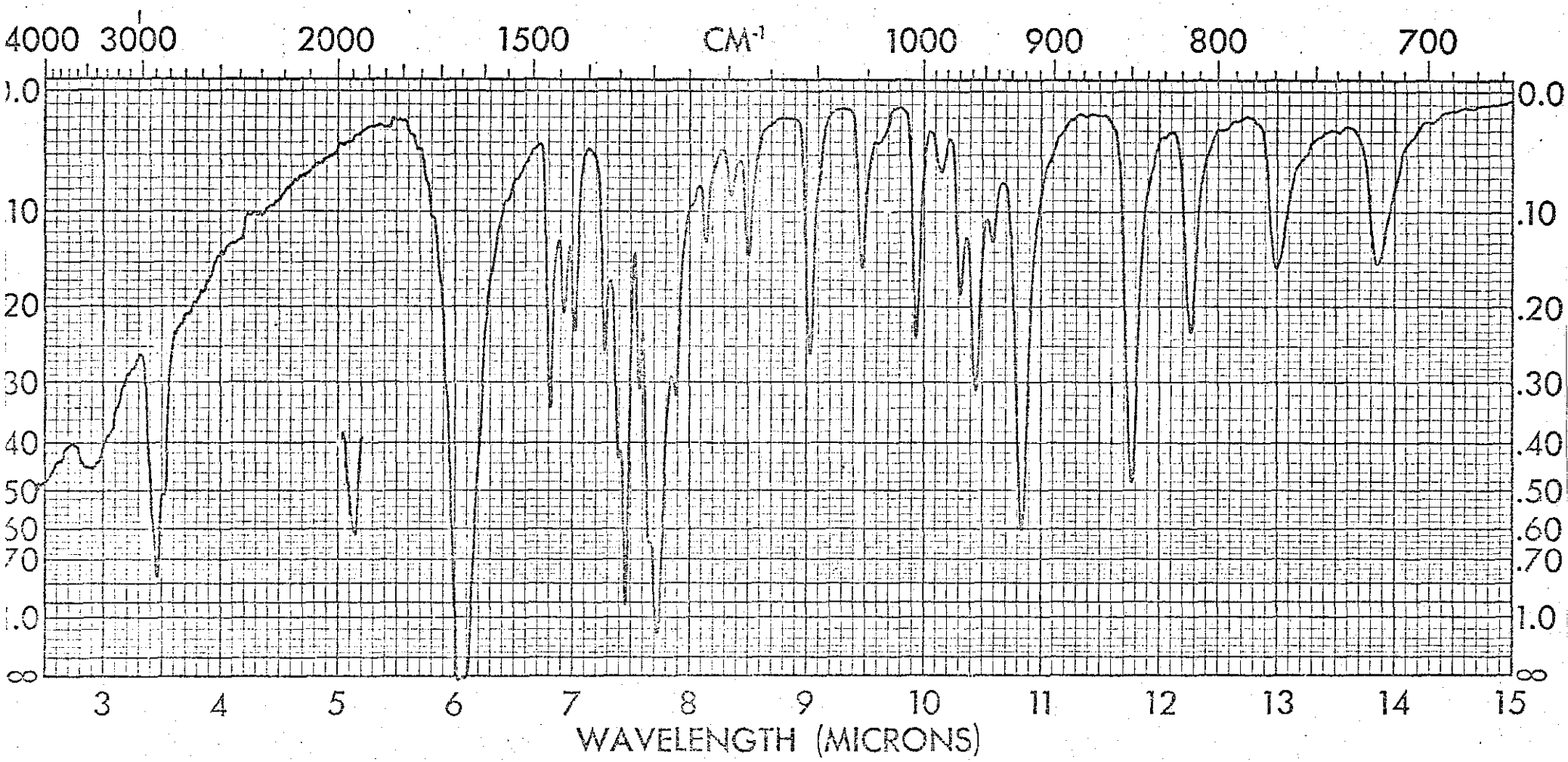

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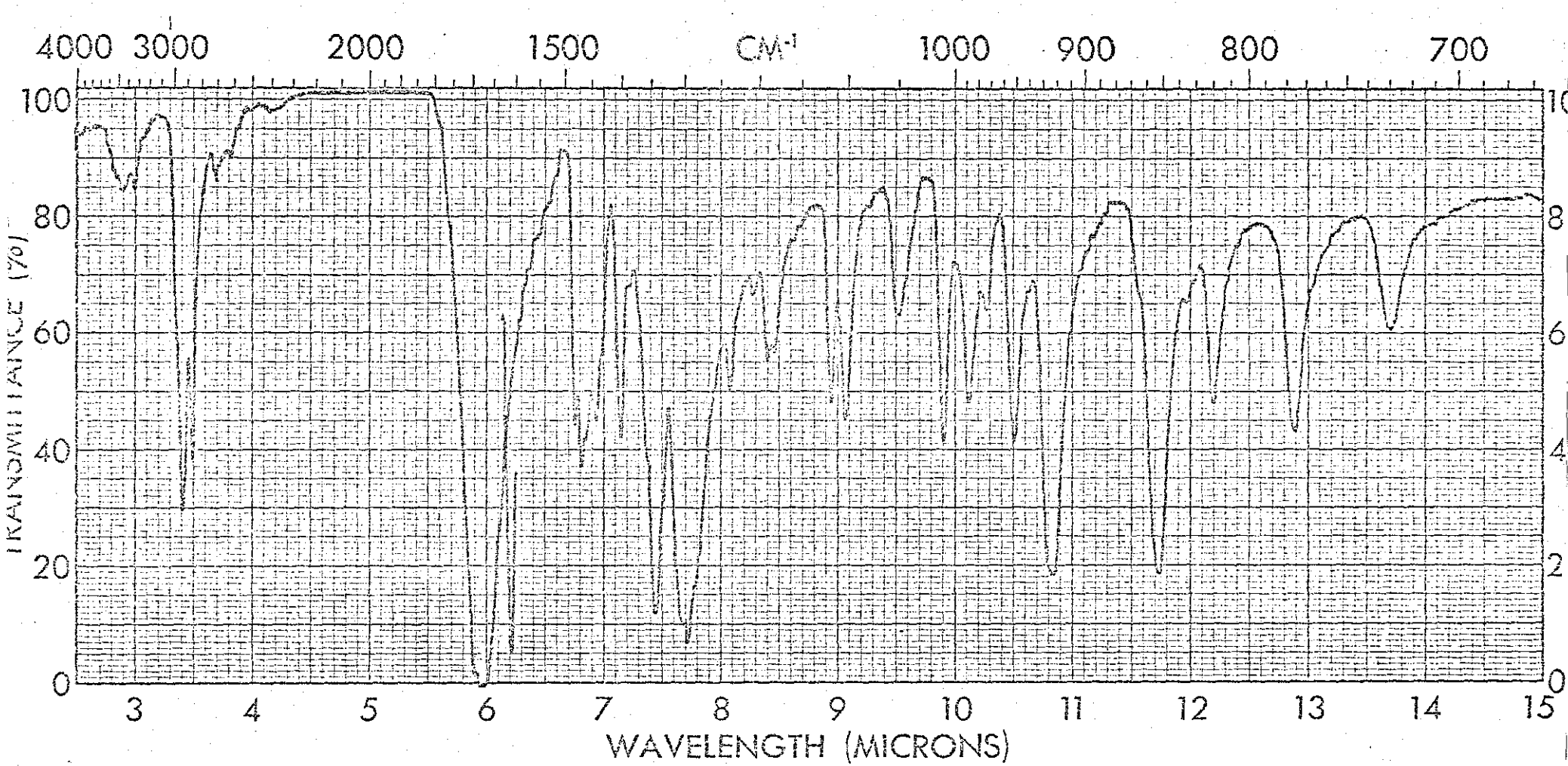

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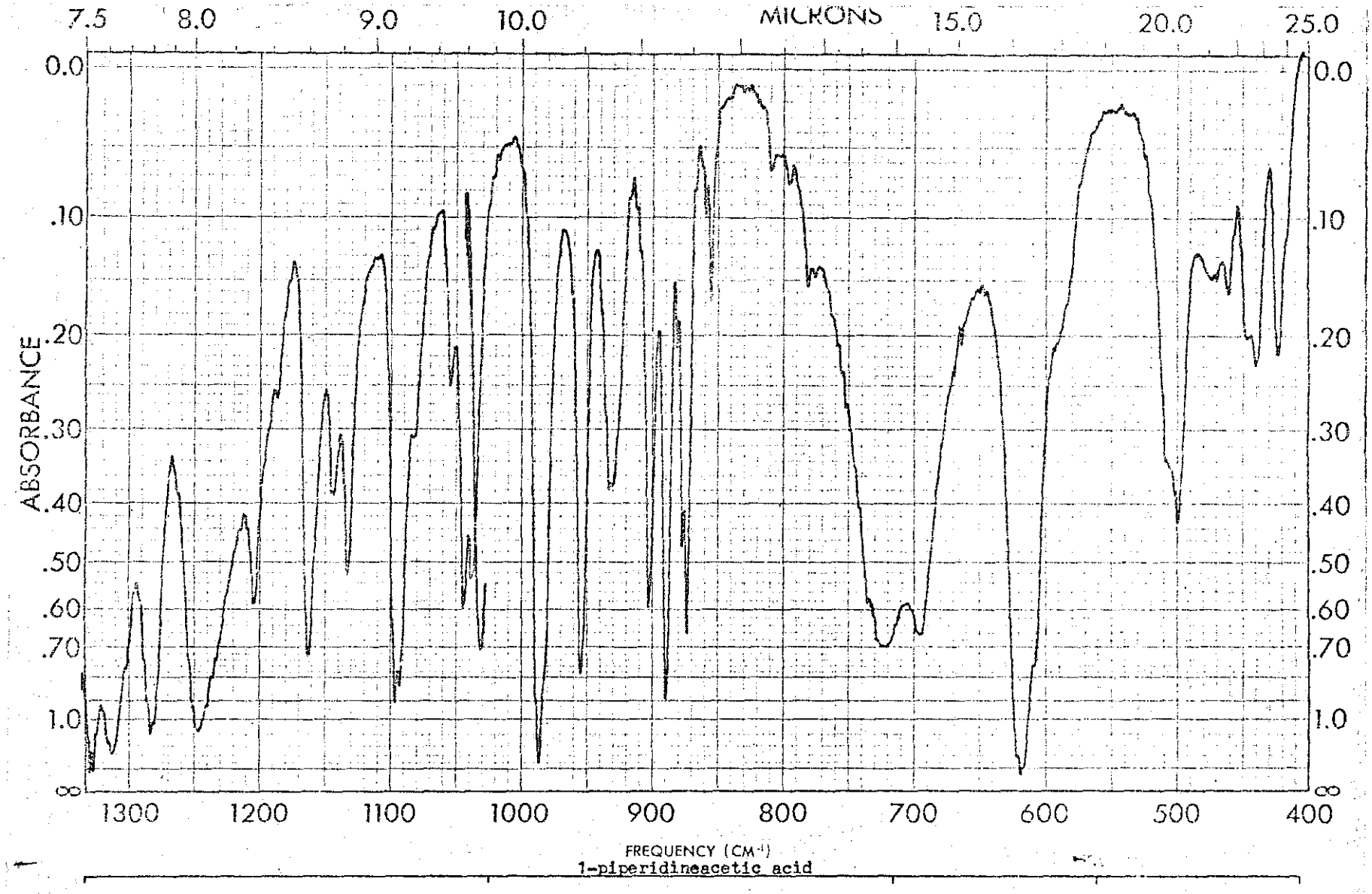
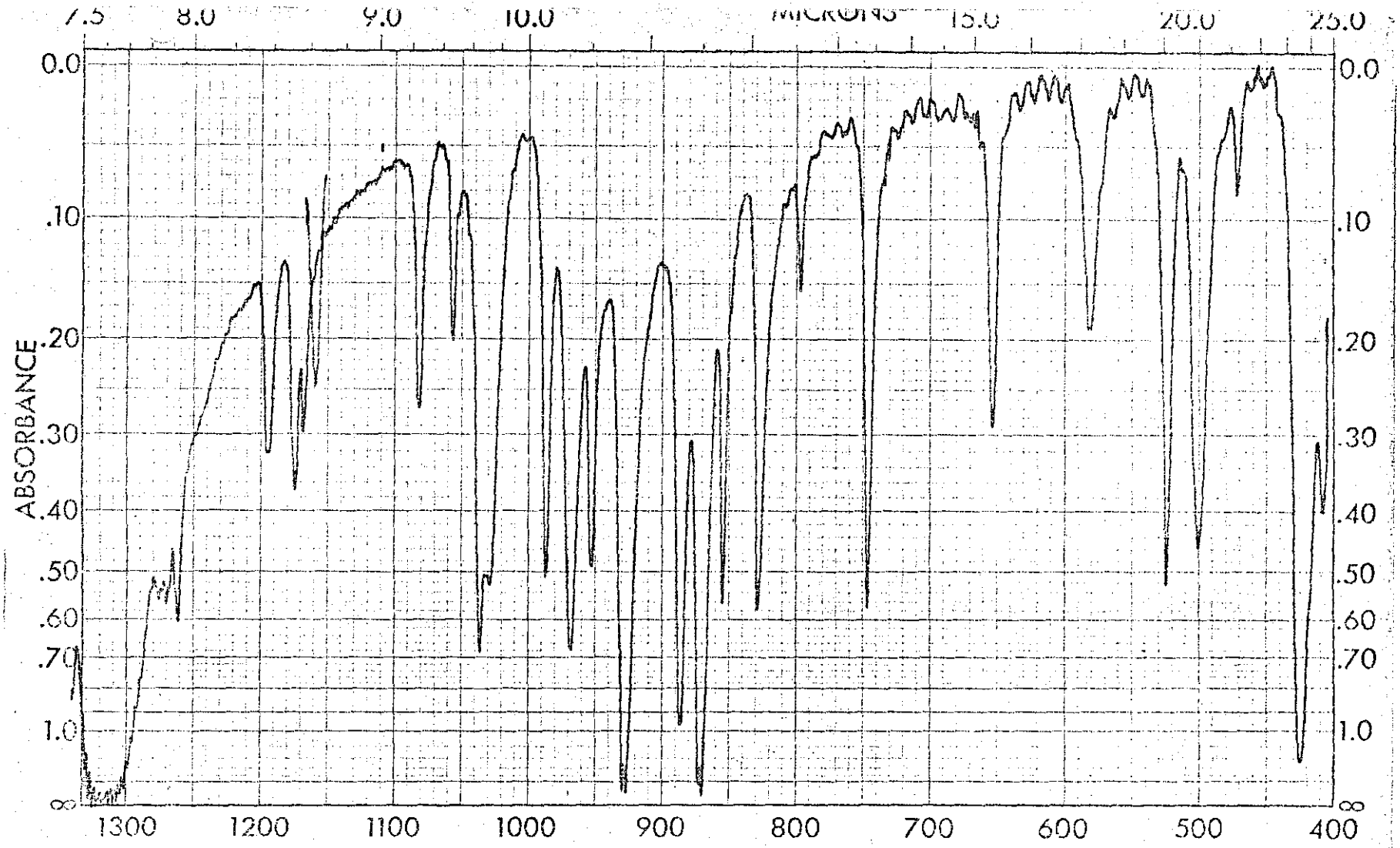


1-piperidineacetic acid



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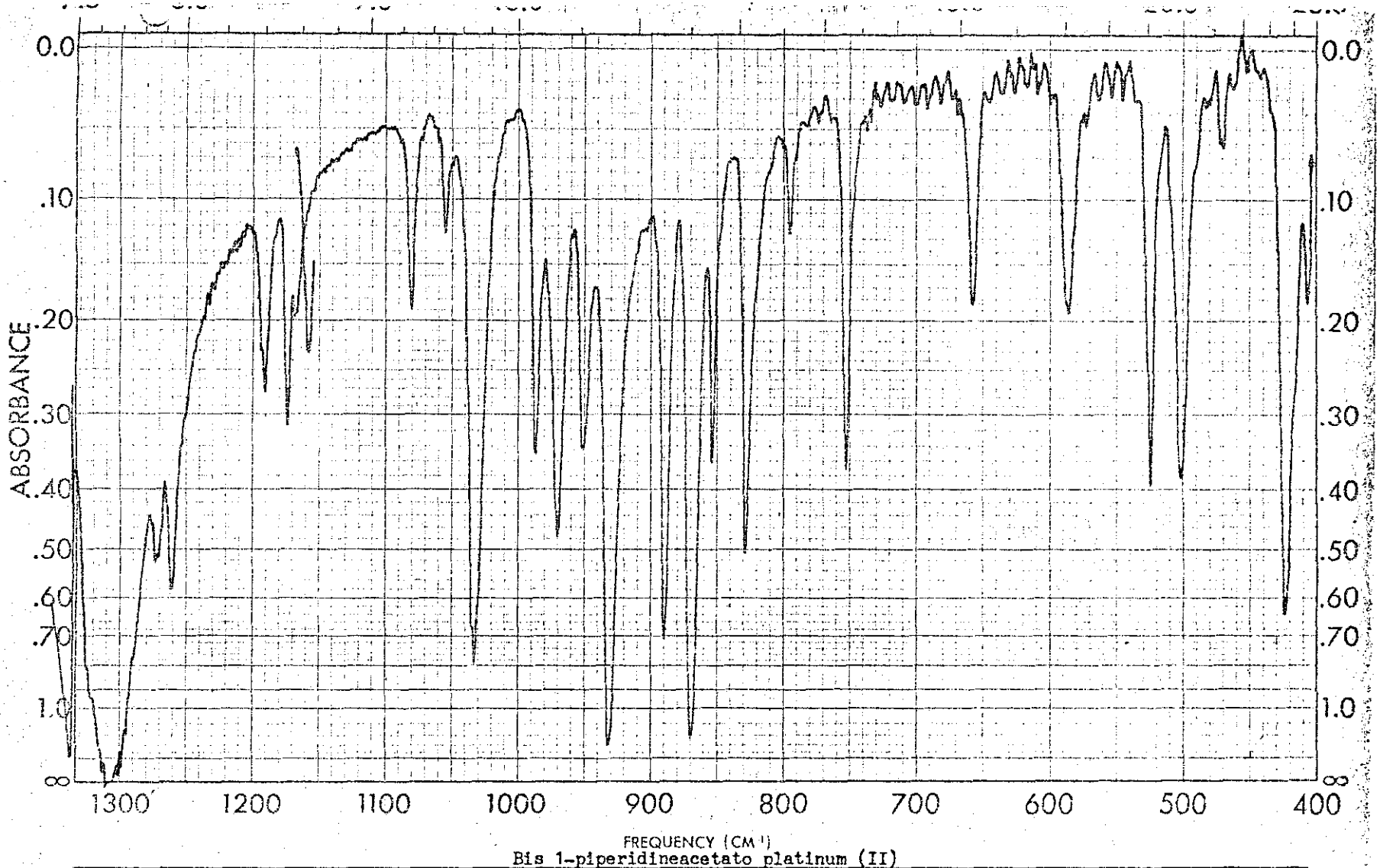

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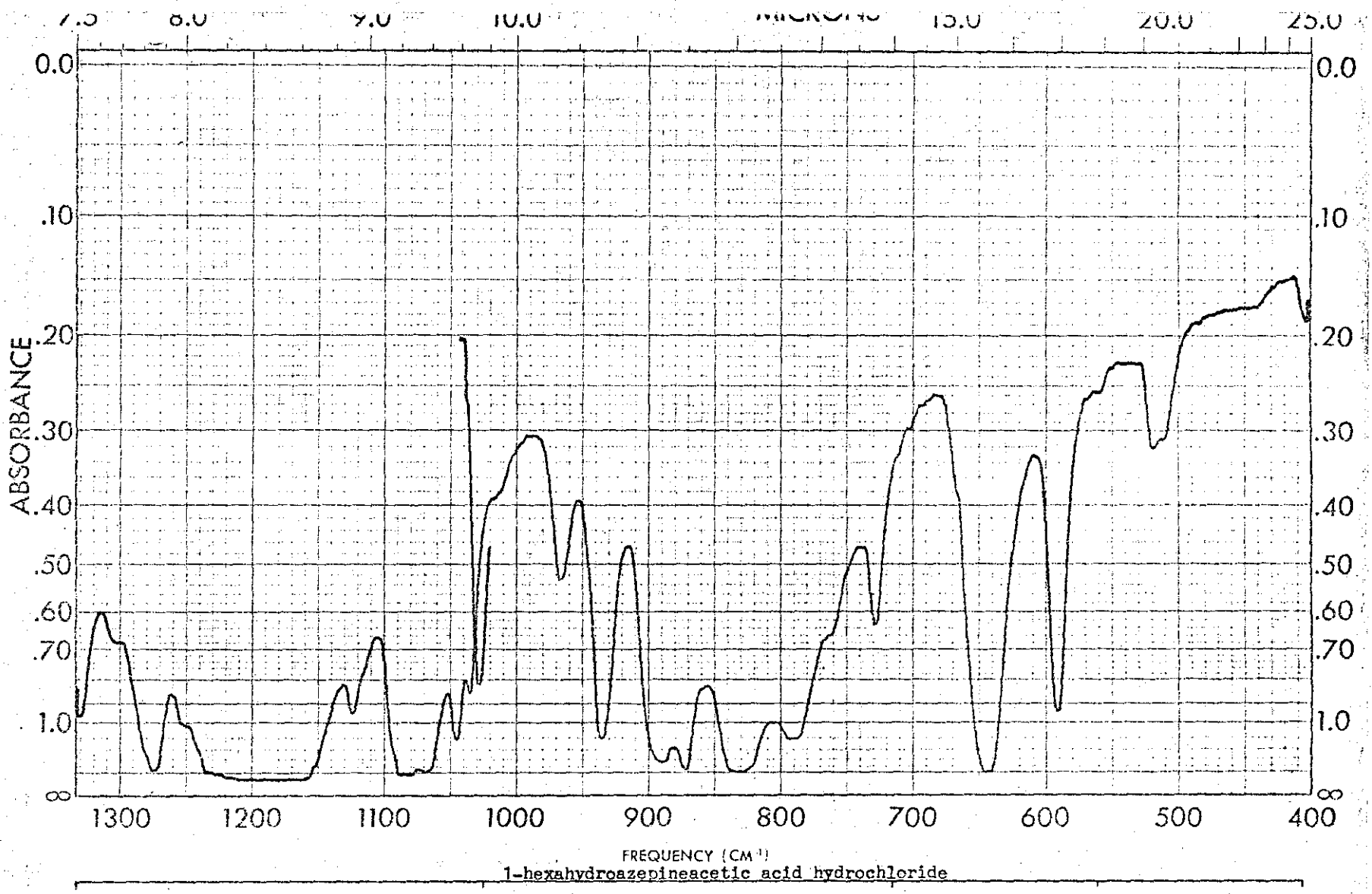
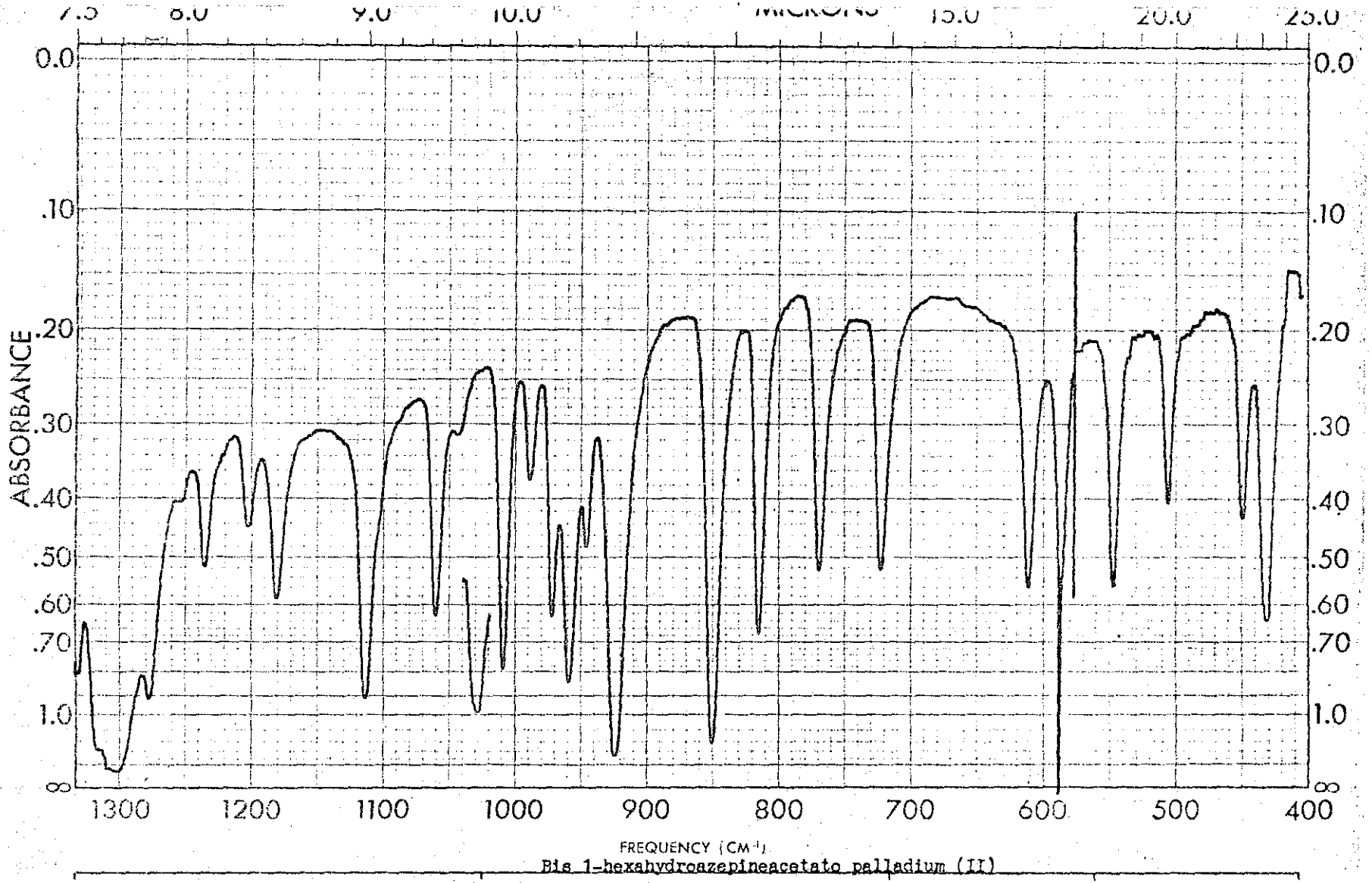


1-hexahydroazepineacetic acid hydrochloride



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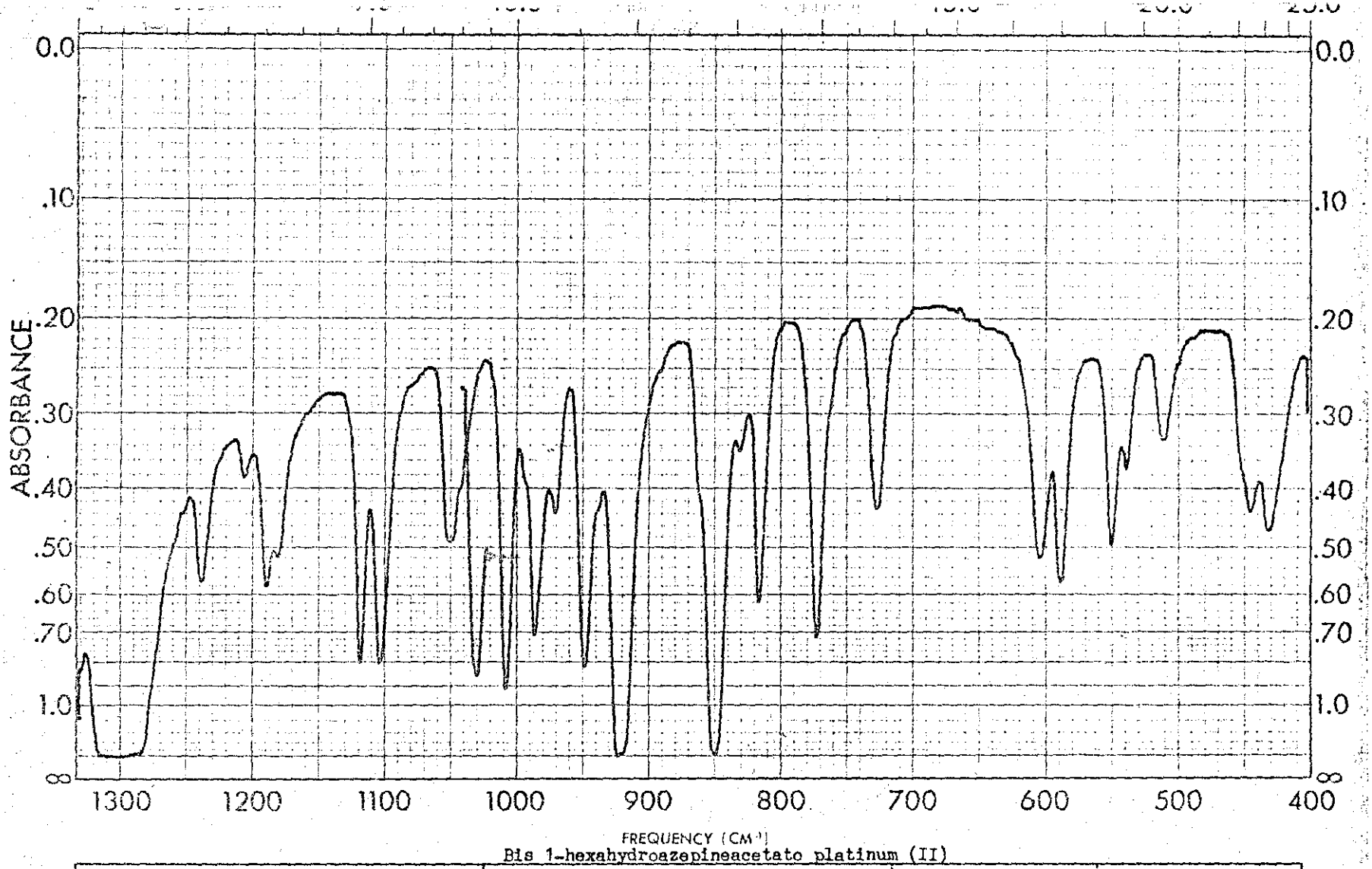
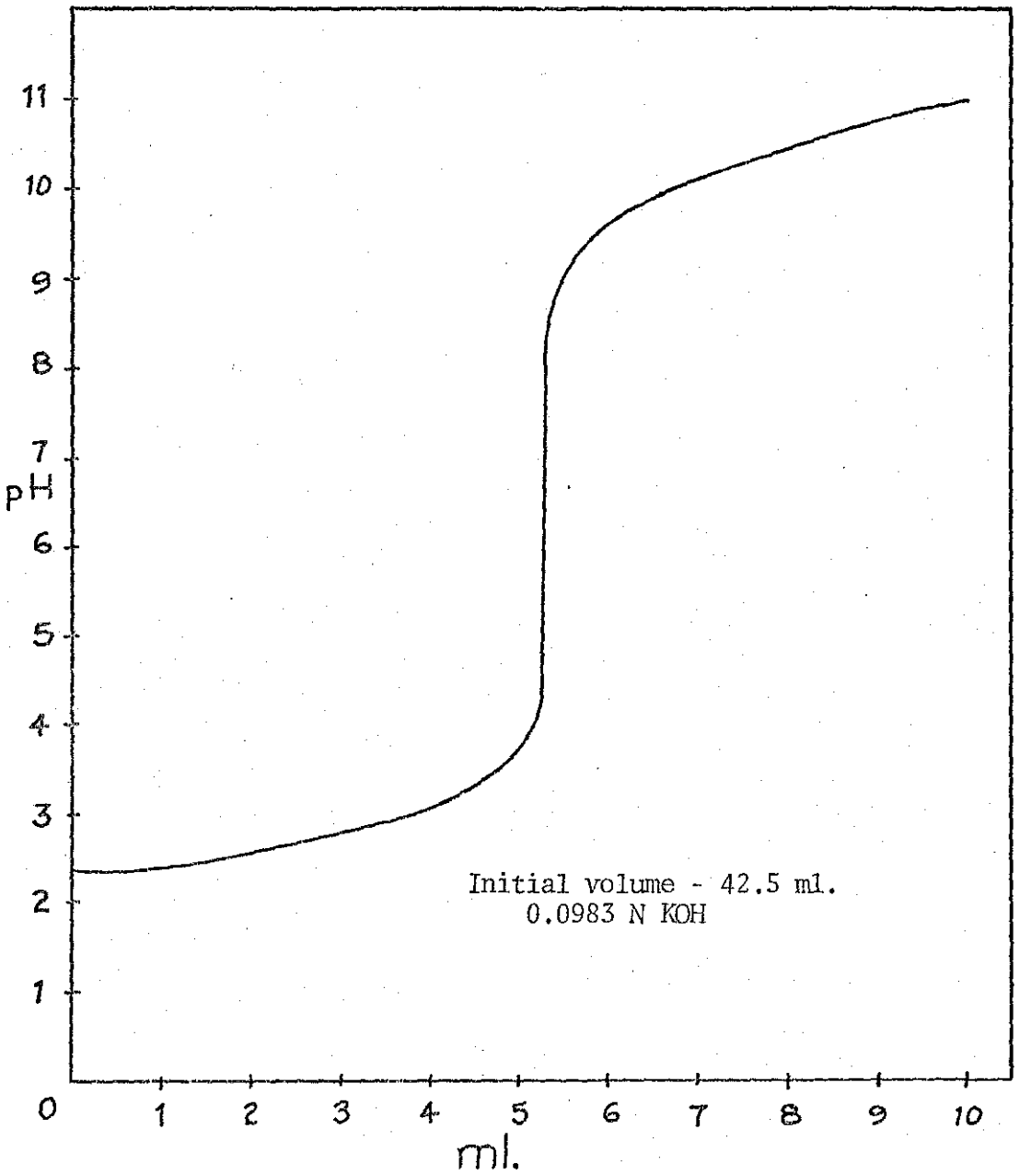


Bis 1-hexahydroazepineacetato platinum (II)

APPENDIX C

TITRATION DATA FOR IONIZATION CONSTANTS



TITRATION CURVE FOR 1-PYRROLIDINEACETIC ACID AT 25° C.

0.08762 g 1-Pyrrolidineacetic acid hydrochloride

0.03728 g KCl

Volume - 42.5 ml.

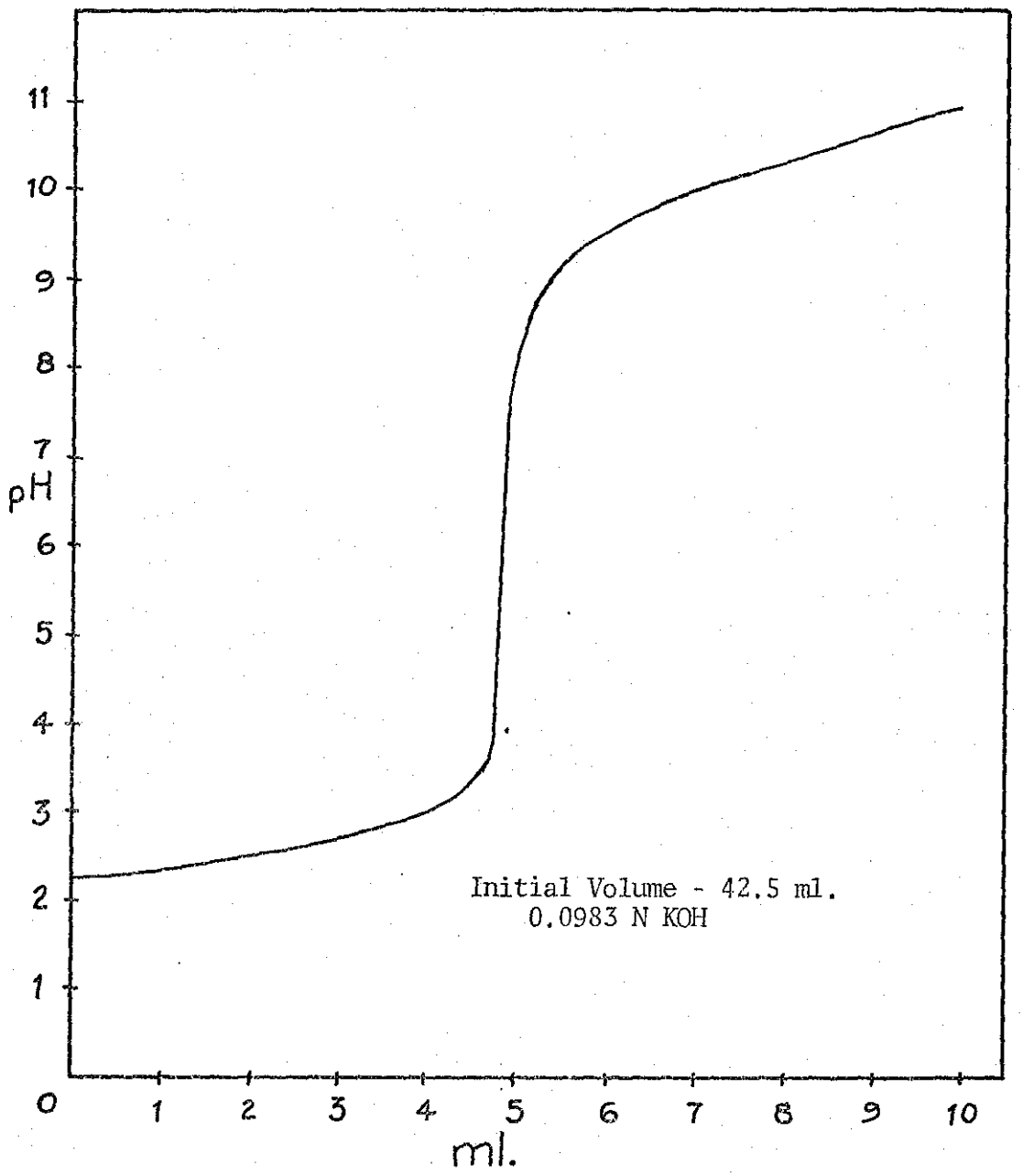
0.0983 N KOH

Volume	pH
0.00	2.31
0.50	2.37
1.00	2.44
1.50	2.51
2.01	2.58
2.50	2.66
3.00	2.77
3.50	2.88
4.00	3.03
4.50	3.26
5.00	3.68
5.50	9.01
6.04	9.65
6.50	9.90
7.02	10.12
7.50	10.28
8.01	10.43
8.50	10.56
9.01	10.68
9.50	10.81
10.00	10.95

TITRATION DATA FOR

1-PYRROLIDINEACETIC ACID

25°C.



TITRATION CURVE FOR 1-PIPERIDINEACETIC ACID AT 25°C.

0.08921 g 1-Piperidineacetic acid hydrochloride

0.03728 g KCl

Volume - 42.5 ml.

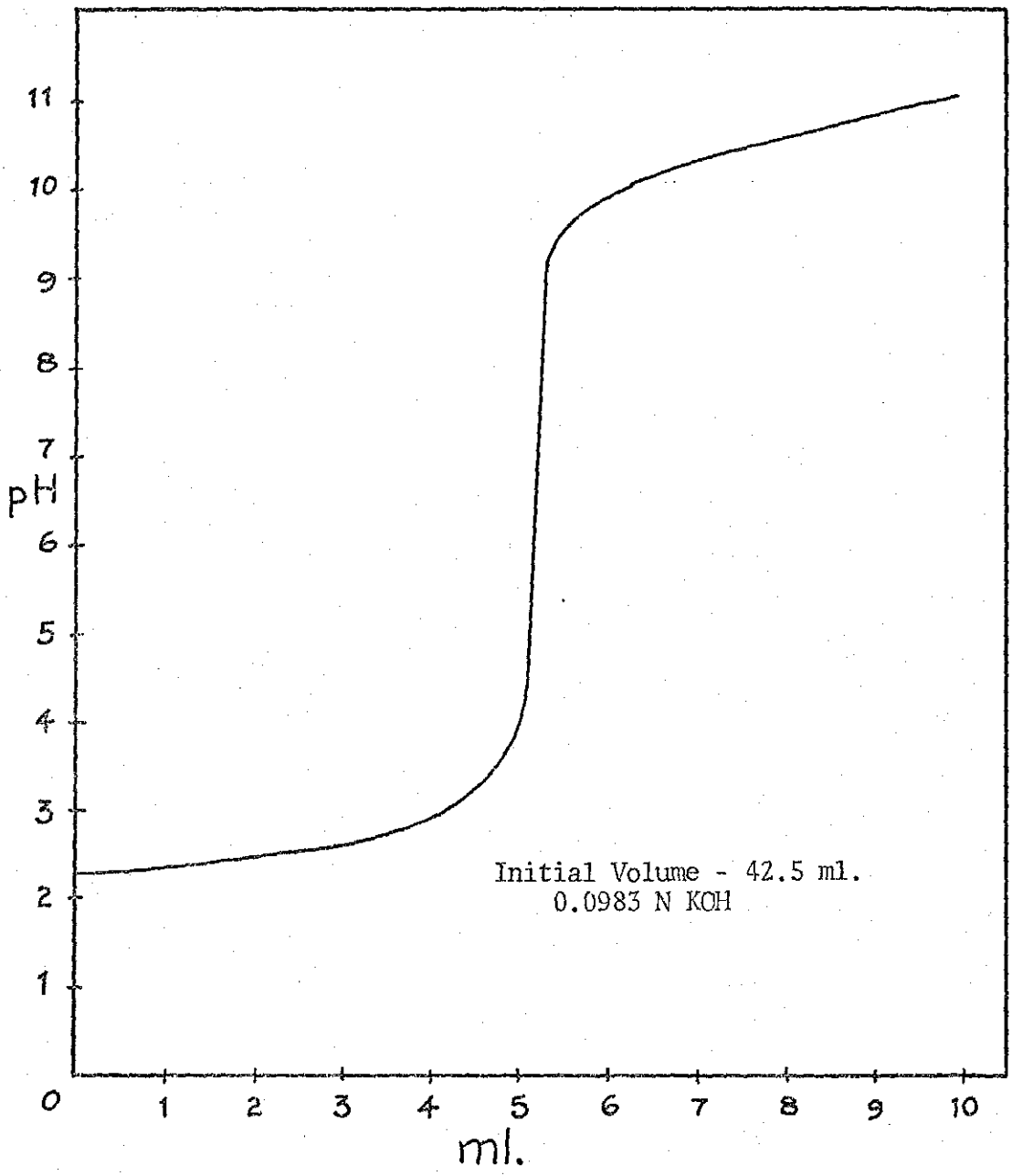
0.0983 N KOH

Volume	pH
0.00	2.23
0.51	2.29
1.01	2.35
1.51	2.43
2.00	2.50
2.50	2.60
3.00	2.70
3.50	2.84
4.00	3.02
4.60	3.46
5.10	8.40
5.50	9.20
6.00	9.57
6.51	9.80
7.00	9.99
7.50	10.12
8.00	10.30
8.51	10.46
9.00	10.62
9.50	10.79
10.00	10.96

TITRATION DATA FOR

1-PIPERIDINEACETIC ACID

25°C.



TITRATION CURVE FOR 1-HEXAHYDROAZEPINEACETIC ACID AT 25°C.

0.09977 g 1-Hexahydroazepineacetic acid hydrochloride

0.03728 g KCl

Volume - 42.5 ml.

0.0983 N KOH

Volume	pH
0.00	2.24
0.50	2.28
1.03	2.35
1.50	2.42
2.01	2.49
2.50	2.58
3.00	2.68
3.51	2.81
4.01	2.97
4.54	3.27
5.04	4.03
5.40	9.27
5.62	9.59
6.02	9.89
6.50	10.10
7.00	10.29
7.50	10.45
8.00	10.57
8.51	10.71
9.02	10.82
9.52	10.96
9.99	11.07

TITRATION DATA FOR

1-HEXAHYDROAZEPINEACETIC ACID

25°C.

APPENDIX D

TITRATION DATA FOR STABILITY CONSTANTS

0.08241 g K_2PdCl_4

0.08398 g 1-Pyrrolidineacetic acid hydrochloride

Volume - 45.0 ml.

0.0983 N KOH

Volume	pH
0.00	2.04
0.50	2.07
1.00	2.11
1.50	2.15
2.01	2.19
2.52	2.23
3.00	2.27
3.50	2.31
4.00	2.37
4.50	2.43
5.02	2.49
5.50	2.55
6.00	2.62
6.50	2.71
7.01	2.81
7.51	2.93
8.00	3.06
8.50	3.30
9.00	3.52
9.53	4.01

TITRATION DATA FOR

$Pd(PyrAA)_2$

$25^{\circ}C.$

0.08625 g K_2PdCl_4

0.09710 g 1-Piperidineacetic acid hydrochloride

Volume - 45.0 ml.

0.0983 N KOH

Volume	pH
0.00	2.08
0.56	2.11
1.10	2.15
1.50	2.18
2.00	2.20
2.50	2.24
3.01	2.29
3.50	2.33
4.00	2.38
4.50	2.43
5.00	2.49
5.50	2.55
6.00	2.62
6.50	2.70
7.00	2.80
7.50	2.91
8.00	3.04
8.50	3.22
9.22	3.54
9.49	3.70
10.00	4.19

TITRATION DATA FOR

$Pd(PipAA)_2$

25°C.

0.08346 g K_2PdCl_4

0.10295 g 1-Hexahydroazepineacetic acid hydrochloride

Volume - 45.0 ml.

0.0983 N KOH

Volume	pH
0.00	2.13
0.50	2.16
1.02	2.19
1.52	2.22
2.00	2.25
2.50	2.30
3.03	2.35
3.50	2.38
4.00	2.43
4.50	2.48
5.00	2.55
5.50	2.61
6.00	2.67
6.51	2.75
7.08	2.86
7.54	2.96
8.00	3.13
8.50	3.27
9.02	3.47
9.50	3.75
10.00	4.27

TITRATION DATA FOR

$Pd(HexAA)_2$

$25^{o}C.$

0.10368 g K_2PtCl_4

0.09200 g 1-Pyrrolidineacetic acid hydrochloride

Volume - 45.0 ml.

0.0983 N KOH

Volume	pH
0.00	2.27
0.50	2.33
0.76	2.37
1.00	2.40
1.25	2.43
1.52	2.46
1.80	2.50
2.00	2.53
2.26	2.57
2.50	2.62
2.81	2.67
3.00	2.70
3.25	2.75
3.58	2.83
4.00	2.94
4.50	3.12
4.74	3.23
5.00	3.41
5.20	3.60
5.52	4.53
6.00	8.98

TITRATION DATA FOR

$Pt(PyrAA)_2$

25°C.

0.10651 g K_2PtCl_4

0.09510 g 1-Piperidineacetic acid hydrochloride

Volume - 45.0 ml.

0.0983 N KOH

Volume	pH
0.00	2.20
0.50	2.26
1.00	2.33
1.50	2.39
2.00	2.46
2.50	2.55
3.00	2.66
3.50	2.77
4.00	2.93
4.50	3.18
5.00	3.67
5.50	8.30

TITRATION DATA FOR

$Pt(PipAA)_2$

$25^{o}C.$

0.10119 g K_2PtCl_4

0.10044 g 1-Hexahydroazepineacetic acid hydrochloride

Volume - 45.0 ml.

0.0983 N KOH

Volume	pH
0.00	2.24
0.50	2.30
0.75	2.32
1.01	2.35
1.25	2.38
1.50	2.42
1.75	2.45
2.00	2.48
2.25	2.52
2.51	2.57
3.10	2.69
3.50	2.80
3.75	2.86
4.01	2.96
4.50	3.19
5.00	3.70
5.50	8.66

TITRATION DATA FOR

$Pt(HexAA)_2$

$25^{o}C.$