FRANK MICHAEL D'ITRI Ph. D.

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THE SYNTHESES AND COMPLEXATION OF SOME 1,5- CYCLOPOLYMETHYLENETETRAZOLES AND BITETRAZOLES

Thesis for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY
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THE SYNTHESES AND COMPLEXATION OF SOME
1,5-CYCLOPOLYMETHYLENETETRAZOLES
AND BITETRAZOLES

presented by

Frank Michael D'Itri

has been accepted towards fulfillment
of the requirements for

Ph. D. degree in Chemistry

Major professor

Date August 6, 1968

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ABSTRACT

THE SYNTHESES AND COMPLEXATION OF SOME 1,5-CYCLOPOLYMETHYLENETETRAZOLES AND BITETRAZOLES

by Frank Michael D'Itri

The purpose of this investigation was to study the influence of substituent groups on the physicochemical and pharmacological properties of the respective 1,5-cyclopolymethylenetetrazoles and bitetrazoles.

A series of 1,5-cyclopolymethylenetetrazoles were synthesized with the hydrocarbon chain containing 3,4,6, 7,8,9, and 11 methylene groups (hereafter abbreviated as C_nMT where n indicates the number of methylene groups in the compound). The donor properties of these tetrazoles were investigated by spectrophotometric and potentiometric techniques.

The spectrophotometric study consisted of the measurement of the cyclopolymethylenetetrazole-iodine charge-transfer complex formation constants for the reaction $C_nMT + I_2 \rightleftharpoons C_nMT \cdot I_2$ in the 5-35° interval. The solvent was 1,2-dichloroethane, and the data were obtained with a Beckman model DU spectrophotometer equipped with Beckman thermospacers to control the temperature of the sample compartment.

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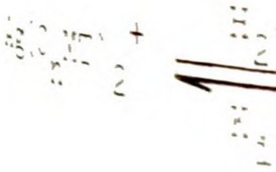
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The enthalpy and entropy changes for the complexing reactions were determined from the temperature coefficient of the stability constant. The donor properties of cyclopolymethylenetetrazoles were rather weak, and the formation constant values at 25° ranged from 1.42 to 2.64 liter mole^{-1}. There does not seem to be a simple correlation between the length of the hydrocarbon chain and the stability of the iodine complex.

The potentiometric study consisted of the determination of the dissociation constants for the complexes formed between silver(I) nitrate and the water soluble 1,5-cyclopolymethylenetetrazoles (tri, tetra, penta, hexa, and heptamethylenetetrazole). The stoichiometry of the reaction is given by the following equation.

$$Ag(C_nMT)_2^+ \underset{K_i}{\overset{H_2O}{\rightleftharpoons}} Ag^+ + 2C_nMT$$

Data were obtained with a Beckman expanded scale pH meter and a two compartment cell equipped with a Corning NAS 11-18 sodium ion electrode, a Beckman silver billet electrode or a silver plated on platinum electrode immersed in the silver solutions connected by means of a "salt-bridge" of 1.0 M potassium nitrate solution to a saturated calomel reference electrode. The concentrations of free silver ion in solutions of the respective silver(I) nitrate-1,5-cyclopolymethylenetetrazole complex was

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determined by comparing the observed potential readings with the calibration curve. A constant ionic strength with 0.1 and 0.4 M potassium nitrate was employed. Therefore, the activity coefficients of the silver ion can be considered to remain constant in all the solutions studied. These complexes of the general formula $Ag(C_nMT)_2^+$ were all nearly equally stable. The pK_f values at 25° ranged from -2.91 to -3.13 with the exception of the heptamethylenetetrazole-silver(I) complex which differed by about 0.3 pK_f unit. Once again, no simple correlation appears to exist between the length of the hydrocarbon chain and the stability of the respective silver(I) complex.

The crystalline complexes, bis(trimethylenetetrazole)-silver(I) and bis(tetramethylenetetrazole silver(I) nitrate analogous to bis(pentamethylenetetrazole)silver(I) nitrate (1) were prepared and characterized.

1,1'-Diphenyl-5,5'-bitetrazole was prepared to study its coordination properties. Attempts to prepare solid complexes with copper(II) perchlorate hexahydrate dehydrated with 2,2-dimethoxypropane in various solvents (2,3) were unsuccessful, and all of the starting material was recovered unreacted. The complexing ability of 1,1'-diphenyl-5,5'-bitetrazole in 1,2-dichloroethane and nitromethane was studied by the method of continuous variations with iodine and copper(II) perchlorate

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hexahydrate respectively. The spectrophotometric data indicated that, surprisingly, the bitetrazole does not form complexes with the above Lewis acids.

In the course of this investigation the following new 6,6-dihalocyclopolymethylenetetrazoles and bitetrazoles were synthesized.

1. 6,6-Dichlorotetramethylenetetrazole
2. 6,6-Dibromotetramethylenetetrazole
3. 6,6-Dichloropentamethylenetetrazole
4. 6,6-Dibromopentamethylenetetrazole
5. 6,6-Dichlorohexamethylenetetrazole
6. 5,5'-Diphenyl-1,1'-bitetrazole
7. 1,4-Bis(5-phenyl-1-tetrazolyl)-n-butane

The attempted preparations of bis(1-phenyl-5-tetrazolyl)methane, 1,2-bis(1-phenyl-5-tetrazolyl)ethane, 1,1'-dimethyl and 1,1'-di-tert-butyl-5,5'-bitetrazole were unsuccessful. In each case the respective nmr, infrared, and mass spectra of the isolated reaction product indicated that the expected compound was not obtained. The most plausible explanation for the failure of these syntheses is the availability of alkyl hydrogen atoms which facilitate a rearrangement of the imide chloride intermediate.

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THE SYNTHESES AND COMPLEXATION OF SOME 1,5-CYCLOPOLYMETHYLENETETRAZOLES AND BITETRAZOLES

By

Frank Michael D'Itri

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1968

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4/3/69

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ACKNOWLEDGMENTS

The author gratefully expresses his sincere appreciation to Dr. A. I. Popov for his friendship, guidance, counsel, and encouragement throughout the course of the author's graduate studies.

Gratitude is also extended to the Department of Chemistry, Michigan State University, the Socony Mobil Oil Company, and the National Institutes of Health of the Department of Health, Education, and Welfare for financial aid.

Thanks are extended to Professor William E. Stone, Department of Physiology, University of Wisconsin, Madison, Wisconsin, for the determination of the pharmacological properties of the various cyclopolymethylenetetrazoles.

The author also wishes to express appreciation to W. J. McKinney for suggestions, information, and the computer program used in this study and to R. H. Erlich and R. G. Hamilton for their valuable technical assistance.

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INTRODUCTION

There is a growing awareness of the importance of the physicochemical approach to the problems of molecular biology. While biological systems are much more complex than those usually studied by the chemist, numerous investigations in recent years have applied physicochemical techniques and concepts to various biological processes, including the mechanism of drug action.

The biological mechanism of drug action is one of the most interesting and important phases of modern research. Because a drug molecule must attach itself to a cell membrane, some type of mechanism must exist which would involve physical and chemical interactions. These interacting forces could be in the form of charge-transfer, covalent, and hydrogen bonding, as well as steric hindrance and London forces.

The importance of charge-transfer complexes in drug action has been illustrated in the publications of A. Szent-Gyorgyi (1,2). He states that the charge-transfer reaction may be one of the most important, frequent, and fundamental biological reactions. Pullman and Pullman (3), recognizing that purines are important growth factors in biogenetic processes, have investigated their respective electron donor and acceptor properties. Russian workers (4)

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have recently studied complexes of biologically active materials with electron spin resonance spectroscopy. They concluded that antibiotics such as penicillin, streptomycin, biomycin, and similar related antibiotics are strong electron donors and that this property is related to their biological activity. Recently, the importance of physicochemical factors in convulsant disorders has been ably illustrated by D. B. Tower (5) while Friess, Standaert and Reber investigated the influences of stereochemical factors in convulsant activity of aminocyclanol derivatives (6).

It is known that pentamethylenetetrazole increases the electrical activity in the brain and that the action is due directly to the compound itself rather than to its metabolic product (7). It is, therefore, not inconceivable that physicochemical properties of pentamethylenetetrazole and of similar tetrazoles are related to this pharmacological activity. In particular, it was of interest to study the complexing abilities of tetrazoles. It should be noted that these compounds have four nitrogen atoms, each capable of donating a pair of electrons to form σ bonds. Because of their conjugated double bond system, they could also be capable of forming weak π type complexes.

Many of the studies of tetrazoles have been done because of their pharmacological properties. Pentamethylenetetrazole (hereafter abbreviated C_5MT) is known to be a strong convulsive agent with a long clinical history.

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Less well-known are the substituted pentamethylene-tetrazole derivatives and other 1,5-cyclopolymethylene-tetrazoles and bitetrazoles although they are also pharmacologically active. Gross and Featherstone (8-12) investigated substituted pentamethylenetetrazoles and found that the addition of a methyl group to the pentamethylene chain increased the stimulating action of the parent compound. Furthermore, as the methyl group is moved toward the "symmetrical" 8-position, the activity becomes more pronounced. An increase in the size of the substituent group in the 8-position shows a variable effect in that 8-isopropylpentamethylenetetrazole has a minimum convulsant dose of 3 mg/kg (compared with 50 mg/kg for pentamethylenetetrazole). On the other hand, 8-sec-butyl and 8-t-amylpentamethylenetetrazole show a depressant rather than a stimulant activity. Substitution of larger groups in other positions of the pentamethylene chain also decreases the convulsant activity of pentamethylenetetrazole (8). Thus, pentamethylenetetrazole has a wide range of physiological activity. The specific activity depends on seemingly minor changes in the nature and/or the position of the substituent group.

In this research problem the factors affecting the nucleophilic properties of tetrazoles, particularly the influence of substituent groups on the formation and strength of charge-transfer complexes, are investigated.

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While a simple correlation cannot be expected between the physicochemical property of a compound and its physiological activity, the ability of the tetrazole derivatives to form charge-transfer complexes must be established to determine whether or not this ability is an important factor in such mechanisms.

Previous research conducted in this laboratory (13-17) showed that pentamethylenetetrazole acted as a fairly strong ligand toward the first row transition metal ions in non-aqueous solvents like 2,2-dimethoxypropane (hereafter abbreviated DMP). Solid complexes of pentamethylenetetrazole were prepared with manganese(II), iron(II), cobalt(II), nickel(II), copper(II), and zinc(II) perchlorate according to the following equation:

$$M^{II}(ClO_4)_2 \cdot 6H_2O + 6C_5MT \xrightarrow{DMP} M^{II}(C_5MT)_6(ClO_4)_2$$

The characteristics of a ligand which influence the stability of a given complex are: basicity of the ligand, number of metal chelate rings per ligand, size of the chelate ring, steric effects, resonance effects, and the ligand atom (18). Among these, a major factor influencing the stability of coordination compounds is the Bronsted basicity of the ligand. Whereas pentamethylenetetrazole forms an octahedral complex with a copper(II) ion, attempts to prepare complexes with pyridine and substituted pyridines have been unsuccessful (19).

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The coordinating properties of a nitrogen-containing ligand should be reflected, to a large extent, by its proton affinity. In the case of pentamethylenetetrazole, however, this parallelism does not exist because pentamethylenetetrazole does not possess a basic character in aqueous solution and only acts as a weak base in glacial acetic acid (20). Therefore, exploration of the factors affecting the nucleophilic properties of substituted tetrazoles with varying convulsant activity can add to the study of this aspect of chemistry in the following areas of consideration in this research project.

1. The synthesis of molecules which contain two tetrazole rings bridged by a methylene chain and which would act as polydentate ligands.

2. The synthesis of other 1,5-cyclopolymethylenetetrazoles.

3. The investigation of respective donor properties of these new tetrazoles by determining at various temperatures their respective complexing abilities with appropriate Lewis acids.

Thermodynamic values obtained for the complexation reaction are then related to the donor and, where possible, the physiological properties of the respective tetrazole. Special emphasis is placed on the following variables.

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1. The influence the substituted group on a given tetrazole has on the free energy, enthalpy, and entropy of complex formation.

2. The relative donor strength of a homologous series of tetrazoles to their respective pharmacological properties.

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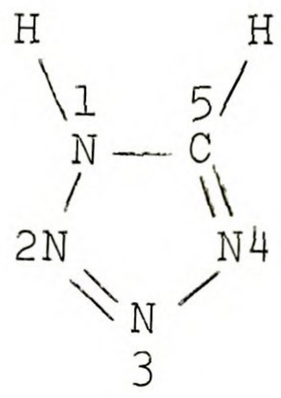
HISTORICAL PART

Tetrazoles are five membered, heterocyclic ring compounds which contain one carbon and four nitrogen atoms linked by three single and two double bonds. The tetrazole ring is numbered so the nitrogen single bonded to the carbon is the 1-position. The remaining three nitrogens are then numbered consecutively two through four with the carbon at the 5-position. The parent compound may exist in tautomeric forms (I) and (II) (21,22).



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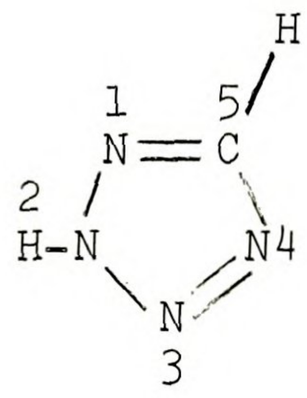

(II)

It has been found that 97% of an equilibrium mixture of (I) and (II) exists in the form (I) (23).

The tetrazole ring is unusual among cyclic systems in that it offers only two points of substitution, in position 1 or 2 and in position 5. A great number of substituted tetrazoles are known with a variety of organic substituents that replace the respective tetrazole protons. F. R. Benson (24,25) has extensively reviewed the

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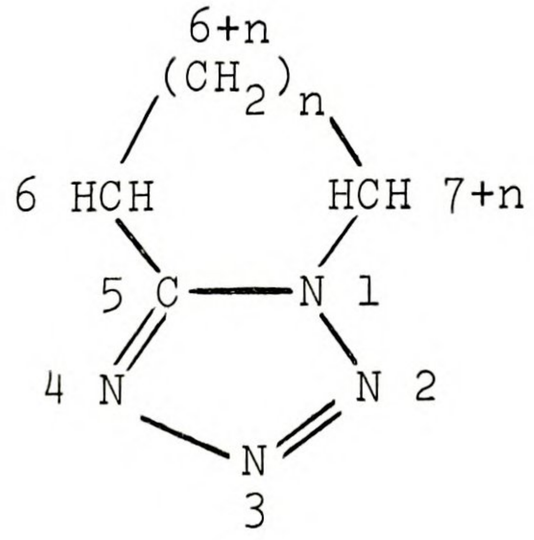
literature pertaining to the preparation of tetrazoles in organic chemistry. Therefore, this discussion will be limited to the aspects of the subject relevant to this particular research project.

The cyclopolymethylenetetrazoles (III) represent a special class of substituted tetrazole derivatives in which the polymethylene chain forms a second ring fused to the tetrazole ring.



(III)

where n = 1, 2, 3, 4, 5, 6, 7, etc.

The reaction between equimolar quantities of carbonyl compounds and hydrazoic acid in the presence of a strong mineral acid was studied in detail by K. F. Schmidt (26-28). He found that organic acids were transformed into primary amines, that aldehydes yield nitriles and formyl derivatives of amines, and that ketones yield amides. With the hydrazoic acid present in large excess aldehydes and ketones yield substituted tetrazoles. Cyclic ketones react normally,

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and the first cyclopolymethylenetetrazole to be synthesized was pentamethylenetetrazole obtained form the reaction of cyclohexanone and two or more moles of hydrazoic acid.

It is well known that pentamethylenetetrazole is a powerful stimulant and convulsant that has been widely used in chemotherapy. Surprisingly, however, neither the higher nor the lower homologues of pentamethylenetetrazole have been investigated to any significant extent. In fact, a literature search indicates that only two reports exist on the preparation of tri- and tetramethylenetetrazole (29,30), and two other reports on the corresponding hexa- and heptamethylenetetrazoles (31,32). Ruzicka et al. (31, 32) have applied the Schmidt reaction to higher cyclic ketones and have prepared the respective cyclopolymethyl-enetetrazoles: hexa-, hepta-, and tetradecamethylene-tetrazole. They were synthesized from cycloheptanone, cyclooctanone, and cyclopentadecanone.

Von Kereszty (29,30) patented an interesting internal condensation of an azidoalkanenitrile used to prepare tri- and tetramethylenetetrazoles. For this purpose, 4-azidobutyronitrile and 5-azidovaleronitrile were treated with chlorosulfonic acid. Syntheses of 6-methyl-8-ethyltrimethylenetetrazole, 7,9-dimethyltetramethylene-tetrazole and 6-carbethoxytetramethylenetetrazole, are also claimed in this patent. Carpenter (33) attempted to prepare penta- and hexamethylenetetrazole by condensation of

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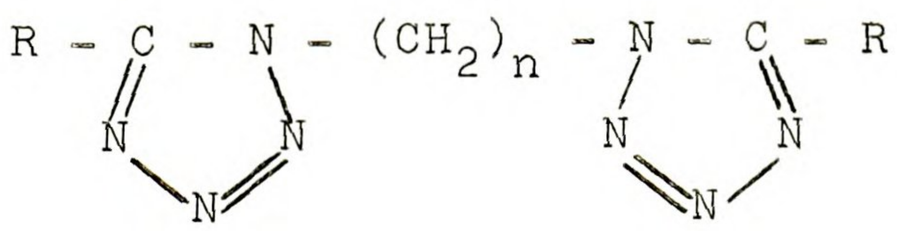
6-azidocapronitrile and 7-azidoheptanonitrile in an effort to extend von Kereszty's cyclization to higher members of the series. Carpenter readily duplicated von Kereszty's reactions for tri- and tetramethylenetetrazole, but no penta- or hexamethylenetetrazoles could be detected even by careful chromatographic analysis of the reaction products. Carpenter explains these results by the following mechanism. A high degree of orientation of the cyano and azido groups is required in the transition state of the cyclization process. Tetramethylenetetrazole was also prepared by hydrogenation of pyridotetrazole and its C-alkyl derivatives in the presence of a noble metal catalyst (30). Recently, Boyer et al. (34) reduced pyridotetrazole over palladium in the presence of acetic acid to tetramethylenetetrazole in nearly quantitative yields.

Because tetrazoles offer two nonequivalent positions for the attachment of substituent groups, compounds containing two tetrazole rings joined by a methylene bridge can be of the α,ω-bis(5-substituted-1-tetrazolyl)-n-alkane type (IV) or the α,ω-bis(1-substituted-5-tetrazolyl)-n-alkane type (V).



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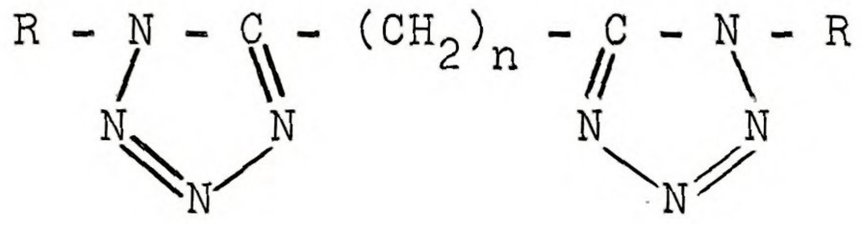

(V)

where R = C_6H_5, H, CH_3 and n = 0,1,2,3,4, etc.

The α,ω-bis(5-substituted-1-tetrazolyl)-n-alkane type compounds (IV) are not recorded in the literature, and references to the α,ω-bis(1-substituted-5-tetrazolyl)-n-alkane compounds (V) are very sparse. Oliveri-Mandala (35) first prepared 5,5'-bitetrazole by reacting 5-cyanotetrazole with hydrazine hydrate in alcohol, followed by successive treatments with sodium nitrite and hydrochloric acid. Because this compound behaves as a weak acid, the corresponding heat sensitive sodium, copper (II), and shock sensitive mercury(II) salts were easily prepared (36). Cohen et al. (37) modified the high pressure method of Mihina and Herbst (38) for the conversion of alkane nitriles into 5-substitutedtetrazoles and prepared 1,4-bis(5-tetrazolyl)-n-butane from adiponitrile. Recently, Wehman (39) of this laboratory used the same method to prepare 5,5'-bitetrazole, 1,3-bis(5-tetrazolyl)-n-propane, and 1,4-bis(5-tetrazolyl)-n-butane. Kauffmann and Ban (40) prepared 1,4-bis(5-tetrazolyl)-n-butane, 1,6-bis(5-tetrazolyl)-n-hexane, and 1,8-bis(5-tetrazolyl)-n-octane by a novel method. Aliphatic diamidrazones of the type $H_2NN = C(NH_2) - (CH_2)_n - C(NH_2) = NNH_2$ were prepared by treating the corresponding dinitriles with sodium hydrazine in a hydrazine-diethyl ether

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mixture. Treatment of the aliphatic diamidrazone with nitrous acid yielded the corresponding bitetrazole. The authors could not prepare bis(5-tetrazolyl)methane or 1,2-bis(5-tetrazolyl)ethane by this method, nor have preparations of these compounds been reported by any other method.

Thus far, only three syntheses for the α,ω-bis(1-substituted-5-tetrazolyl)-n-alkanes have been reported. 1,1'-dimethyl-5,5'-bitetrazole was prepared by the action of diazomethane on 5,5'-bitetrazole in an ether medium (36). The preparation of 1,4-bis(1-methyl-5-tetrazolyl)-n-butane was accomplished by treating a warm aqueous solution of the sodium salt of 1,4-bis(5-tetrazolyl)-n-butane with dimethyl sulfate (37). Stolle (41) prepared 1,1'-diphenyl-5,5'-bitetrazole by the reaction of N,N'-diphenyloxalimidyl chloride with sodium azide in boiling ethanol for about twelve hours.

The physiological activity of various substituted tetrazoles is well-known and has generated a great deal of research seeking to understand the nature of the drug-receptor, physicochemical interactions. Determining the properties of these drugs which are responsible for or related to their respective pharmacological activity would be invaluable in the study of the physiological effects of these drugs on the central nervous system as well as being a guide for the synthesis of new, more active drugs.

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Gross and Featherstone (9) studied the pharmacology of a large number of substituted tetrazoles and concluded that the physiological activity of these drugs on the central nervous system appeared to be a function of the general type of substitution on the ring. They concluded that larger alkyl substituents in position 5 diminish the depression of the electrical activity of the central nervous system whereas increasing the size of the alkyl substituent in position 1 increases stimulation.

Von Issekutz, Leizinger, and Novak (42) noted that the effect of pentamethylenetetrazole on the central nervous system was increased two or three fold by introducing a methyl group in the 6 position and 20-30 fold if the methyl group was substituted on the "symmetrical" 8 position. Gross and Featherstone (8) confirmed the findings of von Issekutz and his co-workers and extended the study by including 23 additional alkyl substituted pentamethylenetetrazoles. In order to determine the maximum enhancement of activity, the structures of the alkylated pentamethylenetetrazoles were varied systematically, and an effort was made to correlate these structural changes with changes in the pharmacological activity. The authors concluded their study with the following observations. The introduction of a single substituent on the 8 position of the pentamethylenetetrazole structure enhances the analeptic and convulsant activity of the parent substance only when

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the group is small or closely packed as in the case of methyl, isopropyl, or tert-butyl. Substitution of alkyl groups in any other position, di- or tri-substitutions, or the formation of quaternary salts decreased the activity of the compound. The isopropyl group appeared to be unique because, in any given case, it was generally associated with the most active compounds.

As early as 1949, Schueler et al. (43) tried to correlate the pharmacological activity of a series of substituted tetrazoles with an activity range from severe convulsive stimulation to deep depression with their respective ultraviolet absorption spectra. Generally, those substituted tetrazoles that have alkyl substituents and that exert stimulative action showed little or no absorption in the region of 220 mμ. The tetrazole derivatives with aryl substituents which exert a depressant activity showed two absorption bands in the regions of 290 and 225 mμ respectively. The 225 mμ band has an absorption ten times greater than that of the 290 mμ band. As the depressant activity of the series of tetrazoles decreased, it was accompanied by a hypochromic effect of the band at 225 mμ only. On the other hand, for increasingly stimulative activity, both absorption bands underwent the hypochromic effect. Apparently, there is some correlation between the physiological activity of the tetrazoles and their respective absorption spectra.

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Pentamethylenetetrazole, substituted pentamethylenetetrazoles, and 1,5-dialkyltetrazoles have surprisingly weak basic properties in aqueous solutions. The first hint of the basic character of these compounds came from the distribution studies performed by Dister (7). He noted that the distribution coefficient (organic)/(aqueous) was larger for basic media. This would indicate that pentamethylenetetrazole can behave as a weak base. Popov and Holm (20) titrated pentamethylenetetrazole potentiometrically in glacial acetic acid with perchloric acid in the same solvent and found that pentamethylenetetrazole does possess weak basic properties in acetic acid. Golton(44) investigated the distribution of pentamethylenetetrazole between various aqueous solutions and carbon tetrachloride as a function of pH. A value of 10^{-14} was obtained for the apparent protonization constant of pentamethylenetetrazole in water. The above results, as well as the titratability in glacial acetic acid, confirmed the extremely weak basic nature of pentamethylenetetrazole. A more detailed treatment of the proton affinity of pentamethylenetetrazole, substituted pentamethylenetetrazoles, and 1,5-dialkyltetrazoles by Popov and Marshall (45,46) was carried out in anhydrous formic acid to enhance the basic character of these weak bases. They determined potentiometrically the pK_b values of these tetrazoles in this solvent to be of intermediate strength, around 2, with very slight

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differences and attempted to relate the base strength of the tetrazoles to their respective physiological activity. The overall correlation of their study was not definitive. Nonetheless, it showed significantly that the most active compound tested was most basic and the most inactive compound was least basic.

As part of a general investigation of the physical properties of certain nervous system stimulants, Popov and Holm (47) determined the dipole moment of pentamethylenetetrazole, 8-t-butyl- and 8-sec-butylpentamethylenetetrazole in benzene solution to be 6.14, 6.20, and 6.18 Debyes respectively. Because 8-t-butylpentamethylenetetrazole has a minimum convulsant dose of 3 mg/kg of body weight compared to 750 mg/kg for 8-sec-butylpentamethylenetetrazole (8), they concluded that there was no simple correlation between the physiological activity of the compounds and their dipole moments.

Person et al. (48), in their infrared spectra study of iodine monochloride charge transfer complexes, found that the spectrum of the I-Cl fundamental stretching vibration was very sensitive to the strength of the interaction between the halogen and the donor molecule with which it is complexed. As the formation constant of the complex increased, the fundamental band shifted to lower frequencies while the intensity of the absorption band increased. Pentamethylenetetrazole caused a shift of the

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ICl peak from 375 to 310 cm^{-1}. Benzene and pyridine formed respective weaker and stronger complexes that shifted the ICl peak to 355 and ~270cm^{-1} respectively. Therefore, they concluded that pentamethylenetetrazole is a moderately strong donor molecule in a mixture of equal parts carbon tetrachloride and 1,2-dichloroethane.

Person *et al.* (49), found similar changes in the far-infrared spectrum of iodine cyanide which indicates that it forms charge-transfer complexes with electron donor molecules of different strengths. These changes in the I-C stretching motion were reflected by a decrease in frequency with an accompanying large increase in intensity and some increase in the half-intensity widths of the respective absorption bands. The decrease in frequency resulting from complexation was correlated with the donor strength of the molecule complexing with iodine cyanide. The electron donor nature of pentamethylenetetrazole was again indicated in the shift of the I-C asymetrical stretch of ICN from 486 to 453 cm^{-1} in benzene. Because the absorption maximum of the ICN-pentamethylenetetrazole charge-transfer band occurs in the ultraviolet region not easily studied by conventional spectrophotometric techniques, Popov *et al.* (50) modified the approach developed by Benesi and Hildebrand for use in the far-infrared region. They calculated formation constants of 1.2± 0.4, 15± 3, and 51± 5 for the dioxane-ICN, pentamethylenetetrazole-ICN and pyridine-ICN complexes in benzene respectively.

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Brubaker (51) prepared and characterized two crystalline forms of bis(5-aminotetrazolato)copper(II). The method of continuous variation clearly indicated that a 1:2 metal to tetrazole complex was formed in solution. The hypsochromic shift and accompanying hyperchromic effect suggest coordination rather than simple salt formation. Spectrophotometric studies in aqueous solution gave an equilibrium constant of 10^{12} for the formation of the complex. Further studies showed that similar behavior is observed with tetrazole, 5-phenyltetrazole and 1-ethyltetrazole. Brubaker found that there is very little interaction between the copper(II) ion and 1,5-dimethyltetrazole. This fact, together with the relatively low formation constant values for $Ag(C_5MT)_2NO_3$ ($\sim 10^2$) (20), indicates that a replaceable ring hydrogen is required to form this type of complex.

Brubaker and Daugherty (52) found that nickel(II) forms only impure and poorly characterized complexes when its salts react with various 5-substitutedtetrazoles. Copper(II) complexes (53) with 5-substitutedtetrazoles are obtained in good purity simply by mixing aqueous solutions of the reactants.

Brubaker and Gilbert (54) prepared various dichlorobis-(1-substitutedtetrazole)cobalt(II), nickel(II), platinum(II), and zinc(II) complexes. The solid complexes, with the exception of the zinc complex, are insoluble in common

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solvents. They decompose upon heating. This property suggests the possibility of polymeric structures. As early as 1961 Brubaker (53) suggested the following three possible methods of coordination between metal ions and tetrazoles.

1. One of the nitrogens of the tetrazole ring acts as a Lewis base and donates its pair of electrons to the central metal ion.
2. The central metal ion may coordinate to the π-electron system of the tetrazolate anion.
3. Since the tetrazolate anion seems to satisfy two coordination sites on the copper ion, coordination could occur by the formation of bonds to two different nitrogen atoms of the tetrazole ring.

Recently, Garber et al. (55,118) performed a vibrational analysis of sodium tetrazolate. By means of a normal coordinate analysis calculation on the tetrazolate ion, they made the vibrational assignments for the molecule. From these results, the assignments of the genuine vibrational modes of 1-methyltetrazole were made. The complexes of bis(1-methyl-5-tetrazolyl)nickel(II), bis(1-cyclohexyl-5-tetrazolyl)nickel(II), bis(tetrazolate)copper(II)monohydrate and 1-methyl-5-tetrazolyllithium 0.5THF(tetrahydrofuran) were also prepared. The fact that the transition metal complexes were insoluble in all common solvents

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suggested a polymeric structure. They decomposed when heated, and the nickel complexes were sensitive to the atmosphere. The reflectance spectra indicate that the respective nickel(II) and copper(II) atoms of the complexes are in an octahedral or tetragonal environment and, therefore, are six coordinate. To account for these spectral data, the authors suggest that two of the six bonds to each nickel are Ni-C bonds while the other four are Ni-N bonds. The only arrangement found possible with framework molecular models has the two Ni-C and each pair of Ni-N bonds trans forming an infinite array. The 4-N and the 2- or 3-N would then be bound to the nickel atom.

During previous research conducted in this laboratory (13,15), anhydrous complexes of pentamethylenetetrazole were prepared with iron(II), manganese(II), cobalt(II), nickel(II), and zinc(II) perchlorates by treating the ligand with the respective hydrated transition metal perchlorates in 2,2-dimethoxypropane solutions. Pentamethylenetetrazole is a weakly coordinating ligand and cannot effectively compete with water for the coordination sites of the central metal ion. For this reason, 2,2-dimethoxypropane was utilized to dehydrate the metal perchlorates in solution and, therefore, to exclude water as a competing ligand (57-62). In all cases, six moles of pentamethylenetetrazole were coordinated to the central metal ion. This was not expected because pentamethylenetetrazole is a rather bulky ligand. Powder X-ray

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diffraction studies as well as the magnetic and spectral properties of these complexes indicate that they are isomorphous and have an octahedral configuration.

Far-infrared studies (17) of these complexes show the appearance of two new bands located in the 302-276 and 236-198 cm^{-1} regions. These bands were tentatively assigned to the metal-nitrogen asymmetrical stretching and bending vibrations. Three copper complexes (16) with the compositions $Cu(C_5MT)_2Cl0_4$, $Cu(C_5MT)_4(Cl0_4)_2$ and $Cu(C_5MT)_6(Cl0_4)_2$ were also isolated and characterized. And the electron spin resonance spectra for $Cu(C_5MT)_6(Cl0_4)_2$, $Cu(C_5MT)_4(Cl0_4)_2$ and $Mn(C_5MT)_6(Cl0_4)_2$ were obtained (14). For hexakis(pentamethylenetetrazole)manganese(II) perchlorate dispersed in hexakis(pentamethylenetetrazole)-zinc(II) perchlorate, the data indicate that the metal-ligand bonds are 91 per cent ionic with essentially octahedral symmetry. For the copper complexes, high resolution spectra of the copper nuclear hyperfine splittings were obtained in the undiluted sample. The symmetry for $Cu(C_5MT)_6(Cl0_4)_2$ is tetragonal with distortion from the octahedral symmetry influenced by both a local Jahn-Teller effect and lattice distortion. The $Cu(C_5MT)_4(Cl0_4)_2$ exhibits a definite tetragonal symmetry, and the copper-pentamethylenetetrazole complexes are approximately 80 per cent ionic. The bonding of the pentamethylene-tetrazole ligand appears to be similar to that of pyridine

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Recently, Bowers and Popov (63) prepared anhydrous complexes of pentamethylenetetrazole with first row transition metal chlorides and bromides. Complexes of the type $M^{II}(C_5MT)\ X_2$ and $M^{II}(C_5MT)_2X_2$ were isolated. They were insoluble in polar and non-polar solvents and have high melting or decomposition points. Magnetic and spectral evidence indicate that the metal ions in the $M^{II}(C_5MT)X_2$ complexes are in octahedral environments while the $M^{II}(C_5MT)_2X_2$ complexes may be tetrahedral. The $M^{II}(C_5MT)\ X_2$ compounds are probably polymeric and contain halogen bridges whereas complexes containing two molecules of the ligand are probably monomeric and have a tetrahedral structure.

In order to study the electron donor properties of pentamethylenetetrazole complexes, Popov et al. (64) determined spectrophotometrically the formation constants of the 1:1 C_5MT complexes with iodine monochloride, iodine monobromide, and iodine in carbon tetrachloride solution to be 2,000, 150, and 7.5 respectively. Only the pentamethylenetetrazole-ICl complex could be obtained as a solid crystalline form which could be purified by recrystallization from chloroform. Vaughn et al. (65) extended this work by the spectrophotometric investigation of the complexes of iodine monochloride with 7-methyl,

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8-sec-butyl, and 8-t-butyl pentamethylenetetrazole. Repeated attempts were made to isolate the respective solid iodine monochloride complexes of these pentamethylenetetrazole derivatives; however, only oily residues which decomposed on standing were obtained. The formation constants of the three complexes were determined, and in all cases the complexes were slightly stronger than the corresponding complex for the unsubstituted pentamethylenetetrazole.

Rheinboldt and Stellinger (66), Dister (7), and Zwikker (67) have reported the preparation of pentamethylenetetrazole-silver complexes, however, the stabilities of complexes in water were never determined. Popov and Holm (20) prepared silver complexes in acetonitrile with the general formula $(Tz)_2AgNO_3$, with pentamethylenetetrazole substituted pentamethylenetetrazoles and 1-cyclohexyl-5-methyltetrazole. The stabilities of these complexes were determined potentiometrically in acetonitrile, and the approximate formation constants were of the order of 10^2. Only the $Ag(C_5MT)_2NO_3$ complex was obtained in the crystalline form by the slow evaporation of an aqueous solution of the complex. The above results demonstrate that loss of the ring hydrogens is not necessary for coordination to occur. The coordination probably occurs, as will be discussed later, through one of the nitrogen atoms of the ring. They also determined

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polarographically that the pentamethylenetetrazole complexes with cobalt(II), thallium(I), and cadmium nitrate were essentially completely dissociated in aqueous solution.

Harris et al. (68) prepared microcrystalline complexes of iron(II) conforming to the general formula Fe(tetrazolato)$_2 \cdot 2H_2O$. They used the anions of 5-chlorotetrazole, 5-trifluoromethyltetrazole and 5-nitrotetrazole. With infrared and Mossbauer studies, they proposed the formation of an analog to ferrocene when the tetrazole has strongly electronegative groups on the carbon. Harris et al. (69) obtained the reflectance spectra of divalent metal complexes with the 5-trifluoromethyltetrazolyl anion. Based on the correlation of these reflectance spectra with previously obtained magnetic susceptibility and spectral data in the visible region, they re-evaluated the proposed structure of the Fe(tetrazolato)$_2 \cdot 2H_2O$ complexes. The new experimental evidence indicated that the structure of the iron(II) and respective copper(II), cobalt(II), and nickel(II) 5-trifluoromethyltetrazole complexes are octahedral or distorted octahedral σ-bonded complexes involving coordination by tetrazolyl anion and water. Wehman and Popov have extended the evidence that complexation occurs (70) through one of the ring nitrogen atoms. A study of the charge-transfer complexes of mono- and disubstituted tetrazoles with π-electron acceptors has shown that, while such complexes do exist in solution, they

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are extremely unstable and are largely dissociated even in concentrated solution. Furthermore, the formation constants of the benzene-tetracyanoethylene and pentamethylenetetrazole-tetracyanoethylene complexes are comparable, but the formation constant of iodine monochloride with pentamethylenetetrazole is larger by three orders of magnitude than that of the benzene-ICl complex (64). The above results seem to indicate that in the iodine monochloride complex of pentamethylenetetrazole, complexation occurs through one of the nitrogen atoms on the tetrazole ring. Recently, the crystal and molecular structure of the iodine monochloride complex of pentamethylenetetrazole was carried out with X-ray crystallographic techniques (71). Pentamethylenetetrazole acts as a unidentate ligand. The planar tetrazole pentagon with the linear ICl group is bonded to the number four nitrogen atom and is essentially co-planar with the tetrazole ring. This configuration precludes the π-electron bonding suggested by Harris et al. (68). The crystal structure of dichlorobis(1-methyltetrazole)zinc(II) complex has also been determined (72) and gives further support to σ-type bonding. Crystals of this complex show the zinc atom in an approximately tetrahedral environment but co-planar with the tetrazole rings and with coordination through the four position of the tetrazole ring.

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EXPERIMENTAL PART

I. General

A. Melting points.--The melting points were measured on a Fisher-Johns melting point apparatus which was calibrated with the Arthur H. Thomas Company (Philadelphia, Pa.) micro-melting point standards.

B. Microanalysis.--The microanalyses were carried out by the Spang Microanalytical Laboratory in Ann Arbor, Michigan.

C. Nuclear Magnetic Resonance Spectra.--The nuclear magnetic resonance spectra were all recorded on a Varian Model A-60 NMR spectrometer and calibrated relative to an internal standard of tetramethylsilane.

D. Mass Spectra.--The mass spectra were all obtained on a Consolidated Electrodynamics Corporation Model 21-103C spectrometer with an ionizing voltage of 56 volts.

E. Infrared Spectra.--Infrared spectra in the 5000-650 cm^{-1} region were recorded on a Unicam SP. 200 spectrometer with potassium bromide discs or with Nujol between sodium chloride plates. The spectra in the 650-100 cm^{-1} region were obtained on a Perkin-Elmer Model 301 Far-Infrared Double-Beam Spectrophotometer with various choppers, mirrors, and filters. Spectra were obtained with Nujol

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F. Near Infrared, Visible, and Ultraviolet Absorption Spectra.--These spectra were recorded on a Cary Model 14 recording or Beckman DU spectrophotometer.

G. Constant Temperature Bath.--A Waco refrigerated constant temperature bath designed by the Wilkens-Anderson Company, Chicago, Illinois, was used.

H. Reflectance Spectra.--The reflectance spectra were all obtained on a Beckman model DK-2 Spectrophotometer equipped with a diffuse reflectance attachment located at the Dow Chemical Company in Midland, Michigan.

II. Chemicals

A. The following chemicals were used and purified as described herein.

1. Pentamethylenetetrazole: All C_5MT was obtained from the Knoll Pharmaceutical Corporation under the registered name "Metrazol." The C_5MT was purified by recrystallization from anhydrous ether. The crystals obtained were washed with small volumes of chilled ether. Residual ether was removed under vacuum, and the crystals were stored in an evacuated desiccator over phosphorus pentoxide. The melting point of the crystals was 60.5-61°. The literature value is 61° (64).

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2. 1,2-Dichloroethane: 1,2-Dichloroethane is usually prepared commercially by adding chlorine to ethylene. The impurities were primarily produced by a substitution reaction involving chloroethane as well as by other impurities present in the ethylene. Because 1,2-dichloroethane forms many azeotropes it is difficult to purify by fractional distillation. For example, binary azeotropes are formed with water, ethanol, methanol, trichloroethylene, carbon tetrachloride, and 2-propanol (73).

The fractional distillation method described by Vogel (64) was followed. The crude 1,2-dichloroethane (5 liter batches) was first washed with 600 ml of a 5% aqueous sodium hydroxide solution followed by three washings with 500 ml portions of distilled water. The solution was stored over anhydrous calcium chloride for twenty-four hours. The washed 1,2-dichloroethane was refluxed over barium oxide for twenty-four hours and fractionally distilled. The fraction which was retained had a boiling point of 82.5° [lit. (74) 83°].

3. Iodine: Fisher Certified Reagent grade iodine was sublimed over a mixture of potassium iodide and barium oxide. It was then resublimed over a few lumps of barium oxide to remove any impurities caused by splattering in the first sublimation (75).

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4. Silver Nitrate: Fisher Certified Reagent grade silver nitrate was purified according to the directions of Rosa and Vinal (76).

5. Water: The water used in the potentiometric portion of this study was prepared by passing distilled water through a mixed bed resin obtained from Crystalab Research Laboratories. The specific conductance of such water ranged from 5-7 x 10^{-7} $ohms^{-1}$ cm^{-1} (77).

B. The following chemicals were used without further purification in the synthesis and preparation of the reagent solutions.

1.	Aniline	Eastman Organic Chemicals
2.	2-Azacycloheptanone	Aldrich Chemical Co.
3.	2-Azacyclohexanone	Aldrich Chemical Co.
4.	2-Azacyclooctanone	Aldrich Cehmical Co.
5.	2-Azacyclotridecanone	Aldrich Chemical Co.
6.	Barium Oxide	Barium and Chemicals, Inc.
7.	Benzamide	Eastman Organic Chemicals
8.	Benzoic Acid	Matheson Coleman and Bell Co.
9.	Benzoyl Chloride	J. T. Baker Chemical Co.
10.	Bromine	Dow Chemical Co.
11.	t-Butyl Amine	Eastman Organic Chemicals
12.	Chlorosulfonic Acid	Matheson Coleman and Bell Co.
13.	4-Chlorobutyronitrile	Columbia Organic Chemical Co.
14.	5-Chlorovaleronitrile	Columbia Organic Chemical Co.
15.	Cobalt(II) Perchlorate Hexahydrate	G. Frederick Smith Chemical Co.

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31. Nickel
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32. Phosph
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34. Potass
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38. Sodium
39. Succin
40. Sulfur

16.	Copper(II) Perchlorate Hexahydrate	G. Frederick Smith Chemical Co.
17.	Cyclododecanone	Aldrich Chemical Co.
18.	Cycloheptanone	Aldrich Chemical Co.
19.	Cyclooctanone	Aldrich Chemical Co.
20.	Cyclononanone	Aldrich Chemical Co.
21.	1,4-Diaminobutane	Aldrich Chemical Co.
22.	1,2-Diaminoethane	G. Frederick Smith Chemical Co.
23.	1,6-Diaminohexane	Aldrich Chemical Co.
24.	1,3-Diaminopropane	Aldrich Chemical Co.
25.	1,3-Dibenzoylhydrazine	Aldrich Chemical Co.
26.	1,2-Dichloroethane	Fisher Scientific Co.
27.	Diethyl Malonate	Matheson Coleman and Bell Co.
28.	N,N-Dimethylaniline	Eastman Organic Chemicals
29.	N,N'-Dimethyloxamide	Aldrich Chemical Co.
30.	Ethyl Oxalate	Matheson Coleman and Bell Co.
31.	Nickel(II) Perchlorate Hexahydrate	G. Frederick Smith Chemical Co.
32.	Phosphorus Pentachloride	Allied Chemical Co.
33.	2-Piperidone	Aldrich Chemical Co.
34.	Potassium Cyanide	Fisher Scientific Co.
35.	Potassium Nitrate	Allied Chemical Co.
36.	Sodium Azide	Eastman Organic Chemicals
37.	Sodium Bisulfite	Fisher Scientific Co.
38.	Sodium Carbonate	Fisher Scientific Co.
39.	Succinyl Chloride	Aldrich Chemical Co.
40.	Sulfuryl Chloride	Eastman Organic Chemicals

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41.	Tetrabutylammonium Hydroxide (25% in methanol)	Matheson Coleman and Bell Co.
42.	Zinc(II) Chloride	Mallinckrodt Chemical Works
43.	Zinc(II) Perchlorate Hexahydrate	G. Frederick Smith Chemical Co.

The common laboratory reagents and solvents were used without further purification and are not listed here.

III. Preparation of Precursors to Cyclopolymethylenetetrazoles

A. 4-Azidobutyronitrile.--The method outlined by Carpenter (33) was used. A mixture of 100 grams of 4-chlorobutyronitrile (1.033 moles), 124 grams of sodium azide (1.94 moles), and 500 ml of diethylene glycol was stirred at 100° for 24 hours in a one liter, three-necked, round bottom flask fitted with a stirrer, reflux condenser, and an alcohol thermometer. The crude product was isolated by steam distillation, and the 4-azidobutyronitrile was separated from the aqueous layer. The aqueous layer was then extracted with three 300 ml portions of ethyl ether for an additional yield of product. The crude product was then dried by filtration through a 3 mm layer of anhydrous sodium sulfate and distilled under reduced pressure (bp 54° at 0.25 mm). The final product (75.4 grams, 70% yield) was a colorless liquid with a refractive index of 1.4574 at 23.5°.

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The infrared and nmr spectra of this compound appear in Appendix I as Figures 1 and 2 respectively.

B. 5-Azidovaleronitrile.--Starting with 5-chlorovaleronitrile, this compound was prepared in the manner previously described for the preparation of 4-azidobutyronitrile. The boiling point of the product was 62° at 0.5 mm, and the final product (70.0 grams, 57% yield) was a colorless liquid which has a refractive index of 1.4605 at 24.0°. The infrared and nmr spectra of this compound appear in Appendix I as Figures 3 and 4 respectively.

C. Hydrazoic acid.--The method outlined by Braun (78) was used to prepare solutions of hydrazoic acid in benzene. The benzene solution of hydrazoic acid was prepared by suspending 210 grams of practical grade sodium azide (3.23 moles) in the same weight of warm water. The mixture was placed in a 3 liter, three-necked, round bottom flask equipped with a dropping funnel, stirrer, and thermometer, and one liter of benzene was added to the slurry. After the slurry was cooled to 0°, 85 ml of concentrated sulfuric acid (1.60 moles) were added to the vigorously stirred slurry by means of a dropping funnel. During the addition of the sulfuric acid, the temperature was maintained between 0° and 10° by means of an external ice bath. After the addition of the sulfuric acid, the

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mixture was cooled to about 5°, and the benzene layer, with the hydrazoic acid dissolved in it, was decanted from the almost solid sludge of hydrated sodium sulfate. The hydrazoic acid-benzene solution was stored over anhydrous sodium sulfate. Whenever necessary, toluene or chloroform solutions of hydrazoic acid can be prepared by this same method. The normality of the hydrazoic acid was determined by extracting two milliliters of the benzene-hydrazoic acid solution into water in a stoppered flask and titrating the acid with standard sodium hydroxide using phenolphthalein as the indicator.

CAUTION: Hydrazoic acid vapors are highly toxic, and all reactions involving its use should be carried out in a good hood. The use of heavy metals such as mercury in thermometers or seals should also be avoided because of the explosive nature of mercury(II) azide.

IV. Preparation of the Various Cyclopolymethylenetetrazoles

A. Trimethylenetetrazole.--Von Kereszty's method (29) modified by Carpenter (79) was used for this preparation. A solution of 11.0 grams of 4-azidobutyronitrile (0.099 mole) in 100 ml of chloroform dried over calcium chloride was added from a dropping funnel to a well-stirred solution of 11.30 grams of chlorosulfonic acid (0.097 mole) in 100 ml of chloroform. The rate of addition was controlled to maintain the temperature of the reaction

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mixture between 20 and 40°. A white, solid complex precipitated from the solution when the 4-azidobutyronitrile-chloroform solution was added. The mixture was stirred in a flask for 12 additional hours, cooled to 0°, and made basic with 50 ml of 25% aqueous sodium hydroxide solution. The neutralized mixture was stirred for an additional twenty minutes. The chloroform layer was then removed and evaporated to dryness. The crude product was dissolved in 100 ml of water, made acidic with 15 ml of concentrated sulfuric acid, and the unreacted 4-azidobutyronitrile was oxidized with a 0.2 N potassium permanganate solution. Trimethylenetetrazole was extracted from the aqueous layer with four 100 ml portions of chloroform. The final purification was accomplished by recrystallizing approximately 10 grams of trimethylenetetrazole from a solvent mixture of 50 ml of carbon tetrachloride and 10 ml of ethanol. The colorless crystals that were obtained melted at 110°, [lit. (29) mp 110°]. The yield of trimethylenetetrazole (total 8.18 grams) based on 4-azidobutyronitrile was 74%. The infrared, nmr, and mass spectra of this compound appear in Appendix I as Figures 5, 6, and 7 respectively.

Anal. Calcd. for $C_4H_6N_4$: C, 43.63%; H, 5.49%; N, 50.88%.

Found: C, 43.74%; H, 5.41%; N, 51.04%.

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B. Tetramethylenetetrazole.--The above compound was prepared starting with 11.00 grams of 5-azidovaleronitrile (0.089 mole) in the manner previously described for the preparation of trimethylenetetrazole. However, an oil formed instead of a white solid precipitate when the 5-azidovaleronitrile-chloroform mixture was added to the chlorosulfonic acid-chloroform solution. The crude product (6.00 grams, 54.5% yield) was purified in the manner previously described for trimethylenetetrazole. It was recrystallized from a carbon tetrachloride-ethanol solvent mixture. The colorless crystals which were obtained melted at 117° [lit.(29) mp 115°]. The yield (total 4.80 grams) based on 5-azidovaleronitrile was 43.5%. The infrared, nmr, and mass spectra of this compound appear in Appendix I as Figures 8, 9, and 10 respectively.

Anal. Calcd for $C_5H_8N_4$: C, 48.37%; H, 6.50%; N, 45.13%.

Found: C, 48.46%; H. 6.41%; N, 45.20%.

C. Pentamethylenetetrazole.--This compound is commercially available and was not prepared in this laboratory. As a matter of completeness, however, and for comparison purposes, the infrared, nmr, and mass spectra appear in Appendix I as Figures 11, 12, and 13 respectively.

D. Hexamethylenetetrazole.--A mixture of twelve grams of cycloheptanone (0.107 mole) and 20 grams of hydrazoic acid (0.466 mole, 188 ml of 2.5 N hydrazoic acid-benzene

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solution) was added to 100 ml of freshly distilled benzene to make a total volume of approximately 300 ml. This mixture was then added over a period of 45 minutes to a well-stirred, ice cooled mixture of 60 ml of concentrated sulfuric acid and 100 ml of benzene. After the reaction was completed, ice and water were carefully added to the mixture. Two layers were formed. The aqueous layer was cooled to 0° and neutralized with 50% aqueous sodium hydroxide solution. The crude product (12.0 grams, 79.5% yield) was extracted from the aqueous layer with ethyl ether, purified in the manner described for trimethylene-tetrazole, and recrystallized from hexane. The melting point of the crystals was 68° [lit. (31) 68°]. The yield of the product (total 6.80 grams) based on cycloheptanone was 46%. The infrared, nmr, and mass spectra of this compound appear in Appendix I as Figures 14, 15, and 16 respectively.

Anal. Calcd for $C_7H_{12}N_{14}$: C, 55.24%; H, 7.95%; N, 36.81%.
Found: C, 55.32%; H, 7.93%; N, 36.61%.

E. Heptamethylenetetrazole.--Eighty ml of concentrated sulfuric acid were added to an ice cooled mixture of 20.80 grams of hydrazoic acid (0.484 mole, 323 ml of 1.5 N hydrazoic acid-benzene solution) in a one liter, three-necked, round-bottom flask equipped with a mechanical stirrer, dropping funnel, and thermometer. A solution of 20 grams of cyclooctanone (0.159 mole) dissolved in 80 ml

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of benzene was added from a dropping funnel. The reaction mixture was stirred for an additional 20 minutes and then poured into an ice-water mixture, at which point two liquid layers were formed. The aqueous layer was cooled to approximately 5° and neutralized with 50% aqueous sodium hydroxide solution. The neutralization was followed by three successive extractions with ethyl ether. The benzene layer, which contained only a small fraction of the product, was also evaporated, and the oily residue was added to the evaporated ethyl ether residue. The recovered crude product (23.90 grams, 90.5% yield) was an oil which was purified further by distillation under vacuum. The fraction with a boiling range of 140-150° at 0.5 mm was collected [lit. (31) 145-146° at 0.1 mm]. The oil was difficult to crystallize, and seed crystals were first obtained by freezing a small sample at 0° for approximately 30 days. These crystals were used to induce crystallization of the oil. The first product had a melting point of 40-55°. The crude heptamethylenetetrazole (20 grams, 0.12 mole) was dissolved in 200 ml of a mixture of equal parts of ethanol and water, and the solution was made acidic with 50 ml of concentrated sulfuric acid. Sufficient amount of 0.2 N potassium permanganate (about 25 ml) was added to oxidize the azide impurities. The crude product was then extracted with four 100 ml aliquots of chloroform. Evaporation of the chloroform solution left

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a residue in the form of a yellow oil. The oil was dissolved in 400 ml of ethyl ether, and crystallization of heptamethylenetetrazole was induced when the solution temperature was reduced to approximately -60°. Three or four recrystallizations were required before seeding of the chilled, saturated solution was no longer required. The purified heptamethylenetetrazole was dried *in vacuo*, and the crystals melted at 42-43°. The yield based on cyclooctanone was 75%. It is interesting to note that the only previously published literature report on this compound (31) describes it as an oil impossible to crystallize. The infrared, nmr, and mass spectra of this compound appear in Appendix I as Figures 17, 18, and 19 respectively.

Anal. Calcd for $C_8H_{14}N_4$: C, 57.81%; H, 8.49%; N, 33.70%.
Found: C, 57.94%; H, 8.47%; N, 33.74%.

F. *Octamethylenetetrazole*.--Starting with 5.5 grams of cyclononanone (0.039 mole), this compound was prepared in the manner described for the preparation of heptamethylenetetrazole. The crude product recovered by the evaporation of the ethyl ether was purified as previously described and then recrystallized from a solvent mixture composed of one part benzene to fifty parts hexane. The purified octamethylenetetrazole was obtained as colorless crystals and had a melting point of 117-118°. The yield, based on the cyclononanone, was 73.5% (4.8 grams). The

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infrared, nmr, and mass spectra of this compound appear in Appendix I as Figures 20, 21, and 22 respectively.

Anal. Calcd for $C_9H_{16}N_4$: C, 59.97%; H, 8.95%; N, 31.08%.

Found: C, 60.09%; H, 8.90%; N, 31.08%.

G. Nonamethylenetetrazole.--Starting with 5.0 grams of cyclodecanone (0.031 mole), nonamethylenetetrazole was prepared in the manner described for the preparation of heptamethylenetetrazole. Most of the crude product was recovered from the benzene layer. However, the aqueous layer was extracted three times with 100 ml portions of ethyl ether in order to recover an additional small fraction of the product. The crude product was recrystallized from a solvent mixture composed of one part benzene to twenty parts hexane. The purified nonamethylenetetrazole was obtained as colorless crystals with a melting point of 90-91°. The yield of the reaction (4.8 grams) based on cyclodecanone was 80.0%. The infrared and nmr spectra of this compound appear in Appendix I as Figures 23 and 24 respectively.

Anal. Calcd for $C_{10}H_{18}N_4$: C, 61.82%; H, 9.34%; N, 28.84%.

Found: C, 61.93%; H, 9.31%; N, 28.82%.

H. Undecamethylenetetrazole.--This compound was prepared by adding from a dropping funnel a solution composed of 22.0 grams of cyclododecanone (0.137 mole) dissolved in 50 ml of dry benzene to an ice-cooled mixture

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of 20.8 grams of hydrazoic acid (0.484 mole, 225 ml of a 2.2 N hydrazoic acid-benzene solution) and 80 ml of concentrated sulfuric acid (1.50 mole). The mixture of cyclododecanone was added at a rate adjusted to maintain the reaction mixture temperature at approximately 10°. After this addition was complete, the stirring process was continued for 36 hours at 25°. From this point the reaction mixture was treated in the manner described for heptamethylenetetrazole, but benzene was used instead of ethyl ether to extract the product. The crude product was recrystallized three times from a solvent mixture composed of equal parts of water and ethanol. The purified undecamethylenetetrazole was obtained as colorless crystals in a 66.2% yield (20.1 grams) based on cyclododecanone and had a melting point of 66-67°. The infrared and nmr spectra of this compound appear in Appendix I as Figures 25 and 26 respectively.

Anal. Calcd for $C_{12}H_{22}N_{24}$: C, 64.83%; H, 9.97%; N, 25.20%.

Found: C, 64.84%; H, 9.88%, N, 25.23%.

V. Preparation of Precursors to 6,6-Dihalocyclopolymethylenetetrazoles

A. 2-Benzoyl-2-azacycloheptanone.--A mixture of 135.6 grams (1.20 moles) of 2-azacycloheptanone and 170.1 ml (1.32 moles) of N,N-dimethylaniline was prepared in a 3-liter, three-necked, round-bottom flask equipped with a stirrer, dropping funnel, and an alcohol thermometer. To the

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vigorously stirred solution, 185.7 grams (1.32 moles) of benzoyl chloride were added drop-wise at such a rate that the temperature did not rise above 80°. The mixture was heated and stirred at 90° for three hours, cooled to 70°, and poured into a solution of 24 ml of 2.5 N hydrochloric acid in 1200 ml of distilled water. The oily blue material crystallized after approximately five minutes. The lumps were broken up and collected on a filter, washed with distilled water, and air dried to yield 260 g of the product (99% yield) mp 67-69° [lit. (80,81) 67-69.5°].

B. 2-Benzoyl-7-chloro-2-azacycloheptanone.--A suspension of 217 g (1.00 mole) of 2-benzoyl-2-azacycloheptanone in 55 ml of carbon tetrachloride and 165 ml of cyclohexane was prepared in a 2-liter, three-necked, round-bottom flask equipped with a mechanical stirrer, dropping funnel, and thermometer. To the stirred solution, 85 ml (1.05 moles) of sulfuryl chloride were added. The yellow slurry was maintained at 5-10° by external cooling while the sulfuryl chloride was added. The mixture was then slowly heated to 40° over a period of thirty minutes. When the temperature of the reaction slurry reached approximately 15°, the suspension dissolved completely. The reaction mixture was stirred and its temperature was maintained at 40-42° for 28 hours followed by evaporation to dryness in vacuo. During the 28 hours the yellow reaction mixture turned green and then back to

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gold. The residue was then stirred with 250 ml of isopropyl alcohol at 70° for a few minutes. The suspension was cooled to 0-5° for one hour, filtered, and washed with chilled isopropyl alcohol. The white crystalline product (134 g) was obtained in a 54% yield, mp 121-122° [lit. (82) 122-123°].

C. 2-Chloro-7-azacycloheptanone.--A 500 ml three-necked, round-bottom flask equipped with a stirrer, thermometer, and side arm for sample addition was charged with 168 ml of concentrated sulfuric acid. Dry 2-benzoyl-7-chloro-2-azacycloheptanone (125 g , 0.5 mole) was gradually added to the concentrated sulfuric acid at a rate sufficient to maintain the temperature of the reaction mixture below 25°. The mixture was stirred for one hour without external heating, and the temperature rose to 35°. It was heated to 50° and stirred for two additional hours. The mixture was cooled to 25°, poured into 1 kg of ice in a 4 liter beaker, neutralized with concentrated ammonium hydroxide solution, and extracted with four 500-ml portions of chloroform. The chloroform solution was evaporated to yield a yellow product which was recrystallized from a 10% benzene and 90% ligroin mixture. The white crytalline product (50 g) was obtained in a 68% yield, mp 91-93 [lit. (82) 92.5-93.5°].

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D. 2,2-Dichloro-6-azacyclohexanone.--A stirred slurry of 260 g (1.25 moles) of phosphorus pentachloride in one liter of benzene was prepared in a 2-liter, three-necked, round bottom flask equipped with an efficient mechanical stirrer, dropping funnel, and thermometer. To the stirred slurry a solution composed of 42 g (0.42 mole) of 2-azacyclohexanone (2-piperidone) in 100 ml of benzene was added from the dropping funnel during a period of 20 minutes. The temperature of the reaction mixture was maintained at 30-35° by external cooling during the addition, and then the mixture was heated to 80-85° with continuous stirring for an additional hour. The reaction mixture was concentrated by distillation under reduced pressure on a steam bath. After all the volatile materials had been removed, the oily residue was added to 500 ml of a 10% sodium carbonate solution with vigorous stirring. The sludge was filtered, washed with 200 ml of water, and then washed with 100 ml of chilled ethanol. The crystalline product was recrystallized from boiling ethanol and dried in vacuo to give 30.0 grams of well-formed prisms of 2,2-dichloro-6-azacyclohexanone (42.5% yield) mp 166° [lit. (83) 166°]. The infrared spectrum of this compound appears in Appendix I as Figure 27.

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E. 2,2-Dichloro-7-azacycloheptanone.--Starting with 57 g (0.5 mole) of 2-azacycloheptanone (ε-caprolactam), this compound was prepared in the manner described for the preparation of 2,2-dichloro-6-azacyclohexanone. The product was recrystallized from boiling ethanol and dried *in vacuo* to give 62.8 g of well-formed prisms of 2,2-dichloro-7-azacycloheptanone (34.0% yield) mp 126-127° [lit. (83) 125°]. The infrared spectrum of this compound appears in Appendix I as Figure 28.

F. 2,2-Dichloro-8-azacyclooctanone.--This compound was prepared in 75.8% yield from 25 g (0.197 mole) of 2-azacyclooctanone and phosphorus pentachloride following the procedure described for the preparation of 2,2-dichloro-6-azacyclohexanone. The product was recrystallized from boiling ethanol and dried *in vacuo* to give 29.2 g of well-formed prisms of 2,2-dichloro-8-azacyclooctanone mp 96-97°. The infrared spectrum of this compound appears in Appendix I as Figure 29.

G. 2,2-Dichloro-13-azacyclotridecanone.--Starting with 100 grams (0.506 mole) of 2-azacyclotridecanone, this compound was prepared in the manner described for the preparation of 2,2-dichloro-6-azacyclohexanone. The crude crystalline product was recrystallized from boiling ethanol and dried *in vacuo* to give 95 grams of well-formed prisms of 2,2-dichloro-13-azacyclotridecanone (70.2% yield) mp

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159°. The infrared spectrum of this compound appears in Appendix I as Figure 30.

H. 2,2-Dibromo-6-azacyclohexanone.--A stirred solution of 58 grams (0.58 mole) of 2-azacyclohexanone (2-piperidone) in 400 ml of dry chloroform was prepared in a 1-liter, three-necked, round-bottom flask equipped with a mechanical stirrer and thermometer. A small Erlenmeyer flask was attached to the third opening by means of a large diameter rubber tubing slipped over the opening. Phosphorus pentachloride (242 grams, 1.16 moles) was quickly weighed into the Erlenmeyer flask which was then attached to the apparatus. The phosphorus pentachloride was added to the reaction flask in about one or two gram portions during a period of one hour. Throughout this addition, the reaction mixture was maintained between 3° and 10° by external cooling. After all the phosphorus pentachloride was added, the resulting slurry was allowed to return to room temperature, 1.5 grams of zinc(II) chloride was added, followed by 96 grams (0.6 mole) of bromine. The stirring was continued for five hours. The solvent was removed by vacuum distillation at 40° and 20 mm. The residue was poured into an ice-water mixture, the solid product was dissolved in chloroform, and the solution was treated with 10% aqueous sodium bisulfite solution to remove the last traces of bromine. Evaporation of the chloroform

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solution left a solid residue which was recrystallized from ethanol to yield 80 grams of well-formed prisms of 2,2-dibromo-6-azacyclohexanone, mp 186°. The yield, based on 2-azacyclohexanone, was 53.7%. The infrared spectrum of this compound appears in Appendix I as Figure 31.

I. 2,2-Dibromo-7-azacycloheptanone.--This compound was prepared in 91.5% yield from 33.9 grams (0.30 mole) of 2-azacycloheptanone (ε-caprolactam), phosphorus pentachloride, and bromine following the procedure described for the preparation of 2,2-dibromo-6-azacyclohexanone. The product was recrystallized from boiling ethanol and dried in vacuo to give 74.10 grams of 2,2-dibromo-7-azacycloheptanone mp 162-163° [lit. (80) 162-163.5°]. The infrared spectrum of this compound appears in Appendix I as Figure 32.

J. 2,2-Dibromo-8-azacyclooctanone.--Starting with 50 grams of 2-azacyclooctanone (0.394 mole), this compound was prepared in the manner described to prepare 2,2-dibromo-6-azacyclohexanone. The crude product was recrystallized from ethanol to give 32 grams of well-formed prisms of 2,2-dibromo-8-azacyclooctanone mp 150-151°. The yield based on 2-azacyclooctanone was 28.6%. The infrared spectrum of this compound appears in Appendix I as Figure 33.

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VI. Preparation of the Various 6,6-Dihalocyclopolymethylenetetrazoles

A. 6,6-Dichlorotetramethylenetetrazole.--A stirred solution of 16.8 grams of 2,2-dichloro-6-azacyclohexanone (0.10 mole) in 300 ml of dry benzene was prepared in a 1-liter, three-necked, round-bottom flask fitted with a stirrer, reflux condenser, and surmounted by a calcium chloride drying tube. The third opening was connected to a 500 ml Erlenmeyer flask containing 22.88 grams (0.11 mole) of phosphorus pentachloride. The benzene solution was stirred and heated to 40° while the phosphorus pentachloride was added in ~0.5 gram portions over a period of one hour. The reaction was accompanied by the vigorous evolution of hydrogen chloride. When the formation of the imide chloride was complete, as evidenced by the disappearance of solid phosphorus pentachloride, the reaction mixture was cooled to 20°. The Erlenmeyer flask was then replaced by a dropping-funnel through which 10 grams (0.233 mole, 137 ml of 1.7 N hydrazoic acid-benzene solution) of hydrazoic acid-benzene solution was added, maintaining the temperature of the reaction mixture between 20 and 30° by means of external cooling. After the addition of the hydrazoic acid, the reaction mixture was allowed to stand at room temperature for two hours. It was then gradually warmed to the boiling point on a steam bath and maintained at this temperature until hydrogen chloride evolution ceased (about three hours). The solvent

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was removed by air evaporation, and the residue was treated with ice and water (100 grams of each) to decompose any phosphorus oxychloride that was present. Dry sodium carbonate was then carefully added to neutralize any acid, the presence of which caused the oily residue to solidify. The product was extracted from the mixture with four 100 ml portions of chloroform, evaporated to dryness, and recrystallized twice from ethanol. On cooling, 13.5 grams (70% yield based on the 2,2-dichloro-6-azacyclohexanone) of 6,6-dichlorotetramethylenetetrazole precipitated. The colorless crystals that were obtained melted at 84°. The infrared and nmr spectra of this compound appear in Appendix I as Figures 34 and 35 respectively.

Anal. Calcd for $C_5H_6N_4Cl_2$: C, 31.11%; H, 3.13%; N, 29.02%; Cl, 36.73%.

Found: C, 31.77%; H, 3.26%; N, 28.86%; Cl, 36.90%.

B. 6,6-Dibromotetramethylenetetrazole.--This compound was prepared in the manner previously described for the preparation of 6,6-dichlorotetramethylenetetrazole. Starting with 25.69 grams of 2,2-dibromo-6-azacyclohexanone (0.1 mole), 12 grams of crude product were obtained and recrystallized twice from boiling ethanol. On cooling, 10 grams (36.5% yield) of 6,6-dibromotetramethylenetetrazole precipitated. These colorless crystals melted at 91°. The infrared and nmr spectra of this compound appear in

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Anal. Calcd for $C_5H_6N_4Br_2$: C, 21,30%; H, 2.15%; N, 19.87%; Br, 56.68%.

Found: C, 21.30%; H, 2.19%; N, 20.08%; Br, 56.48%.

C. 6,6-Dichloropentamethylenetetrazole.

1. Method I: This compound was prepared starting with 18.2 grams of 2,2-dichloro-7-azacycloheptanone (0.10 mole) in the manner previously described for the preparation of 6,6-dichlorotetramethylenetetrazole. The crude product was recrystallized from boiling ethanol twice. The resulting colorless crystals melted at 81-82°. The yield (total 17.48 grams) based on 2,2-dichloro-7-azacycloheptanone was 84.5%. The infrared and nmr spectra of this compound appear in Appendix I as Figures 38 and 39 respectively.

Anal. Calcd for $C_6H_8N_4Cl_2$: C, 34.80%; H, 3.94%; N, 27.06%; Cl, 34.24%.

Found: C, 34.77%; H, 3.81%; N, 27.11%; Cl, 34.22%.

2. Method II: Phosphorous pentachloride (31.4 grams, 0.15 mole) was dissolved in 200 ml of hot, dry benzene (50-60°) in a one-liter, three-necked, round-bottom flask equipped with a mechanical stirrer, a reflux condenser surmounted by a calcium chloride tube, and a side arm for sample addition. Dry 2-chloro-7-azacycloheptanone (14.7 grams, 0.10 mole) was gradually added to the hot

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benzene-phosphous pentachloride mixture through the side arm. The reaction was accompanied by vigorous evolution of the hydrogen chloride for a period of one hour. After all of the 2-chloro-7-azacycloheptanone was added, the mixture was cooled to approximately 10°, and 12.9 grams of hydrazoic acid (0.3 mole, 108 ml of a 2.79 N hydrazoic acid-benzene solution) were added by means of a dropping funnel over a period of one hour. After the addition of hydrazoic acid was completed, the reaction mixture was allowed to stand at room temperature for one hour before it was gradually warmed to the boiling point and maintained at this temperature until the hydrogen chloride evolution ceased in approximately two hours. The solvent was removed under reduced pressure, the residue was diluted with 300 ml of water, and the product was extracted with four 200 ml portions of chloroform. The chloroform solution was evaporated to yield a black, viscous oil-like substance.

The crude product was purified by sublimation (1 mm at 170°) to yield an impure white solid (mp 42-58°) which was purified further by a second sublimation and then recrystallization from carbon tetrachloride and absolute alcohol respectively, mp 80-82°. The yield of the product (total 10.35 grams) based on the 2-chloro-7-azacycloheptanone was 50%. This compound is identical with the 6,6-dichloropentamethylenetetrazole. Because the preparation of 6-chloropentamethylenetetrazole was attempted,

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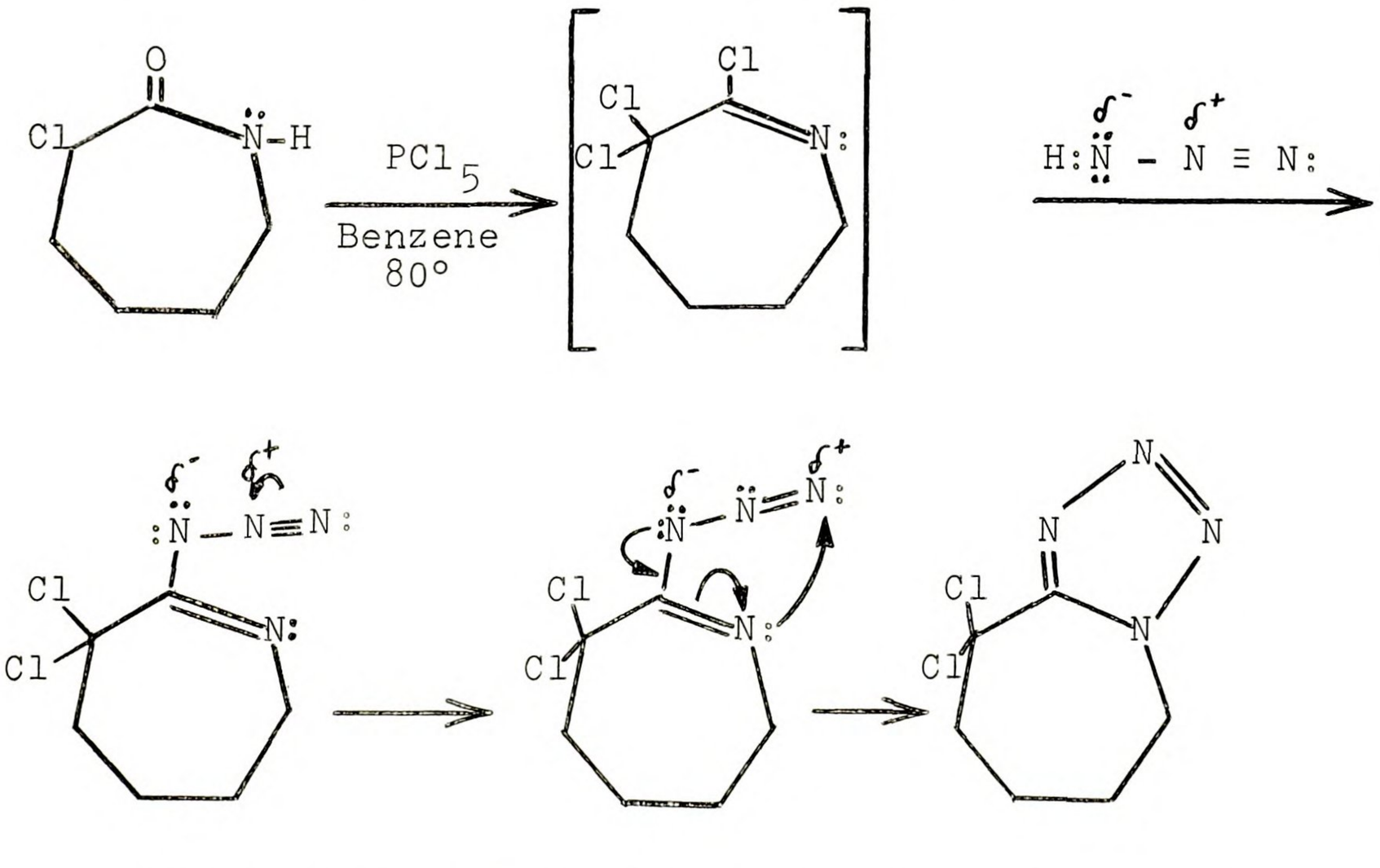
6,6-dichloropentamethylenetetrazole was an unexpected product. In all probability, the addition of dry 2-chloro-7-azacycloheptanone to the hot phosphorus pentachloride-benzene mixture resulted in a further chlorination of the 2 position to cause an imidyl chloride intermediate of 2,2-dichloro-7-azacycloheptanone which, when reacted with hydrazoic acid, added an azido group that rearranged to produce 6,6-dichloropentamethylenetetrazole.



This mechanism is supported by the experimental evidence that all efforts to convert 2-azacycloheptanone directly to 2-chloro-7-azacycloheptanone result only in the formation of 2,2-dichloro-7-azacycloheptanone (80, 82, 84). Therefore, the more efficient way to prepare 6,6-dichloropentamethylenetetrazole would be with 2,2-dichloro-7-azacycloheptanone as the starting material, method I outlined above.

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D. 6,6-Dibromopentamethylenetetrazole.--The preparation of this compound started with 27.10 grams of 2,2-dibromo-7-azacycloheptanone (0.10 mole) in the manner previously described to prepare 6,6-dichlorotetramethylenetetrazole. The crude product was recrystallized from boiling ethanol. Upon cooling, 22.35 grams (75.4% yield) of 6,6-dibromopentamethylenetetrazole precipitated. The colorless crystals thus obtained melted at 117-119°. The infrared and nmr spectra of this compound appear in Appendix I as Figures 40 and 41 respectively.

Anal. Calcd for $C_6H_7N_4Br_2$: C, 24.35%; H, 2.73%; N, 18.93%; Br, 54.00%.

Found: C, 24.38%; H, 2.72%; N, 18.95%; Br, 54.03%.

E. 6,6-Dichlorohexamethylenetetrazole.--Starting with 19.6 grams of 2,2-dichloro-8-azacyclooctanone (0.10 mole), this compound was prepared in the manner described for the preparation of 6,6-dichlorotetramethylenetetrazole. The crude product recovered by evaporating the chloroform was purified by two recrystallizations from ethanol. On cooling, 12.20 grams (55.2% yield) of colorless crystals of 6,6-dichlorohexamethylenetetrazole (mp 63-64°) precipitated. The infrared and nmr spectra of this compound appear in Appendix I as Figures 42 and 43 respectively.

Anal. Calcd for $C_7H_{10}N_4Cl_2$: C, 38.03%; H, 4.56%; N, 25.34%; Cl, 32.97%.

Found : C, 38.56%; H, 4.61%; N, 25.80%; Cl, 31.23%.

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F. Attempted Preparation of 6,6-Dibromohexamethylenetetrazole.--The procedure previously described to prepare 6,6-dichloropentamethylenetetrazole was also used in an attempt to prepare 6,6-dibromohexamethylenetetrazole, starting with 2,2-dibromo-8-azacyclooctanone. The nmr and infrared spectra of the isolated product showed that the expected product was not obtained.

G. Attempted Preparation of 6,6-Dichloroundecamethylenetetrazole.--The procedure previously described to prepare 6,6-dichlorohexamethylenetetrazole was also used in an attempt to prepare 6,6-dichloroundecamethylenetetrazole starting with 2,2-dichloro-13-azacyclotridecanone. However, only starting material could be recovered from the reaction mixture.

VII. Preparation of Precursors to 1,1'-Diphenyl-5,5'-bitetrazole

A. N,N'-Diphenyloxamide.--A mixture of 73 grams of ethyl oxalate (0.50 mole) and 100 grams of aniline (1.07 mole) was heated at 150° for 30 minutes in a 500 ml three-necked, round-bottom flask equipped with a thermometer, reflux condenser, and stirrer. After the ethanol produced during the reaction was removed by distillation, the remaining material solidified as it cooled. The crude product was recrystallized from benzene. Upon cooling, 100 grams of N,N'-diphenyloxamide mp 245° [lit. (85) mp

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244°] precipitated. The yield of the product (total 102.6 grams) based on ethyl oxalate was 85%. The infrared spectrum of this compound appears in Appendix I as Figure 44.

B. N,N'-Diphenyloxalimidyl Chloride.--This compound was prepared by Bauer's method (86). Eighty-five grams of N,N'-diphenyloxamide (0.354 mole) and 170 grams of phosphorus pentachloride (0.817 mole) were suspended in 240 ml of freshly distilled toluene in a 500 ml three-necked, round-bottom flask equipped with a stirrer, a reflux condenser surmounted by a calcium chloride tube, and a thermometer. As the stirred solution was heated, the phosphorus pentachloride dissolved, and a clear yellow solution resulted when the temperature reached 90°. The solution was then refluxed for an additional three hours, and 200 ml of toluene were distilled off. The crude product in the flask solidified when it was cooled to room temperature and then was recrystallized from ligroin. Straw yellow needles of N,N'-diphenyloxalimidyl chloride, mp 115° [lit. (86) mp 115°] were obtained. The reaction yield (total 44.2 grams) based on N,N'-diphenyloxamide was 45%. The product is gradually hydrolyzed back to N,N'-diphenyloxamide by atmospheric moisture. However, if the preparation is carried out rapidly, a dry box is not required. The infrared spectrum of this compound appears in Appendix I as Figure 45.

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VIII. Preparation of Precursors to α,ω-Bis(5-phenyl-1-tetrazolyl)-n-alkanes

A. Bis(α-chlorobenzylidene)hydrazine.--Twenty-four grams of dry 1,2-dibenzoylhydrazine (0.10 mole) were added in one gram portions, over a period of one hour to a solution of 50 grams of phosphorus pentachloride (0.25 mole) in 100 ml of freshly distilled toluene at 90-100°. During the reaction the solution was stirred vigorously and after the reaction was completed, the volatile reaction products and most of the solvent were distilled off at 760 mm. On cooling, the residual liquid yielded 20 grams of crude product which was recrystallized from 300 ml of ethylene glycol monomethyl ether and 18 grams (65% yield) of bis(α-chlorobenzylidene)hydrazine [mp 121-122°, lit. (87) 120-122°] were obtained.

B. N,N'-Dibenzoyl-1,3-diaminopropane.--Benzoyl chloride (140 g, 1.00 mole) was added over a period of 55 minutes to a well-stirred solution of 29.6 grams (0.40 mole) of 1,3-diaminopropane and 60 grams (1.50 mole) of sodium hydroxide in 600 ml of water. An ice bath held the temperature of the reaction solution below 10°. After stirring the slurry for an additional one hour, it was filtered. The solid white product was washed with a large amount of water and then air dried. The crude amide was dissolved in 300 ml of a 1:1 mixture of boiling ethanol

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and benzene, and this solution was diluted with 300 ml of benzene. On cooling, 86.2 grams of N,N'-dibenzoyl-1,3-diaminopropane mp 147° [lit. (88) 147°] precipitated. The reaction yield (total 95.5 grams) based on 1,3-diaminopropane was 85%.

C. N,N'-Dibenzoyl-1,4-diaminobutane.--This compound was prepared starting with 35.2 grams of 1,4-diaminobutane (0.40 mole) in the same manner as the corresponding propane derivative. The melting point of 177° agrees well with the literature value (89). The yield (total 102.0 grams) based on 1,4-diaminobutane was 86.5%.

D. N,N'-Dibenzoyl-1,2-diaminoethane.--This compound was prepared starting with 24 grams of ethylenediamine (0.40 mole) in the manner previously described for the corresponding propane derivative. The melting point of 249° closely corresponds with the literature value (90). The yield (total 91.0 grams) based on 1,2-diaminoethane was 85%.

E. N,N'-Dibenzoyl-1,6-diaminohexane.--This compound was prepared from 46.5 grams of 1,6-diaminohexane (0.40 mole) in the manner previously described for the corresponding propane derivative. The melting point of 165-166° corresponds closely with the literature value (90, 91). The yield (total 104.3 grams) based on 1,6-diaminohexane was 81%.

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F. N,N'-Dibenzoyldiaminomethane.--This compound was prepared by stirring together 20 grams of benzamide (0.165 mole), 40 ml of 40% aqueous formaldehyde (0.531 mole) and 20 ml of 15 N sulfuric acid. As this mixture was heated, dissolution occurred. On further heating, a precipitate formed. The solution was cooled to ice-bath temperature, and then the product was recrystallized twice from absolute ethanol. On cooling, 8.93 grams of N,N'-dibenzoyldiaminomethane [85% yield, mp 225°, lit. (92) mp 220°] were obtained.

IX. Preparation of 1,1'-Diphenyl-5,5'-bitetrazole

Twenty-eight grams of N,N'-diphenyloxalimidyl chloride (0.100 mole) and 26 grams of sodium azide (0.400 mole) were added to 200 ml of 95% ethanol. The mixture was caused to refluxed and stirred for 12 to 14 hours. After the reaction was completed, the white, solid precipitate was filtered, washed with water, and recrystallized twice from absolute ethanol. The white crystalline material melted sharply at 212° [lit. (41,93) 212°]. The infrared spectrum of this compound appears in Appendix I as Figure 46. The nmr spectrum was not obtained because this compound does not possess sufficient solubility in any suitable solvent.

Anal. Calcd for $C_{17}H_{10}N_8$: C, 57.93%; H, 3.47%; N, 38.60%.

Found: C, 57.94%; H, 3.55%; N, 38.51%.

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X. Preparation of α,ω-Bis(5-phenyl-1-tetrazolyl)-n-alkanes

A. 5,5'-Diphenyl-1,1'-bitetrazole.--Bis(α-chlorobenzylidene)hydrazine (14.0 grams, 0.05 mole) and 20 grams of sodium azide (0.305 mole) were added to 100 ml of 95% ethanol and then refluxed and stirred for approximately 12 to 14 hours. On completion of this process, the unreacted azide was removed by filtration, and upon cooling, crystals of the product precipitated. The crude product was then recrystallized from 95% ethanol. It decomposed at 203°, and, if more than a few milligrams were heated, the product exploded. The infrared spectrum of this compound appears in Appendix I as Figure 47. The nmr spectrum was not obtained because this compound does not possess sufficient solubility in any suitable solvent.

Anal. Calcd for $C_{17}H_{10}N_8$: C, 57.93%; H, 3.47%; N, 38.60%.

Found: C, 55.05%; H, 3.56%; N, 41.32%.

B. 1,4-Bis(5-phenyl-1-tetrazolyl)-n-butane.--N,N'-dibenzoyl-1,4-diaminobutane (29.6 grams, 0.100 mole) was added in one gram portions to a stirred, heated (90-100°) solution of 50 grams of phosphorus pentachloride in 150 ml of freshly distilled toluene for an hour. The reaction was completed by allowing the solution to reflux for an additional hour after which 26.6 grams of dry sodium azide (0.400 mole) were added directly to the hot mixture in one gram portions over the period of one hour.

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The mixture was then refluxed and stirred for 12 to 14 hours. The solvent was evaporated, and the crude product recovered was washed with 200 ml of water. The material, insoluble in water, was recrystallized from glacial acetic acid, and 1.89 grams of 1,4-bis(5-phenyl-1-tetrazolyl)-n-butane (mp 225-226°) were obtained. The reaction yield based on N,N'-dibenzoyl-1,4-diaminobutane was 3.44%. The infrared spectrum of this compound appears in Appendix I as Figure 48. The nmr spectrum was not obtained because this compound does not possess sufficient solubility in any suitable solvent.

Anal. Calcd for $C_{18}H_{18}N_8$: C, 62.41%; H, 5.24%; N, 32.35%.
Found: C, 62.34%; H, 5.14%; N, 32.41%.

XI. Preparation of Precursors to α,ω-Bis(1-phenyl-5-tetrazolyl)-n-alkanes

A. N,N'-Diphenylmalonamide.--Diethyl malonate (320 grams, 2 moles) and aniline (400 grams, 4.30 moles) were mixed together, and N,N'-diphenylmalonamide was prepared in the manner previously described for N,N'-diphenyloxamide. The crude product was recrystallized from methanol, and, upon cooling, 502 grams of N,N'-diphenylmalonamide [mp 225°, lit. (94) mp 224-225°] precipitated. The reaction yield based on diethyl malonate was 93.6%. The infrared spectrum of this compound appears in Appendix I as Figure 49.

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B. N,N'-Diphenylsuccinamide.--A mixture of 93 grams of aniline (1 mole) and 1 liter of freshly distilled benzene was prepared in a two liter, three-necked, round-bottom flask equipped with a stirrer, thermometer, and dropping funnel. The flask was cooled by a water-ice bath. A solution of 25 grams of succinyl chloride (0.25 mole) and 200 ml of freshly distilled benzene was slowly added to the well-stirred, cooled solution over a period of two hours. After the reaction was completed, the aniline hydrochloride was extracted with warm water. A residue was left which consisted of almost pure N,N'-diphenylsuccinamide. The crude product was recrystallized from methanol [mp 229°, lit. (95) at 228-229°] and the yield of product (39.0 grams) based on succinyl chloride was 90%. The infrared spectrum of this compound appears in Appendix I as Figure 50.

XII. Attempted Preparation of α,ω-Bis(1-phenyl-5-tetrazolyl)-n-alkanes

Preparations of bis(1-phenyl-5-tetrazolyl)methane and 1,2-bis(1-phenyl-5-tetrazolyl)ethane were attempted from N,N'-diphenylmalonamide and N,N'-diphenylsuccinamide according to the following reaction procedure.

(1) $$\phi\text{-}\underset{\underset{H}{|}}{N}\text{-}\underset{\underset{O}{\|}}{C}\text{-}(CH_2)_n\text{-}\underset{\underset{O}{\|}}{C}\text{-}\underset{\underset{H}{|}}{N}\text{-} \xrightarrow[\text{benzene}]{2PCl_5} \text{-}N{=}\underset{\underset{Cl}{|}}{C}\text{-}(CH_2)_n\text{-}\underset{\underset{Cl}{|}}{C}{=}N\text{-}\phi$$

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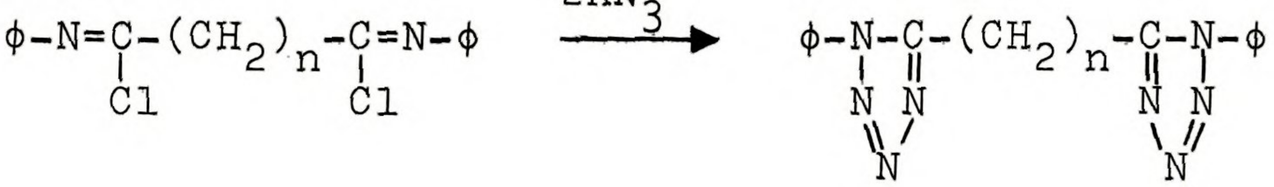
(2) 

where n = 1 and 2, ϕ = C_6H_5.

In each case, the respective nmr, infrared, and mass spectra of the isolated reaction product indicated that the expected compound was not obtained. Because 1,1'-diphenyl-5,5'-bitetrazole can be prepared from N,N'-diphenyloxamide (see p. 57), it is surprising that the related methylene bridged bitetrazoles could not be prepared. The most plausible explanation for the failure of the synthesis is the availability of methylene hydrogens which could facilitate a possible rearrangement.

Von Braun and Rudolph (96) applied the foregoing sequence of reactions only to imide chlorides in which R' was aromatic and R was either aliphatic or aromatic groups. The restriction to imide chlorides derived from anilides was based on earlier work by von Braun and his co-workers (97-99). These authors have shown that the chlorides of aliphatic amides of the type R-CH_2-C(Cl)=NR', where R was either hydrogen or an aliphatic group and R' was either an aliphatic or aromatic group, were so reactive that they could not be isolated. Such imide chlorides readily formed amidine-like condensation products, apparently because of a primary shift of hydrogen from the alpha carbon to the nitrogen atom, followed by a reaction between the tautomeric forms with the elimination of hydrogen chloride.

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(1) $R\text{-}CH_2C(Cl) = N\text{-}R' \rightarrow R\text{-}CH = C(Cl)\ NHR'$

(2) $R\text{-}CH_2C(Cl) = N\text{-}R' + R\text{-}CH = C(Cl)NHR' \rightarrow R\text{-}CH_2\text{-}\underset{\displaystyle |}{C} = N\text{-}R' + R\text{-}CH = C(Cl)\ N\text{-}R' + HCl$

if R represents the $\phi\text{-}N = C(Cl)\text{-}$ fragment and R' represents a phenyl group, this reaction sequence is applicable.

Although von Braun concluded that most imide chlorides were highly unstable, this conclusion was based on attempts to isolate these compounds. The imide chlorides of the α,ω-bis(5-phenyl-1-tetrazolyl)-n-alkanes appear to form in solution with complete stability (100). However, they could not be isolated even under reduced pressures because they decompose into two moles of benzonitrile and the corresponding α,ω-dichloroalkane.

XIII. Preparation of the Precursor of 1,1'-Di-tert-butyl-5,5'-bitetrazole

N,N'-Di-tert-butyloxamide.--A mixture of 146 grams of ethyl oxalate (1.00 mole) and 150 grams of t-butylamine (2.06 moles) was heated at 100° for 24 hours in a 1-liter, three-necked, round-bottom flask equipped with a thermometer, reflux condenser, and stirrer. After the ethanol produced during the reaction was removed by distillation, the remaining material solidified as it cooled. The product was recrystallized from a solution consisting of equal parts of water and

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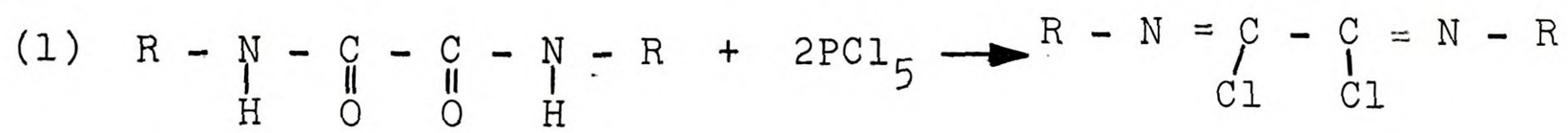
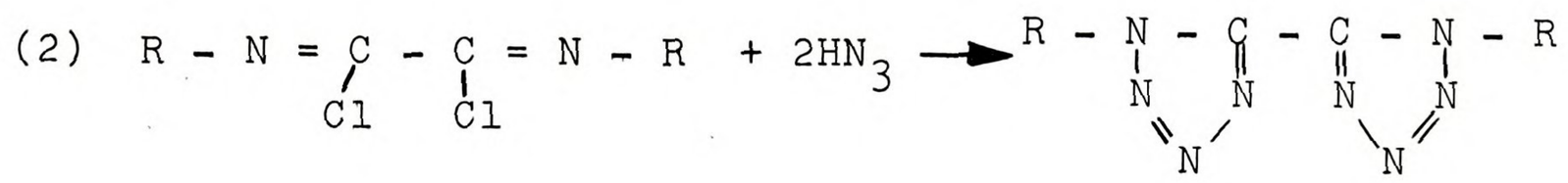
ethanol. When the mixture was cooled, 150 grams of pure product [mp 176°, lit. (101) at 176°C] were recovered. The infrared spectrum of this compound appears in Appendix I as Figure 51.

XIV. Attempted Preparation of 1,1'-Dimethyl- and 1,1'-Di-tert-butyl-5,5'-bitetrazole

A slurry of N,N'-dimethyloxamide or N,N'-di-tert-butyloxamide in benzene reacted with phosphorus pentachloride and then was successively treated with hydrazoic acid in the following manner.

(1) 

(2) 

In each case, the nmr, infrared, and mass spectra of the isolated reaction product showed that the expected bitetrazole was not obtained. It appears that the reaction scheme failed to yield the expected product because of the reactivity of the diimidchloride intermediate. There is evidence of an intramolecular rearrangement (96) in which the diimidchloride eliminates one HCl molecule and an intermolecular rearrangement (96-99) in which a proton shifts from a carbon atom to a nitrogen atom followed by the subsequent elimination of HCl between one molecule each

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of the rearranged and nonrearranged compounds. The further investigation of the mechanisms of these reactions was not pursued because, while highly significant in itself, the effort to prepare these compounds necessitated a detailed exploration of an area of fundamental organic chemistry peripheral to the main goals of this research project.

XV. Spectrophotometric Studies

A. Procedure for Carrying Out Spectrophotometric Measurements.

--The method used to evaluate the equilibrium constants for the reaction $C_nMT + I_2 \xrightarrow{K_f} C_nMT \cdot I_2$ requires that a series of solutions be prepared in an inert solvent with the initial concentration of the absorbing iodine component held constant and the concentration of cyclopolymethylenetetrazole varied over a ten to fifteen-fold range, always in large excess compared with the iodine concentration.

B. Preparation of Solutions.

--Stock solutions of the respective cyclopolymethylenetetrazoles were prepared by direct weighing of the compound into a volumetric flask and dilution to the calibration mark with 1,2-dichloroethane at the appropriate temperature.

Stock iodine solutions were prepared by accurately weighing the solute into a volumetric flask and diluting to the calibration mark with 1,2-dichloroethane at the appropriate temperature.

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C. Spectrophotometric Techniques.--All measurements were made in stoppered one cm matched silica cells with a Beckman DU spectrophotometer equipped with Beckman thermospacers to control the temperature of the sample compartment. The desired temperature was maintained by circulating water from a constant temperature bath (Waco refrigerated constant temperature bath, Wilkens-Anderson Company, 4525 W. Division Street, Chicago 51, Illinois) through the thermospacers. By controlling the temperature of the bath, the temperature of the cell compartment was regulated to within ±0.1° for each of the following four temperatures: 5.0, 15.0, 25.0, and 35.0°. Dry nitrogen circulation through the cell compartment was essential during the absorbance measurements at the lower temperatures in order to remove moisture and to prevent cell fogging. The absorbances of each of the iodine solutions of a given cyclopolymethylenetetrazole were measured at several of the wavelengths near the complex absorption maximum.

D. Spectrophotometric Measurements.--Solutions with known concentrations of iodine and of the respective cyclopolymethylenetetrazole were prepared at 5.0, 15.0, 25.0, and 35.0° ±0.1° respectively. The iodine concentrations of these solutions were such (approximately 10^{-3} M) that the absorbances in the region of the complex absorption maximum were approximately 0.5. Measured amounts of these stock solutions were mixed in 25 ml volumetric flasks so

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as to obtain the desired final concentrations. The solutions were diluted to the mark with 1,2-dichloroethane which had previously been brought to the respective temperature in the constant temperature bath. Samples of these solutions were transferred to 1-cm glass stoppered silica absorption cells and placed in the thermostatted cell compartment. After the temperature equilibrium was attained (~fifteen minutes), the absorbance values were measured at 430, 420, 410, and 400 mμ. Pure 1,2-dichloroethane was used as the reference solvent.

E. Recovery Procedures for the Cyclopolymethylenetetrazoles.--The recovery techniques for all the cyclopolymethylenetetrazoles are essentially the same. Solutions containing the water soluble cyclopolymethylenetetrazoles were first treated with an aqueous sodium thiosulfate solution in order to reduce the iodine. The respective cyclopolymethylenetetrazole was then extracted from the aqueous phase with chloroform. The tetrazole recovered by evaporation of the chloroform was then purified further by recrystallization from an appropriate solvent. The cyclopolymethylenetetrazoles which were insoluble in water were dissolved in a one to one ethanol-water solvent solution before the above purification procedure was carried out.

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F. Calculation of Equilibrium Constants as a Function of the Temperature.--The formation constants were calculated using Ketelaar's (102) improvement of the Benesi-Hildebrand method where, in the case of an addition reaction between iodine and a cyclopolymethylenetetrazole

$$C_nMT + I_2 \longrightarrow C_nMT \cdot I_2$$

the formation constant is given by

$$K_f = \frac{[C_nMT \cdot I_2]}{[C_nMT][I_2]} = \frac{\varepsilon_t - \varepsilon_{I_2}}{\varepsilon_c - \varepsilon_t} \cdot \frac{1}{C_B}$$

where

ε_{I_2} = the molar absorptivity of pure iodine in the pure solvent.

ε_t = the apparent molar absorptivity, calculated by dividing the total absorbance at the appropriate wavelength by the total iodine concentration.

ε_c = the molar absorptivity of the cyclopolymethylene-tetrazole-iodine complex.

C_B = equilibrium concentration of the cyclopolymethylenetetrazole.

If $C_B^{\text{total}} >> C_{I_2}^{\text{total}}$, then $C_B \approx C_B^{\text{total}}$

This equation can be rearranged to

$$\frac{1}{\varepsilon_t - \varepsilon_{I_2}} = \frac{1}{(\varepsilon_c - \varepsilon_{I_2})K_f C_B} + \frac{1}{\varepsilon_c - \varepsilon_{I_2}}$$

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The only unknown factors here are ε_c and K_f, a plot of $\frac{1}{\varepsilon_t - \varepsilon_{I_2}}$. vs. $\frac{1}{C_B}$ should therefore produce a straight line. From the slope and intercept of this line, the formation constant and molar absorptivity of the complex can be determined respectively.

Once the formation constants for the respective cyclopolymethylenetetrazole-iodine complexes are known at several different temperatures, they may be used to calculate the free energy, enthalpy, and entropy for the complexation reaction from the well known relationships

$$\Delta G^\circ = - RT \ln K_f$$

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

$$\log K_f = \frac{-\Delta H^\circ}{2.303\ RT} + \frac{\Delta S}{2.303\ R}$$

where ΔG° is the standard free energy change in cal/mole, ΔH° is the standard enthalpy change in cal/mole, and ΔS° is the standard entropy change in cal/mole deg. A plot of $\log K_f$ vs. $1/T$ should give a straight line with a slope of $-\Delta H^\circ/2.303R$ and an intercept of $\Delta S^\circ/2.303R$.

G. Treatment of the Spectrophotometric Data.--The respective formation constants were determined by using the spectrophotometric data taken at each of four temperatures for the cyclopolymethylenetetrazole solutions in 1,2-dichloroethane. These data, given in Tables I through VI,

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were treated using a regression analysis performed on a CDC 3600 computer with points over three standard deviations off the line being rejected. The program was written by W. J. McKinney and is listed in Appendix II.

The iteration was performed on the Ketelaar equation in the following manner. The experimental values of $1/C_B$ and $1/\varepsilon_t-\varepsilon_{I_2}$ were used in Ketelaar's equation to calculate a value for the concentration of the complex which was subtracted from each value of C_B to give a new array. The process was then repeated until successive values of K_f agreed within 0.1%.

The iteration procedure for solving Ketelaar's equation offers a distinct advantage in the evaluation of formation constants from experimental data. The values converged rapidly and reproducibly at all wavelengths. This method made it possible to use lower concentrations of the donors to avoid the possibility of a change in the physical properties of the solvent in solutions with high concentrations of the base. It is assumed that the activity coefficients of uncharged species equal the unity at the concentrations of iodine and cyclopolymethylenetetrazoles that were used (<0.6 M). The values of the respective formation constants, therefore are expressed in concentration units.

TABLE
Trime

[C_3MT	ε_{I_2}	K_f
0.000		
0.042		
0.084		
0.126		
0.168		
0.210		
0.252		
0.294		
0.336		
0.379		
0.429		
0.499		

	ε_{I_2}	K_f
0.000		
0.045		
0.090		
0.135		
0.180		
0.225		
0.270		
0.315		
0.360		
0.405		
0.443		
0.528		

TABLE I.--Absorbances and Formation Constants for the Trimethylenetetrazole-Iodine Complex in Purified 1,2-Dichloroethane.

$[C_3MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
		5.0°, $[I_2] = 1.09 \times 10^{-3}$ M		
0.000	0.162	0.087	0.043	0.022
0.042	0.257	0.184	0.133	0.095
0.084	0.341	0.266	0.208	0.158
0.126	0.406	0.336	0.273	0.212
0.168	0.461	0.397	0.331	0.259
0.210	0.517	0.450	0.380	0.303
0.252	0.566	0.502	0.427	0.344
0.294	0.601	0.541	0.464	0.375
0.336	0.637	0.581	0.499	0.407
0.379	0.670	0.618	0.538	0.438
0.429	0.707	0.658	0.574	0.468
0.499	0.745	0.698	0.615	0.501
ε_{I_2}	148.62	79.82	39.45	20.18
K_f	2.31±0.04	2.09±0.02	2.05±0.03	1.93±0.03
		15.0°, $[I_2] = 1.07 \times 10^{-3}$ M		
0.000	0.150	0.082	0.042	0.021
0.045	0.236	0.176	0.126	0.092
0.090	0.307	0.253	0.194	0.151
0.135	0.374	0.321	0.256	0.204
0.180	0.430	0.381	0.311	0.251
0.225	0.477	0.435	0.361	0.294
0.270	0.519	0.479	0.402	0.326
0.315	0.560	0.523	0.445	0.365
0.360	0.595	0.560	0.482	0.395
0.405	0.624	0.596	0.511	0.424
0.443	0.663	0.635	0.550	0.462
0.528	0.698	0.675	0.588	0.494
ε_{I_2}	140.12	76.64	39.25	19.63
K_f	1.85±0.04	1.87±0.05	1.72±0.05	1.65±0.06

TABLE

$[C_3MT]$	ε_{I_2}	K_f
0.000		
0.040		
0.079		
0.119		
0.158		
0.198		
0.237		
0.277		
0.316		
0.356		
0.403		
0.448		

$[C_3MT]$	ε_{I_2}	K_f
0.000		
0.048		
0.097		
0.145		
0.194		
0.242		
0.291		
0.339		
0.388		
0.436		
0.516		
0.582		

TABLE I--Continued.

$[C_3MT)$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
	25.0°, $[I_2] = 1.48x10^{-3}$ M			
0.000	0.205	0.110	0.055	0.029
0.040	0.289	0.191	0.128	0.087
0.079	0.367	0.273	0.200	0.146
0.119	0.446	0.349	0.270	0.201
0.158	0.494	0.398	0.316	0.237
0.198	0.559	0.459	0.372	0.287
0.237	0.600	0.512	0.419	0.326
0.277	0.646	0.561	0.462	0.361
0.316	0.694	0.608	0.510	0.402
0.356	0.738	0.648	0.546	0.431
0.403	0.774	0.683	0.574	0.451
0.448	0.816	0.727	0.615	0.486
ε_{I_2}	138.51	74.32	37.16	19.59
K_f	1.56±0.08	1.24±0.10	1.36±0.09	1.33±0.09
	35.0°, $[I_2] = 1.10x10^{-3}$ M			
0.000	0.150	0.082	0.041	0.021
0.048	0.215	0.147	0.098	0.067
0.097	0.273	0.202	0.147	0.106
0.145	0.327	0.258	0.198	0.149
0.194	0.373	0.302	0.237	0.177
0.242	0.417	0.344	0.276	0.208
0.291	0.464	0.398	0.332	0.268
0.339	0.504	0.441	0.373	0.307
0.388	0.537	0.470	0.401	0.328
0.436	0.567	0.502	0.433	0.355
0.516	0.602	0.535	0.458	0.368
0.582	0.635	0.568	0.487	0.392
ε_{I_2}	136.36	74.55	37.27	19.09
K_f	1.18±0.05	1.14±0.08	1.10±0.06	1.00±0.23

TABLE I
Tetram

$[C_4MT]$	ε_{I_2}	K_f
0.000		
0.041		
0.083		
0.124		
0.165		
0.207		
0.248		
0.287		
0.331		
0.372		
0.396		
0.481		

	ε_{I_2}	K_f
0.000		
0.042		
0.084		
0.126		
0.168		
0.210		
0.252		
0.294		
0.337		
0.379		

TABLE II.--Absorbances and Formation Constants for the Tetramethylenetetrazole-Iodine Complex in Purified 1,2-Dichloroethane.

$[C_4MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
		5.1°, $[I_2] = 1.12x10^{-3}$ M		
0.000	0.167	0.090	0.045	0.022
0.041	0.327	0.264	0.214	0.172
0.083	0.445	0.393	0.345	0.288
0.124	0.527	0.478	0.420	0.345
0.165	0.602	0.561	0.494	0.411
0.207	0.665	0.624	0.561	0.467
0.248	0.709	0.679	0.615	0.517
0.287	0.751	0.728	0.662	0.560
0.331	0.788	0.768	0.700	0.592
0.372	0.820	0.803	0.741	0.627
0.396	0.857	0.835	0.776	0.663
0.481	0.907	0.904	0.855	0.749
ε_{I_2}	149.11	80.36	40.18	19.64
K_f	4.13±0.13	4.09±0.16	4.07±0.23	4.16±0.35
		14.8°, $[I_2] = 8.89x10^{-4}$ M		
0.000	0.126	0.067	0.035	0.018
0.042	0.234	0.186	0.150	0.119
0.084	0.316	0.281	0.237	0.195
0.126	0.386	0.353	0.312	0.263
0.168	0.441	0.417	0.375	0.319
0.210	0.486	0.471	0.428	0.367
0.252	0.531	0.515	0.473	0.410
0.294	0.570	0.557	0.515	0.449
0.337	0.600	0.590	0.546	0.477
0.379	0.624	0.618	0.579	0.504
ε_{I_2}	141.73	75.37	39.37	20.25
K_f	3.16±0.06	3.19±0.04	2.98±0.06	2.81±0.07

TABLE

$[C_4MT]$	ε_{I_2}	K_f
0.000		
0.044		
0.087		
0.130		
0.174		
0.217		
0.261		
0.304		
0.348		
0.391		
0.468		
0.530		
0.559		

	ε_{I_2}	K_f
0.000		
0.045		
0.090		
0.135		
0.180		
0.225		
0.271		
0.316		
0.361		
0.406		
0.459		
0.510		

TABLE II--Continued.

$[C_4MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
		25.0°, $[I_2] = 1.48 \times 10^{-3}$ M		
0.000	0.205	0.113	0.058	0.030
0.044	0.354	0.266	0.200	0.150
0.087	0.475	0.392	0.320	0.251
0.130	0.573	0.494	0.418	0.332
0.174	0.656	0.584	0.498	0.404
0.217	0.750	0.681	0.599	0.490
0.261	0.795	0.730	0.642	0.525
0.304	0.852	0.785	0.695	0.575
0.348	0.907	0.848	0.750	0.621
0.391	0.957	0.887	0.790	0.660
0.468	1.017	0.962	0.858	0.724
0.530	1.074	1.024	0.926	0.775
0.559	1.089	1.038	0.945	0.793
ε_{I_2}	138.51	76.35	39.19	20.27
K_f	2.47±0.05	2.40±0.03	2.31±0.07	2.18±0.07
		35.0°, $[I_2] = 1.10 \times 10^{-3}$ M		
0.000	0.151	0.082	0.041	0.021
0.045	0.245	0.178	0.132	0.097
0.090	0.326	0.261	0.210	0.163
0.135	0.397	0.337	0.285	0.232
0.180	0.460	0.403	0.348	0.288
0.225	0.515	0.458	0.402	0.338
0.271	0.567	0.518	0.458	0.400
0.316	0.606	0.564	0.503	0.431
0.361	0.644	0.600	0.540	0.464
0.406	0.677	0.631	0.570	0.487
0.459	0.712	0.671	0.609	0.522
0.510	0.742	0.703	0.640	0.549
ε_{I_2}	137.26	74.55	37.26	19.09
K_f	1.87±0.03	1.74±0.05	1.66±0.05	1.47±0.11

TABLE
Penta

$[C_5MT$	ε_{I_2}	K_f
0.000		
0.044		
0.087		
0.130		
0.174		
0.217		
0.261		
0.304		
0.348		
0.391		
0.447		
0.493		

	ε_{I_2}	K_f
0.000		
0.040		
0.080		
0.119		
0.159		
0.199		
0.239		
0.279		
0.318		
0.358		
0.416		
0.503		

TABLE III-Absorbances and Formation Constants for the Pentamethylenetetrazole-Iodine Complex in Purified 1,2-Dichloroethane.

$[C_5MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
		5.0°, $[I_2] = 1.09 \times 10^{-3}$ M		
0.000	0.163	0.087	0.043	0.021
0.044	0.310	0.247	0.193	0.152
0.087	0.425	0.368	0.312	0.250
0.130	0.511	0.460	0.402	0.327
0.174	0.579	0.535	0.467	0.387
0.217	0.647	0.607	0.538	0.445
0.261	0.690	0.658	0.588	0.486
0.304	0.733	0.700	0.631	0.528
0.348	0.772	0.739	0.671	0.561
0.391	0.798	0.775	0.703	0.589
0.447	0.845	0.821	0.753	0.638
0.493	0.868	0.848	0.777	0.658
ε_{I_2}	149.54	79.82	39.45	19.27
K_f	3.52±0.06	3.53±0.05	3.40±0.07	3.37±0.08
		15.0°, $[I_2] = 1.08 \times 10^{-3}$ M		
0.000	0.153	0.083	0.042	0.022
0.040	0.257	0.203	0.155	0.114
0.080	0.360	0.300	0.245	0.191
0.119	0.438	0.383	0.324	0.261
0.159	0.501	0.450	0.386	0.311
0.199	0.556	0.507	0.440	0.356
0.239	0.606	0.561	0.489	0.401
0.279	0.648	0.606	0.535	0.441
0.318	0.680	0.641	0.570	0.468
0.358	0.716	0.675	0.602	0.498
0.416	0.758	0.722	0.653	0.543
0.503	0.801	0.779	0.706	0.591
ε_{I_2}	141.67	76.85	38.89	20.37
K_f	2.91±0.03	2.84±0.03	2.74±0.04	2.53±0.06

TABLE

| $[C_5MT$ | | |

TABLE III--Continued.

$[C_5MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
	25.0°, $[I_2] = 9.04 \times 10^{-4}$ M			
0.000	0.126	0.070	0.035	0.018
0.039	0.203	0.150	0.110	0.081
0.078	0.271	0.216	0.172	0.134
0.117	0.328	0.281	0.232	0.185
0.156	0.378	0.229	0.282	0.226
0.195	0.423	0.375	0.324	0.264
0.234	0.458	0.416	0.361	0.295
0.273	0.490	0.448	0.392	0.324
0.312	0.523	0.480	0.423	0.350
0.351	0.554	0.516	0.456	0.378
0.389	0.576	0.537	0.479	0.400
0.416	0.590	0.556	0.492	0.412
0.456	0.610	0.576	0.512	0.426
ε_{I_2}	139.38	77.43	38.72	19.91
K_f	2.29±0.04	2.20±0.04	2.16±0.04	2.05±0.04
	35.0°, $[I_2] = 1.10 \times 10^{-3}$ M			
0.000	0.150	0.081	0.041	0.022
0.050	0.249	0.181	0.133	0.096
0.101	0.335	0.268	0.212	0.163
0.151	0.407	0.344	0.285	0.226
0.201	0.467	0.409	0.344	0.275
0.252	0.524	0.467	0.400	0.324
0.302	0.571	0.517	0.446	0.365
0.352	0.615	0.563	0.488	0.403
0.403	0.658	0.602	0.528	0.436
0.453	0.686	0.637	0.563	0.463
0.506	0.716	0.658	0.591	0.488
0.586	0.756	0.709	0.631	0.522
ε_{I_2}	136.36	73.64	37.27	20.00
K_f	1.85±0.02	1.77±0.04	1.65±0.03	1.48±0.06

TABLE
Hexam

[C_6MT	ε_{I_2}	K_f
0.000		
0.035		
0.070		
0.105		
0.141		
0.176		
0.211		
0.246		
0.281		
0.316		
0.350		
0.385		

[C_6MT	ε_{I_2}	K_f
0.000		
0.039		
0.077		
0.116		
0.155		
0.194		
0.232		
0.271		
0.310		
0.348		
0.392		
0.421		

TABLE IV--Absorbances and Formation Constants for the Hexamethylenetetrazole-Iodine Complex in Purified 1,2-Dichloroethane.

$[C_6MT]$	$A_{420m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
		6.5°, $[I_2] = 1.05 \times 10^{-3}$ M		
0.000	0.155	0.083	0.041	0.021
0.035	0.298	0.238	0.192	0.148
0.070	0.413	0.362	0.311	0.255
0.105	0.502	0.458	0.405	0.336
0.141	0.577	0.540	0.487	0.415
0.176	0.669	0.645	0.593	0.511
0.211	0.687	0.662	0.606	0.518
0.246	0.729	0.713	0.653	0.563
0.281	0.767	0.748	0.690	0.598
0.316	0.791	0.788	0.728	0.630
0.350	0.823	0.828	0.772	0.680
0.385	0.855	0.848	0.796	0.699
ε_{I_2}	147.62	78.10	39.05	20.00
K_f	4.29±0.20	4.10±0.20	4.02±0.22	3.61±0.24
		15.1°, $[I_2] = 8.79 \times 10^{-4}$ M		
0.000	0.124	0.065	0.034	0.017
0.039	0.230	0.178	0.139	0.108
0.077	0.315	0.269	0.227	0.182
0.116	0.382	0.343	0.297	0.244
0.155	0.439	0.399	0.354	0.293
0.194	0.484	0.449	0.400	0.334
0.232	0.528	0.498	0.447	0.376
0.271	0.573	0.550	0.496	0.425
0.310	0.594	0.569	0.515	0.438
0.348	0.617	0.599	0.547	0.464
0.392	0.652	0.631	0.583	0.502
0.421	0.660	0.643	0.595	0.512
ε_{I_2}	141.07	73.95	38.68	19.34
K_f	3.35±0.07	3.28±0.08	3.05±0.08	2.89±0.09

TABLE

$[C_6MT]$	
0.000	
0.041	
0.081	
0.122	
0.162	
0.203	
0.243	
0.284	
0.324	
0.365	
0.395	
0.421	
0.453	
0.484	
0.507	
ε_{I_2}	
K_f	

0.000	
0.041	
0.083	
0.124	
0.165	
0.206	
0.248	
0.289	
0.330	
0.372	
0.418	
0.453	
ε_{I_2}	
K_f	

TABLE IV--Continued.

$[C_6MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
	25.0°, $[I_2] = 9.0x10^{-4}$ M			
0.000	0.126	0.071	0.036	0.018
0.041	0.215	0.163	0.125	0.093
0.081	0.291	0.240	0.196	0.155
0.122	0.355	0.309	0.262	0.209
0.162	0.412	0.366	0.316	0.258
0.203	0.456	0.416	0.361	0.299
0.243	0.496	0.459	0.407	0.339
0.284	0.529	0.493	0.439	0.364
0.324	0.565	0.527	0.472	0.397
0.365	0.594	0.560	0.500	0.422
0.395	0.610	0.577	0.514	0.427
0.421	0.622	0.593	0.528	0.442
0.453	0.637	0.609	0.550	0.457
0.484	0.662	0.629	0.569	0.477
0.507	0.668	0.638	0.577	0.483
ε_{I_2}	139.38	78.54	39.82	19.91
K_f	2.52±0.05	2.43±0.04	2.45±0.04	2.37±0.06
	36.0°, $[I_2] = 1.05x10^{-3}$ M			
0.000	0.141	0.077	0.040	0.020
0.041	0.227	0.168	0.126	0.095
0.083	0.309	0.253	0.206	0.166
0.124	0.374	0.323	0.274	0.226
0.165	0.433	0.384	0.334	0.282
0.206	0.484	0.441	0.387	0.330
0.248	0.532	0.487	0.433	0.373
0.289	0.574	0.531	0.478	0.414
0.330	0.614	0.572	0.516	0.448
0.372	0.642	0.608	0.554	0.483
0.418	0.679	0.651	0.600	0.535
0.453	0.704	0.677	0.620	0.550
ε_{I_2}	134.29	73.33	38.10	19.05
K_f	1.89±0.05	1.85±0.04	1.71±0.03	1.65±0.05

TABLE

$[C_6MT]_0$	ε_{I_2}	K_f	ε_{I_2}	K_f
	0.000		0.000	
	0.041		0.041	
	0.081		0.083	
	0.122		0.124	
	0.162		0.165	
	0.203		0.206	
	0.243		0.248	
	0.284		0.289	
	0.324		0.330	
	0.365		0.372	
	0.395		0.418	
	0.421		0.453	
	0.453			
	0.484			
	0.507			

TABLE IV--Continued.

$[C_6MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
	25.0°, $[I_2] = 9.0x10^{-4}$ M			
0.000	0.126	0.071	0.036	0.018
0.041	0.215	0.163	0.125	0.093
0.081	0.291	0.240	0.196	0.155
0.122	0.355	0.309	0.262	0.209
0.162	0.412	0.366	0.316	0.258
0.203	0.456	0.416	0.361	0.299
0.243	0.496	0.459	0.407	0.339
0.284	0.529	0.493	0.439	0.364
0.324	0.565	0.527	0.472	0.397
0.365	0.594	0.560	0.500	0.422
0.395	0.610	0.577	0.514	0.427
0.421	0.622	0.593	0.528	0.442
0.453	0.637	0.609	0.550	0.457
0.484	0.662	0.629	0.569	0.477
0.507	0.668	0.638	0.577	0.483
ε_{I_2}	139.38	78.54	39.82	19.91
K_f	2.52±0.05	2.43±0.04	2.45±0.04	2.37±0.06
	36.0°, $[I_2] = 1.05x10^{-3}$ M			
0.000	0.141	0.077	0.040	0.020
0.041	0.227	0.168	0.126	0.095
0.083	0.309	0.253	0.206	0.166
0.124	0.374	0.323	0.274	0.226
0.165	0.433	0.384	0.334	0.282
0.206	0.484	0.441	0.387	0.330
0.248	0.532	0.487	0.433	0.373
0.289	0.574	0.531	0.478	0.414
0.330	0.614	0.572	0.516	0.448
0.372	0.642	0.608	0.554	0.483
0.418	0.679	0.651	0.600	0.535
0.453	0.704	0.677	0.620	0.550
ε_{I_2}	134.29	73.33	38.10	19.05
K_f	1.89±0.05	1.85±0.04	1.71±0.03	1.65±0.05

TABLE
Heptan

[C_7MT	ε_{I_2}	K_f
0.000		
0.039		
0.078		
0.117		
0.156		
0.195		
0.235		
0.274		
0.313		
0.352		
0.386		
0.452		

	ε_{I_2}	K_f
0.000		
0.037		
0.075		
0.112		
0.149		
0.185		
0.224		
0.261		
0.298		
0.336		
0.374		
0.400		

TABLE V.--Absorbances and Formation Constants for the Heptamethylenetetrazole-Iodine Complex in Purified 1,2-Dichloroethane.

$[C_7MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
		$5.1°$, $[I_2] = 1.12x10^{-3}$ M		
0.000	0.167	0.090	0.045	0.022
0.039	0.337	0.276	0.224	0.178
0.078	0.461	0.414	0.359	0.299
0.117	0.560	0.519	0.464	0.392
0.156	0.640	0.608	0.551	0.470
0.195	0.698	0.670	0.614	0.527
0.235	0.765	0.743	0.687	0.595
0.274	0.797	0.782	0.723	0.625
0.313	0.830	0.817	0.760	0.659
0.352	0.868	0.857	0.795	0.688
0.386	0.906	0.901	0.846	0.745
0.452	0.946	0.941	0.883	0.777
ε_{I_2}	149.54	80.36	40.18	19.64
K_f	4.38±0.08	4.39±0.08	4.21±0.08	3.99±0.10
		$15.1°$, $[I_2] = 8.79x10^{-4}$ M		
0.000	0.124	0.065	0.034	0.017
0.037	0.233	0.181	0.145	0.114
0.075	0.318	0.273	0.231	0.187
0.112	0.397	0.365	0.332	0.292
0.149	0.443	0.409	0.365	0.308
0.185	0.488	0.458	0.412	0.349
0.224	0.535	0.510	0.461	0.396
0.261	0.573	0.551	0.501	0.433
0.298	0.602	0.582	0.532	0.459
0.336	0.637	0.619	0.675	0.501
0.374	0.665	0.652	0.707	0.532
0.400	0.678	0.665	0.718	0.540
ε_{I_2}	141.07	73.95	38.68	19.34
K_f	3.53±0.10	3.47±0.14	3.31±0.49	3.42±0.37

TABLE

$[C_7MT]$	ε_{I_2}	K_f
0.000		
0.039		
0.078		
0.118		
0.157		
0.196		
0.235		
0.274		
0.313		
0.353		
0.391		
0.440		

	ε_{I_2}	K_f
0.000		
0.046		
0.093		
0.139		
0.185		
0.231		
0.278		
0.324		
0.370		
0.417		

TABLE V--Continued.

$[C_7MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
		$25.0°$, $[I_2] = 9.26 \times 10^{-4}$ M		
0.000	0.130	0.070	0.035	0.018
0.039	0.223	0.167	0.125	0.093
0.078	0.297	0.245	0.197	0.153
0.118	0.358	0.311	0.262	0.206
0.157	0.420	0.372	0.321	0.257
0.196	0.462	0.420	0.363	0.293
0.235	0.502	0.459	0.403	0.327
0.274	0.540	0.500	0.440	0.359
0.313	0.579	0.541	0.480	0.394
0.353	0.598	0.566	0.498	0.410
0.391	0.626	0.592	0.527	0.434
0.440	0.654	0.618	0.557	0.456
ε_{I_2}	140.39	75.59	37.80	19.44
K_f	2.71±0.07	2.68±0.05	2.57±0.05	2.58±0.07
		$35.0°$, $[I_2] = 1.10 \times 10^{-3}$ M		
0.000	0.151	0.082	0.041	0.021
0.046	0.258	0.191	0.142	0.105
0.093	0.346	0.284	0.229	0.177
0.139	0.425	0.363	0.305	0.245
0.185	0.485	0.427	0.363	0.293
0.231	0.549	0.488	0.425	0.348
0.278	0.597	0.543	0.474	0.388
0.324	0.641	0.596	0.526	0.437
0.370	0.682	0.636	0.568	0.473
0.417	0.718	0.675	0.608	0.501
ε_{I_2}	137.27	74.55	37.27	19.09
K_f	2.07±0.04	1.95±0.04	1.81±0.05	1.67±0.06

TABLE
Undeca

[C_{11}M											
0.000											
0.038											
0.076											
0.114											
0.152											
0.190											
0.228											
0.267											
0.305											
0.343											
0.376											
ε_{I_2}											
K_f											

TABLE VI--Absorbances and Formation Constants for the Undecamethylenetetrazole-Iodine Complex in Purified 1,2-Dichloroethane.

$[C_{11}MT]$	$A_{430m\mu}$	$A_{420m\mu}$	$A_{410m\mu}$	$A_{400m\mu}$
	25.0°, $[I_2] = 8.27x10^{-4}$ M			
0.000	0.117	0.063	0.032	0.017
0.038	0.184	0.132	0.094	0.067
0.076	0.241	0.190	0.149	0.112
0.114	0.287	0.236	0.190	0.143
0.152	0.333	0.284	0.232	0.181
0.190	0.371	0.324	0.270	0.212
0.228	0.408	0.358	0.305	0.243
0.267	0.439	0.393	0.336	0.273
0.305	0.468	0.426	0.366	0.297
0.343	0.491	0.450	0.393	0.322
0.376	0.516	0.470	0.410	0.334
ε_{I_2}	141.48	76.18	38.69	20.56
K_f	2.11±0.05	2.11±0.05	1.96±0.07	1.72±0.09

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The formation constants at the various temperatures obtained in this study are given in Table VII. Furthermore, by the use of the data given in Table VII, a plot of the relationship between log K_f's and the reciprocals of the absolute temperatures was obtained by drawing a straight line to fit all the points as closely as possible by the least squares method (Figure 1). The standard enthalpy, which was assumed to be independent of temperature over the 30° temperature span studied, was obtained from the slope of the straight line. The entropy change was then calculated for each of the respective temperatures.

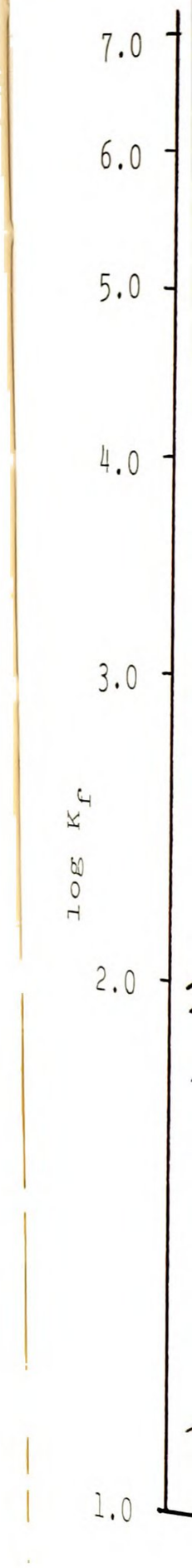
H. Errors in Spectrophotometric Studies.--In order for these measurements to be meaningful the cyclopolymethylenetetrazoles must have a high degree of purity because very small amounts of residual starting material (azide ion or the respective azidoalkanenitrile) will reduce equivalent amounts of iodine to the iodide ion which will react with the remaining iodine to give the triiodide ion. The presence of the triiodide ion is evident from the appearance of the two intense absorption bands at 290 and 365 mμ (103). Thus, if any triiodide ion is formed, a significant error can be introduced due to the effective decrease in the iodine concentration along with the superposition of the 365 mμ triiodide absorption band with a high molar absorptivity on the respective cyclopolymethylenetetrazole-iodine complex absorption

TABLE
C_nMT

Temp.	
35.0°	
25.0°	
15.0°	
5.0°	
35.0°	
25.0°	
14.8°	
5.1°	
35.0°	
25.0°	
15.0°	
5.0°	
36.0°	
25.0°	
15.0°	
6.5°	
35.1°	
25.0°	
15.1°	
5.1°	

TABLE VII-Thermodynamic Constants for the Reaction $C_nMT + I_2 \rightarrow C_nMT \cdot I_2$ in 1,2-Dichloroethane Solutions at 25°.

Temp.	$K_f(\underline{M}^{-1})$	$\Delta G°$(cal/mole)	$\Delta S°$(eu)	ΔH(Kcal/mole)
		Trimethylenetetrazole		
35.0°	1.16±0.06	- 91	-10.8	-3.4
25.0°	1.42±0.09	-215		
15.0°	1.63±0.04	-299		
5.0°	2.10±0.03	-454		
		Tetramethylenetetrazole		
35.0°	1.68±0.05	-318	-15.2	-5.0
25.0°	2.34±0.05	-504		
14.8°	3.08±0.05	-644		
5.1°	4.11±0.22	-782		
		Pentamethylenetetrazole		
35.0°	1.69±0.04	-321	-12.3	-4.1
25.0°	2.18±0.04	-461		
15.0°	2.75±0.04	-579		
5.0°	3.46±0.07	-686		
		Hexamethylenetetrazole		
36.0°	1.78±0.04	-354	-14.2	-4.7
25.0°	2.44±0.05	-529		
15.0°	3.14±0.08	-655		
6.5°	4.01±0.22	-772		
		Heptamethylenetetrazole		
35.1°	2.08±0.05	-446	-11.9	-4.1
25.0°	2.64±0.05	-575		
15.1°	3.42±0.10	-704		
5.1°	4.23±0.08	-797		



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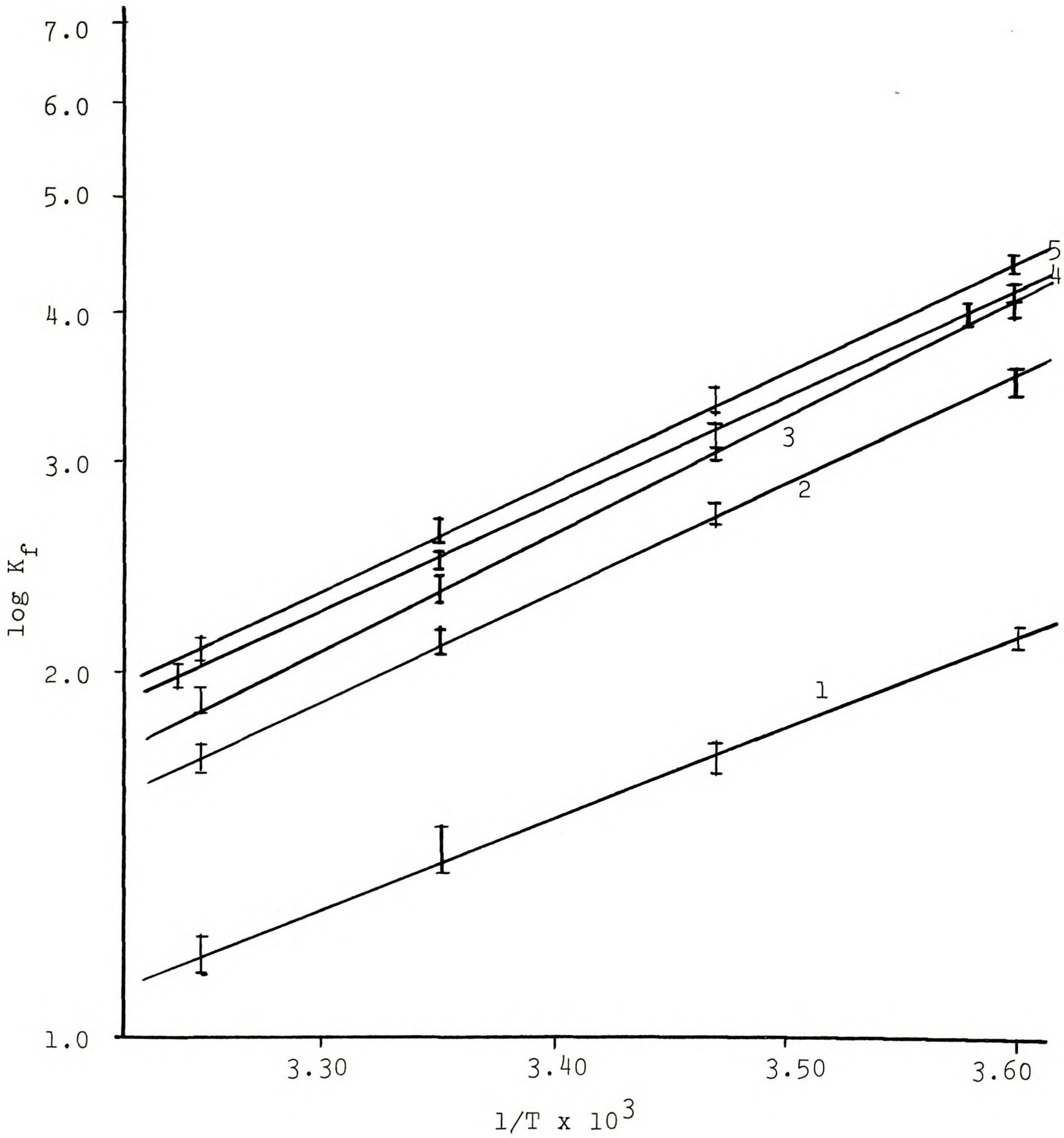

Figure 1.--The relations between log K_f and 1/T for (1) trimethylenetetrazole, (2) pentamethylenetetrazole, (3) tetramethylenetetrazole (4) hexamethylenetetrazole, and (5) heptamethylenetetrazole.

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band at about 430±5mμ. In order to eliminate the interference from the residual azide, crude cyclopolymethylenetetrazole was treated with potassium permanganate in an acid medium prior to the final purification by recrystallization.

After this treatment, no evidence of the triiodide ion was found in the spectra of the respective complexes, not even when the concentrations of cyclopolymethylenetetrazole were four times greater than those used to obtain the needed data. The solvent, 1,2-dichloroethane, was selected because all the cyclopolymethylenetetrazoles were soluble in it at concentrations greater than one molar, and its vapor pressure at 35° was sufficiently low to allow convenient handling. In 1,2-dichloroethane solutions, molecular iodine has an absorbance maximum at 495 mμ. The cyclopolymethylenetetrazoles essentially do not absorb in this spectral region. In all cases the concentrations of tetrazole were kept below 0.5 M. With the increasing tetrazole/I_2 ratio the absorption maximum gradually shifted from 495 to 430 ± 5 mμ. A series of each of the respective cyclopolymethylenetetrazole-iodine mixtures was run on the Cary model 14 spectrophotometer at room temperature to monitor the isosbestic point. The very slight shifting of the isosbestic point can be attributed to the changing character of the solvent as the concentration of the cyclopolymethylenetetrazole was

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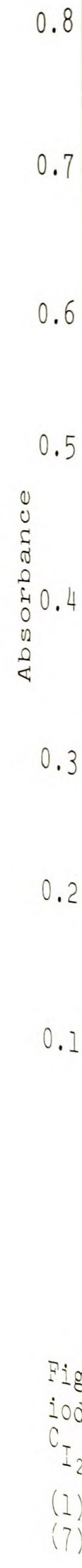
increased (104). This shift, however, was too small to significantly influence the results. A typical set of spectral curves is illustrated in Figure 2.

I. Complexation Studies of 1,1'-Diphenyl-5,5'-bitetrazole.--Attempts to prepare solid complexes of 1,1'-diphenyl-5,5'-bitetrazole with copper(II) perchlorate hexahydrate dehydrated with 1,2-dimethoxypropane in various solvents were not successful. In each case the starting material was recovered unchanged. Therefore, the complexing ability of 1,1-diphenyl-5,5'-bitetrazole in solution was studied spectroscopically by the method of continuous variations. The absorbance of solutions in which the total analytical concentration of bitetrazole and iodine in purified 1,2-dichloroethane was 10^{-3} M were determined with a Beckman model DU spectrophotometer. The measurements were carried out at three different wavelengths. The fact that the concentration of free iodine was not decreased by the addition of 1,1-diphenyl-5,5'-bitetrazole indicated that complexation did not occur. The same experiment was repeated with copper(II) perchlorate hexahydrate (total analytical concentration 0.015 M) in purified nitromethane with the same results.



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C_{I_2}
(1)
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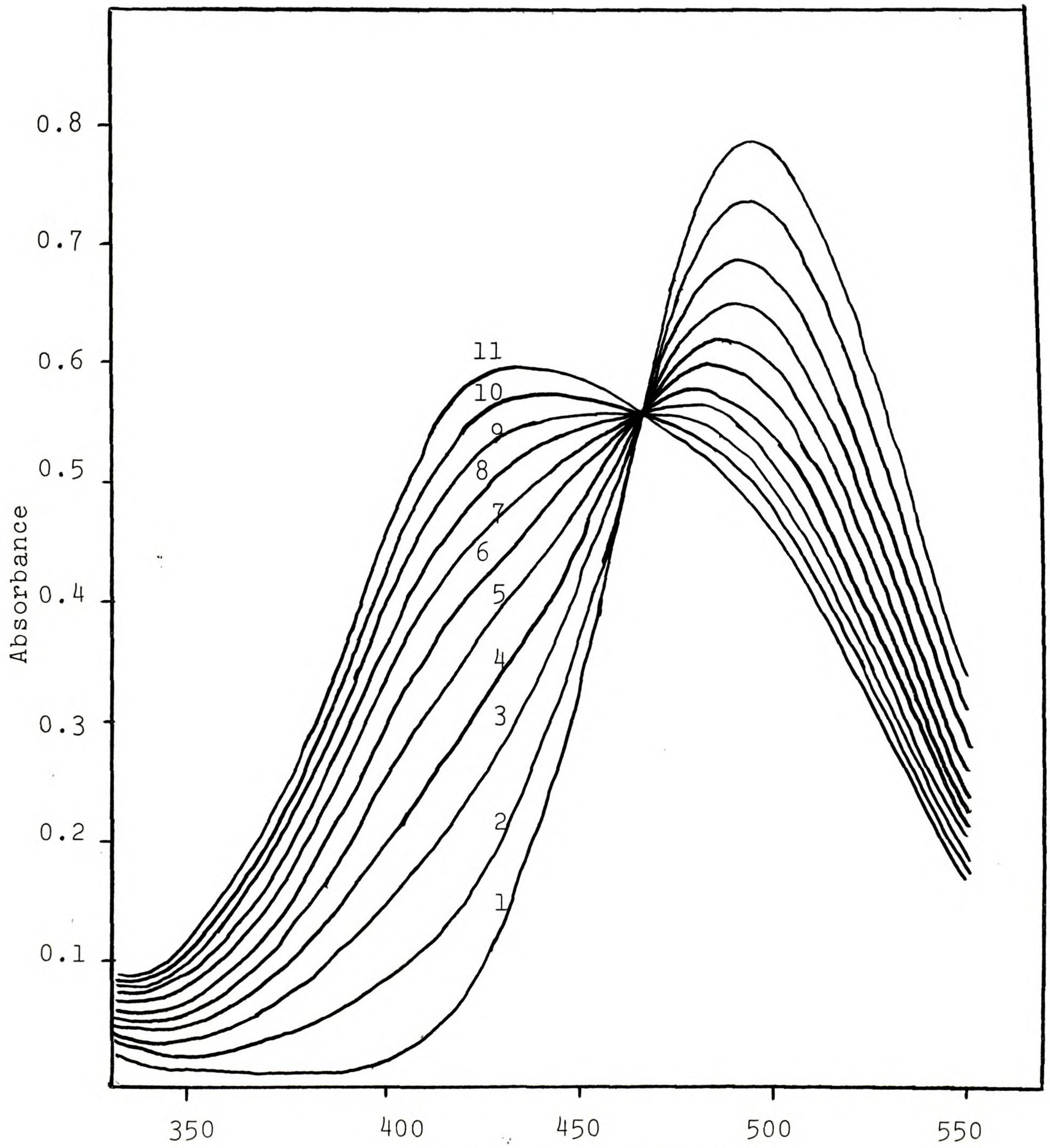

Figure 2.--Absorption spectra of tetramethylenetetrazole-iodine system in 1,2-dichloroethane solutions. $C_{I_2} = 8.89 \times 10^{-4}$ M C_{C_4MT}(M)

(1) 0.00 (2) 0.042 (3) 0.084 (4) 0.126 (5) 0.168 (6) 0.210 (7) 0.252 (8) 0.294 (9) 0.337 (10) 0.379 (1) 0.425.

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XVI. Potentiometric Studies

A. Instrumentation.--A Beckman model 76 expanded scale pH meter with a sensitivity of ±0.3 millivolts was employed in the potentiometric determination of the silver-cyclopolymethylenetetrazole complex dissociation constants. The 0-200 mv full scale was extended by recalibration of the scale against the output of a Biddle-Gray portable potentiometer.

B. Electrodes.--The indicating electrodes used in this study are listed below. A standard Beckman fiber junction calomel electrode was used as the reference electrode in all the potentiometric studies.

1. Corning NAS 11-18 Sodium Ion Electrode (Catalogue Number 476210): The Corning sodium ion electrode is a glass membrane electrode which exhibits high specificity to sodium and some selected univalent ions. The very high apparent selectivity toward silver ions allows this electrode to be used in making direct quantitative determinations of silver ions in solutions. The electrode response is given as follows.

$$E=E^{\circ} + \frac{2.303\ RT}{F} \log (a_{Na^+} + \alpha a_{M^+})$$

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where M^+ is any univalent cation. The values of α define the apparent selectivity referred to in the Corning Technical Information Bulletin EL - 14 and reproduced in Table VIII.

TABLE VIII--Approximate Ion Apparent Selectivity of the Corning NAS 11-18 Sodium Ion Electrode at pH 7.

Na^+/K^+	1000
Ag^+/Na^+	1500
Na^+/Li^+	250
Na^+/NH_4^+	3000

Thus, sodium has an apparent selectivity over potassium ions at pH 7 of 1000 or $\alpha = 0.001$ in the equation when M^+ is a potassium ion. Furthermore, since the apparent selectivity at pH 7 of Ag^+/K^+ is 1.5×10^6, 0.1 and 0.4 M solutions of potassium nitrate were used as the inert electrolyte to maintain a constant ionic strength.

It was important, therefore, to verify the high selectivity of the Corning NAS 11-18 sodium ion electrode to silver ions over potassium ions. In Figure 3, the potentials are given for mixtures of silver and potassium ions as one is varied relative to the other. It can be seen that even a thousand fold excess of potassium over silver ions has very little effect on the response of the electrode toward silver ions.

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2. Silver Electrode on Platinum Base.

a. Construction and cleaning of silver electrode: The electrode base was made of platinum wire 0.040 to 0.045 cm in diameter fused into glass tubes, leaving about 1 cm of wire outside the tube. The end of the platinum wire is fused into a small ball. The finished electrode was cleaned prior to electroplating by dipping the electrode for five minutes in boiling concentrated nitric acid.

b. The silver-plating solution: In the preparation of the electrode, the salt used for the silver-plating solution was potassium dicyanoargentate(I). The nearly pure salt $KAg(CN)_2$ was obtained as colorless crystals by the addition of an excess of silver cyanide (45 gm) to a boiling aqueous solution of potassium cyanide (20 grams of KCN dissolved in 90 ml of water) (105). After stirring the solution for about 30 minutes, the undissolved silver cyanide was filtered off, and the solution was cooled. The precipitated potassium dicyanoargentate(I) was purified further by a double recrystallization from water.

The silver-plating solution was 0.05 M potassium dicyanoargentate(I) (10 g/l). Because cyanide ions tend to be absorbed in the silver-plated electrode and influence the potential (106), the cyanide concentration was reduced to a minimum by adding enough 0.1 M silver nitrate

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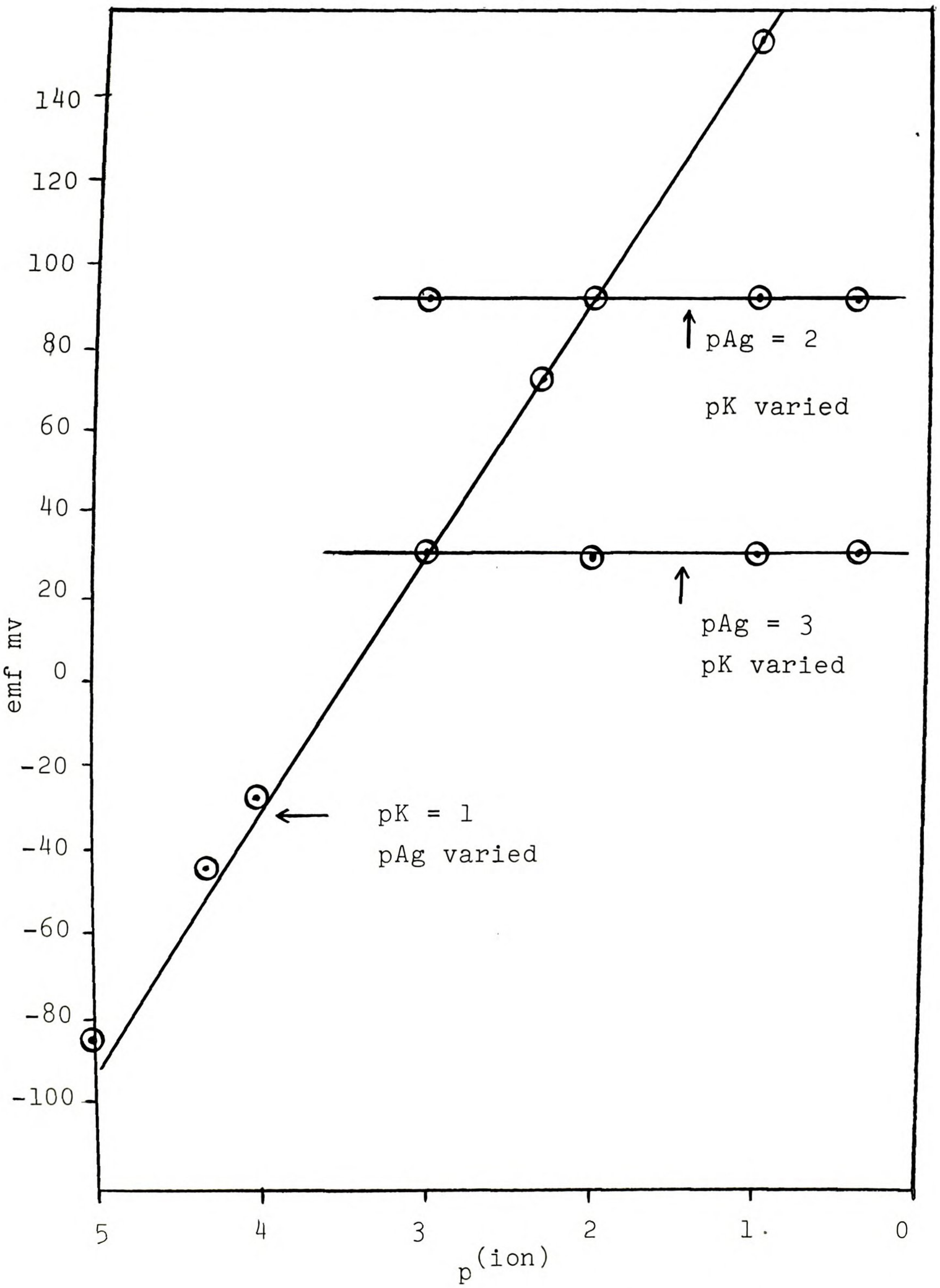

Figure 3.--Response of the corning NAS 11-18 sodium ion electrode to silver ions relative to potassium ions.

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solution to produce a faint cloud of silver cyanide. The precipitate was filtered off.

c. Electrolysis of the silver electrode: An H-type electrolysis cell (Figure 4a) in which the anode and cathode compartments are connected with a fine porosity glass frit was used to prevent contamination of the electroplating solution by the oxidation products in the anode reaction, principally precipitated silver cyanide and hydrocyanic acid. The platinum electrode to be silver plated was inserted into the cathode compartment through a hole drilled through a teflon stopper. A platinum anode was used since silver anodes polarized too readily (107).

The source of current was a Heath constant current module attached to a Heath operational amplifier system (model EUW 19B). The platinum wire was silver plated by electrolysis for approximately 15 hours at a total current of 0.2 milliampere. A layer of about 1.12×10^{-4} equivalent of silver was deposited on the platinum wire. After completion of the electrolysis, the electrode was washed in distilled water and then immersed in 6 M ammonium hydroxide for one hour to dissolve the outer layers of the silver plate and free as much of the absorbed cyanide ion as possible. Finally, the electrodes were washed for four hours in distilled water. The water was changed

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every twenty minutes during the process. The electrode was stored in distilled water in subdued light.

3. Beckman Silver Billet Electrode (Catalogue Number 39261): The Beckman silver billet electrode was employed to measure the free silver ion. This electrode has a large area of silver metal which provides more rapid electrode response, increases thermal stability, and minimizes polarization effects.

The electrode was prepared by cleaning the metallic surface with a mild detergent and scouring power. The surface was rinsed in distilled water and then immersed in a beaker of stirred, distilled water at 50° for two hours, and then it was again repeatedly rinsed in cool, distilled water. Prior to immersion of the electrode in the solution to be measured, it was washed in distilled water and dried with tissue paper. Finally, the electrode was stored in distilled water in subdued light.

C. The Cell Used in the Potentiometric Measurements.--All of the potentiometric measurements were carried out in the cell shown in Figure 4b. To alleviate the errors caused by the precipitation of silver as a result of the potassium chloride leaking out of the calomel reference electrode, the experimental silver solution was separated from the reference compartment by a bridge filled with 1 M potassium nitrate. Prior to each measurement, the cell was cleaned and

4a.--Silver Electroplating Cell

a. cathode compartment
b. anode compartment
c. fine porosity glass frit
d. platinum wire to be silver plated
e. platinum electrode
f. teflon stopper

4b.--Silver Potentiometric Cell

a. silver electrode half cell
b. reference electrode half cell
c. $\overline{\$}$ 14/20 joint
d. fine porosity glass frit
e. electrolyle chamber
f. calomel electrode
g. teflon stopcock
h. respective silver electrode
i. teflon stopper

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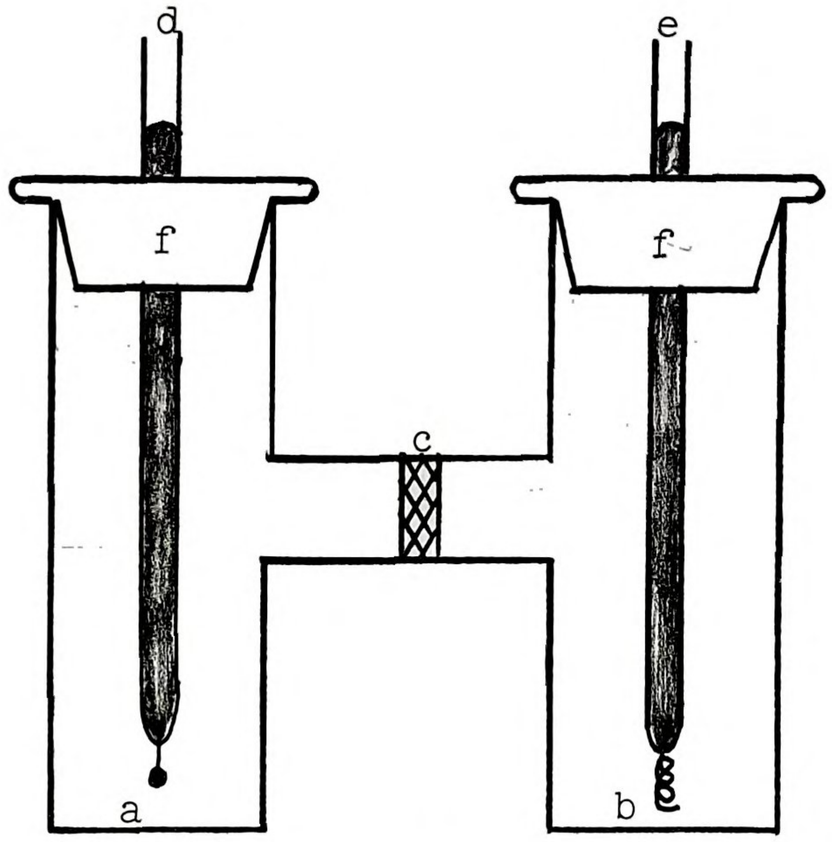
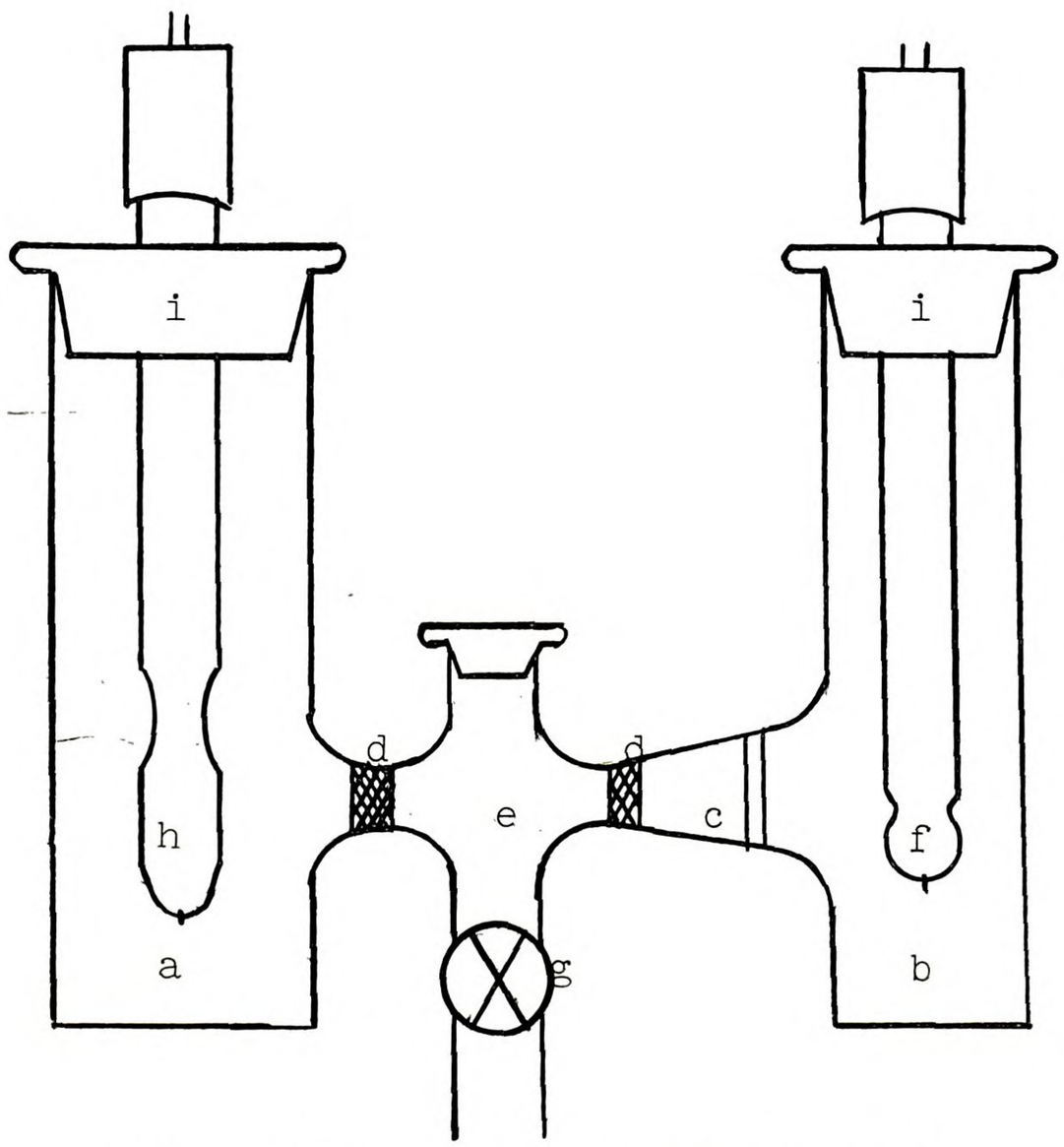


4a. Silver electroplating cell.



4b. Silver potentiometric cell.

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rinsed with distilled water. Then 50 ml of 12 M ammonium hydroxide followed by 200 ml of distilled water was passed through the frits of the electrolyte compartment. The cell was prepared for a potentiometric measurement by passing 25 ml of acetone through the frits followed by a dry air stream to eliminate the bulk of residual acetone and drying for two hours in an oven at 110°.

D. Potential Measurements.--To insure minimum contamination of the silver solution under investigation by the reference electrode solution, the following procedure was used. Fifty milliliters of each silver solution was measured into the silver electrode half cell; and its level was adjusted so that it was at least 1/2" higher than the level of the 1 M potassium nitrate in the reference electrode half cell. The equilibrium potential usually stabilized after ten minutes and if, after this period, three successive potential measurements taken at five minute intervals corresponded to within 0.5 mv, the mean value was recorded.

The liquid junction potential is included in the fixed "standard potential" of the reference electrode. It has been assumed that the liquid junction potential and the potential of the reference electrode remain constant throughout the measurements.

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A variation of ± 0.3 mv was found to be inherent in every potential reading listed. This caused an uncertainty in the pK_i values of ± 0.02 pK_i units.

E. Response of Respective Electrodes.--To measure the concentration of free silver ions, a calibration curve was obtained by varying the concentration of silver ions and measuring the potential of the respective silver indicating electrode versus the reference electrode.

Table IX lists the data used to form the working calibration curves of each of the respective electrodes for solutions of silver nitrate in 0.1 and 0.4 M potassium nitrate. In all cases the potentiometric measurements yielded a straight line plot of emf versus the silver ion concentration. The slope of the line was 0.059 ± .002 as predicted by the Nernst equation. The measurements were carried out over a pAg range of 2 to 5. Figures 5 and 6 depict the respective working calibration curves.

F. Calculations of the Instability Constants.--

The results of instability measurements on the 2:1 cyclopolymethylenetetrazole-silver(I) nitrate complexes have been calculated on the basis of the following equation.

$$Ag(C_nMT)_2^+ \rightleftharpoons Ag^+ + 2C_nMT$$

and the instability constant for the complex is given by

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TABLE IX--Silver Nitrate Working Calibration Curves for the Respective Silver Electrodes.

Molar Concentration of Silver Ion $x10^4$	Silver Electrode on Platinum Base mv	Beckman Silver Billet Electrode mv	Corning NAS 11-18 Sodium mv
a. 0.1 M Potassium Nitrate as the inert electrolyte			
100	441.3	433.0	+92.5
50	423.0	415.1	+72.0
10	385.0	374.3	+31.0
5	368.5	357.0	+ 7.5
1	325.5	314.0	-28.3
0.5	304.1	300.5	-44.0
0.1	---	---	-66.0
0.05	---	---	-86.0
b. 0.4 M Potassium Nitrate as the inert electrolyte			
100	431.2	433.0	+91.5
50	414.0	415.1	+71.2
10	377.1	372.2	+31.5
5	361.9	356.1	+ 8.5
1	317.8	318.5	-30.0
0.5	301.0	299.8	-43.3
0.1	---	---	-66.2
0.05	---	---	---

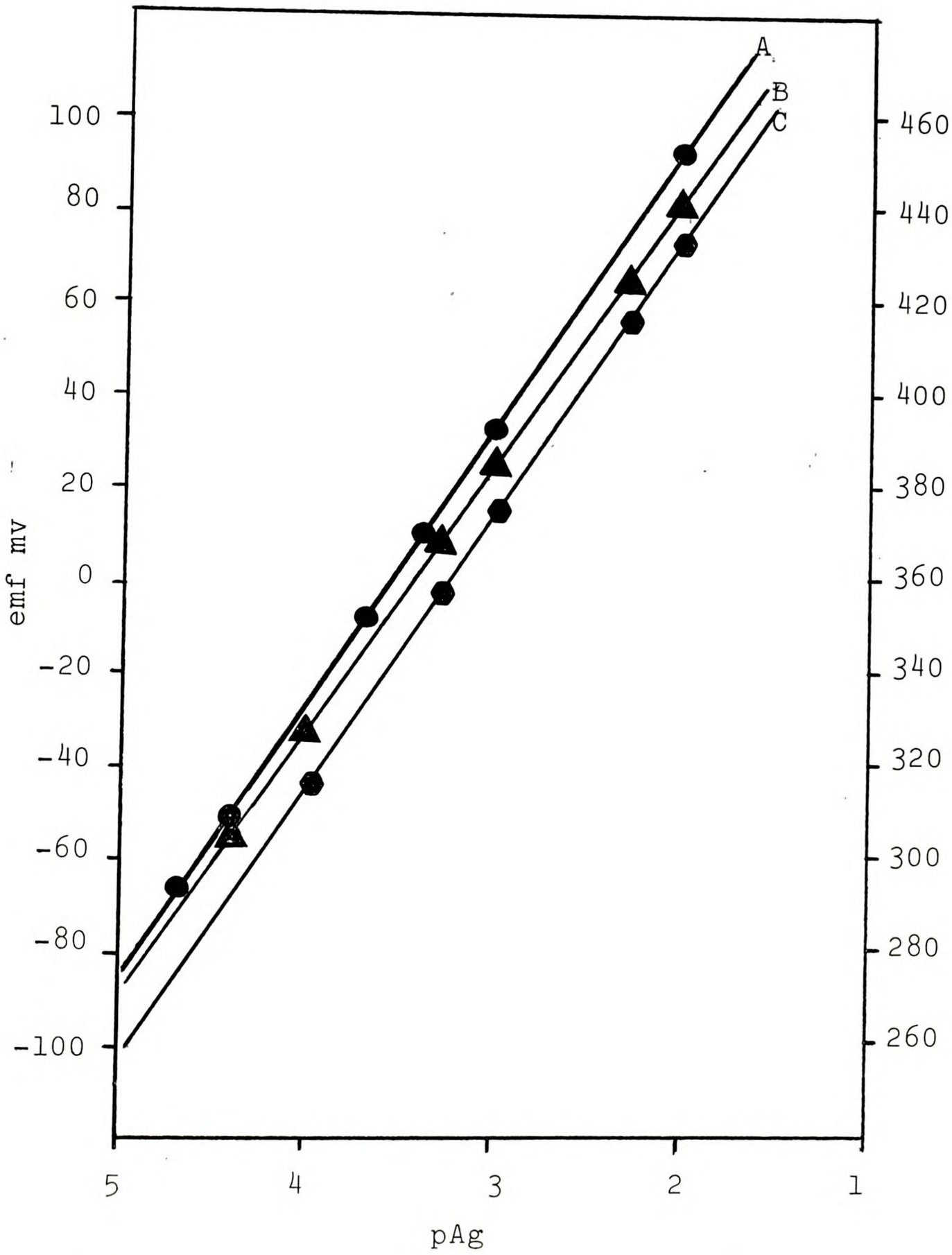

Figure 5.--Silver nitrate working calibration curves 0.1 M aqueous potassium nitrate solutions. (A) Corning NAS 11-18 sodium ion electrode (left scale); (B) Silver plated on platinum electrode (right scale); (C) Beckman silver billet electrode (right scale).

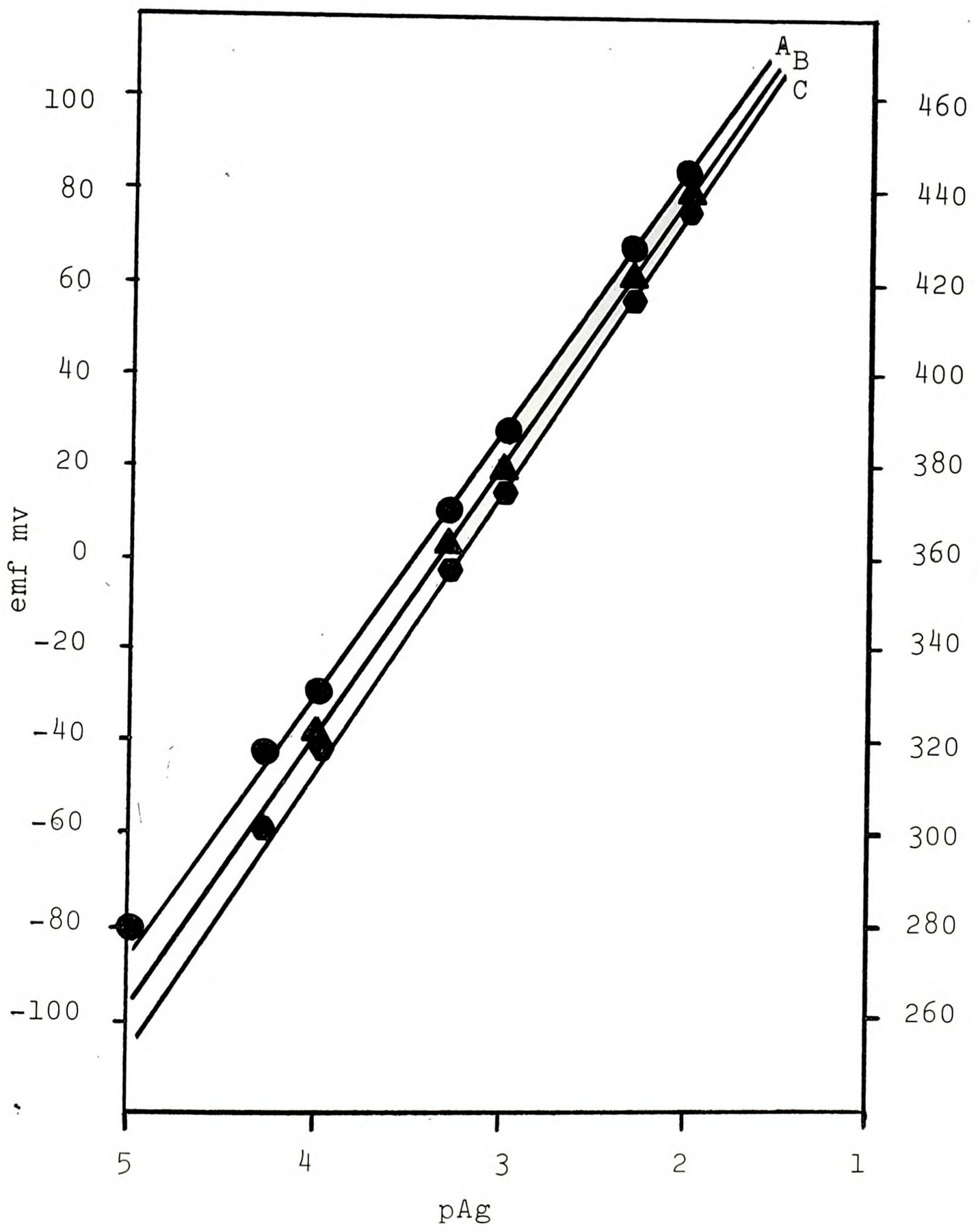

Figure 6.--Silver nitrate working calibration curves 0.4 M aqueous potassium nitrate. (A) Corning NAS 11-18 sodium ion electrode (left scale); (B) Silver plated on platinum electrode (right scale); (C) Beckman silver billet electrode (right scale).

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$$K_i = \frac{[Ag^+]\,[C_nMT]^2}{[Ag(C_nMT)_2^+]} \cdot \frac{f_{Ag^+}\, f^2_{C_nMT}}{f_{Ag(C_nMT)_2}}$$

where

$[Ag^+]$ = equilibrium concentration of free silver ion

$[C_nMT]$ = equilibrium concentration of free cyclopolymethylenetetrazole

$[Ag(C_nMT)_2^+]$ = equilibrium concentration of the respective cyclopolymethylenetetrazole-silver(I) complex

f_{Ag^+}, f_{C_nMT}, and $f_{Ag(C_nMT)_2^+}$ = the activity coefficients for the respective species

The instability constant equation is derived from consideration of the equilibrium in aqueous solutions and is simplified by the assumption that the activity coefficients of ions of the same charge are approximately the same at any given ionic strength while those of uncharged species equal unity.

From the mass balance relationships the following equations are obtained.

$$[C_{Ag^+}]_t = [Ag^+] + [Ag(C_nMT)^+] + [Ag(C_nMT)_2^+]$$

$$[C_{C_nMT}]_t = [C_nMT] + [Ag(C_nMT)^+] + 2[Ag(C_nMT)_2^+]$$

where

$[C_{Ag^+}]$ = the total analytical concentration of silver

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$[C_{C_nMT}]_t$ = the total analytical concentration of the respective cyclopolymethylenetetrazole

$[Ag(C_nMT)^+]$ = the 1:1 cyclopolymethylenetetrazole-silver(I) complex

If $[C_{C_nMT}]_t >> [C_{Ag^+}]_t$ then concentration of the 1:1 cyclopolymethylene-silver(I) complex in solution is assumed to be small and may be neglected. Therefore, the instability constant expression becomes

$$K_i = \frac{[Ag^+]\left([C_{C_nMT}]_t - 2[C_{Ag^+}]_t - 2[Ag^+]\right)^2}{[C_{Ag^+}]_t - [Ag^+]}$$

The overall formation constants of the reaction $Ag^+ + 2\ C_nMT \rightleftharpoons Ag(C_nMT)_2^+$ was then calculated by taking the reciprocal of the instability constant.

The data used to calculated the respective instability constants of the various cyclopolymethylenetetrazoles are listed in Tables X and XI.

XVII. Preparation and Characterization of Transition Metal Complexes with 1,3-bis(5-tetrazolyl)-n-propane and 1,4-bis(5-tetrazolyl)-n-butane

A. Purification of the bitetrazoles.--The author is indebted to Mr. T. C. Wehman of this laboratory for samples of 1,3-bis(5-tetrazolyl)-n-propane and 1,4-bis(5-tetrazolyl)-n-butane (hereafter abbreviated PBT and BBT respectively). The bitetrazoles (hereafter abbreviated

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TABLE X.--Experimental Data from the Potentiometric Studies in 0.1 M Potassium Nitrate Solutions at 25°.

Electrode*	$[C_{Ag^+}]_t$ $X10^4$	$[C_{C_nMT}]_t$ $X10^2$	emf mv	$[Ag^+]$ $X10^4$	K_i $X10^4$	K_f $X10^{-3}$	pK_f
			Trimethylenetetrazole				
Na	100.2	8.71	48.2	18.3	7.48	1.34	-3.13
Na	75.1	9.10	38.0	10.5	8.87	1.13	-3.05
AgB	100.2	8.71	391.0	19.7	9.75	1.03	-3.01
AgB	75.1	9.10	377.5	11.2	9.53	1.05	-3.02
AgP	100.2	8.71	401.5	19.9	9.86	1.01	-3.00
AgP	75.1	9.10	388.3	11.8	10.01	0.990	-2.99
			Tetramethylenetetrazole				
Na	109.4	11.06	31.1	9.9	7.49	1.34	-3.13
Na	60.5	6.50	44.7	14.4	7.81	1.28	-3.11
AgB	109.4	11.06	374.0	10.2	7.73	1.29	-3.11
AgB	60.5	6.50	384.5	16.1	8.95	1.12	-3.05
AgP	109.4	11.06	386.7	10.9	8.29	1.21	-3.08
AgP	60.5	6.50	385.4	16.4	9.16	1.09	-3.04
			Pentamethylenetetrazole				
Na	103.0	11.58	28.0	9.5	8.84	1.13	-3.05
Na	82.5	10.15	30.0	8.2	7.67	1.30	-3.11
AgB	103.0	11.58	375.0	10.4	9.74	1.03	-3.01
AgB	82.5	10.15	371.0	8.7	8.17	1.22	-3.08
AgP	103.0	11.58	385.3	10.3	9.64	1.04	-3.02
AgP	82.5	10.15	380.5	8.5	7.97	1.26	-3.10
			Hexamethylenetetrazole				
Na	105.0	6.72	69.2	38.1	8.48	1.18	-3.07
Na	121.7	12.05	33.0	10.3	8.19	1.22	-3.09
AgB	105.0	6.72	409.2	39.1	8.74	1.14	-3.06
AgB	121.7	12.05	377.5	11.2	8.94	1.12	-3.05
AgP	105.0	6.72	418.0	39.5	8.85	1.13	-3.05
AgP	121.7	12.05	387.5	11.6	9.28	1.08	-3.03
			Heptamethylenetetrazole				
Na	48.1	3.15	69.1	38.0	7.69	1.30	-3.11
Na	30.4	3.31	47.0	17.4	7.45	1.34	-3.13
AgB	48.1	3.15	409.3	39.3	8.80	1.14	-3.06
AgB	30.4	3.31	388.5	17.7	7.72	1.30	-3.11
AgP	48.1	3.15	417.8	39.4	8.90	1.12	-3.05
AgP	30.4	3.31	398.0	17.5	7.54	1.33	-3.12

* Na = Corning NAS 11-18 sodium ion electrode.
AgB = Beckman Silver Billet electrode.
AgP = Silver plated on platinum base electrode.

TABLE XI.--Experimental Data from the Potentiometric Studies in 0.4 M Potassium Nitrate Solutions at 25°.

Electrode*	$[C_{Ag^+}]_t$ X10^4	$[C_{C_nMT}]_t$ X10^2	emf mv	$[Ag^+]$ X10^4	K_i X10^4	K_f X10^{-3}	pK_f
			Trimethylenetetrazole				
Na	104.3	8.60	44.5	21.0	9.36	1.07	-3.03
Na	70.0	7.44	33.0	13.1	7.68	1.30	-3.11
Na	82.4	10.11	24.0	9.2	8.41	1.19	-3.08
AgB	104.3	8.60	395.0	23.5	10.64	0.940	-2.97
AgB	70.0	7.44	384.0	15.2	9.13	1.11	-3.05
AgB	82.4	10.11	375.5	11.0	10.05	0.995	-3.00
AgP	104.3	8.60	400.5	25.0	11.40	0.877	-2.94
AgP	70.0	7.44	389.8	16.1	9.77	1.02	-3.01
AgP	82.4	10.11	382.2	12.1	11.63	0.860	-2.93
			Tetramethylenetetrazole				
Na	114.2	8.86	43.5	20.0	8.07	1.24	-3.09
Na	56.4	5.76	39.6	17.1	8.01	1.25	-3.10
Na	27.4	5.85	15.0	6.3	8.12	1.23	-3.09
AgB	114.2	8.86	394.5	23.0	9.44	1.06	-3.03
AgB	56.4	5.76	388.0	18.0	8.56	1.17	-3.07
AgB	27.4	5.85	363.8	7.1	9.31	1.07	-3.03
AgP	114.2	8.86	399.1	23.6	9.71	1.03	-3.01
AgP	56.4	5.76	393.4	18.7	8.99	1.11	-3.05
AgP	27.4	5.85	370.0	7.5	10.00	1.00	-3.00
			Pentamethylenetetrazole				
Na	120.6	12.19	27.2	10.4	8.64	1.16	-3.07
Na	81.3	9.07	25.8	9.7	7.11	1.41	-3.15
Na	20.5	5.40	10.7	5.3	8.32	1.20	-3.08
AgB	120.6	12.19	378.0	12.2	10.23	0.978	-2.99
AgB	81.3	9.07	376.2	11.3	8.41	1.19	-3.08
AgB	20.5	5.40	368.0	6.8	11.70	0.855	-2.93
AgP	120.6	12.19	384.0	13.0	10.95	0.913	-2.96
AgP	81.3	9.07	380.0	10.9	8.08	1.24	-3.09
AgP	20.5	5.40	367.5	6.7	11.45	0.873	-2.94
			Hexamethylenetetrazole				
Na	119.5	6.98	66.0	50.0	9.27	1.08	-3.03
Na	51.7	3.98	54.0	31.1	8.10	1.23	-3.09
Na	68.4	6.58	41.4	18.4	8.63	1.16	-3.07
AgB	119.5	6.98	417.0	55.6	10.52	0.951	-2.98
AgB	51.7	3.98	407.1	37.1	12.31	0.812	-2.91
AgB	68.4	6.58	393.5	22.0	10.85	0.922	-2.97
AgP	119.5	6.98	420.2	54.5	10.30	0.971	-2.99
AgP	51.7	3.98	409.1	35.3	10.81	0.925	-2.97
AgP	68.4	6.58	396.8	21.5	10.48	0.954	-2.98
			Heptamethylenetetrazole				
Na	64.1	3.66	60.0	39.2	4.00	2.50	-3.40
Na	60.2	3.54	57.0	35.0	3.72	2.69	-3.43
Na	41.7	3.28	43.8	20.3	4.47	2.24	-3.35
AgB	64.1	3.66	412.0	45.3	5.22	1.92	-3.28
AgB	60.2	3.54	409.1	40.2	4.72	2.12	-3.33
AgB	41.7	3.28	395.3	23.7	5.12	1.95	-3.29
AgP	64.1	3.66	414.3	43.1	4.72	2.12	-3.33
AgP	60.2	3.54	419.2	38.4	4.33	2.31	-3.36
AgP	41.7	3.28	397.6	22.1	4.53	2.21	-3.34

* Na = Corning NAS 11-18 sodium ion electrode.
AgB = Beckman Silver Billet electrode.
AgP = Silver plated on platinum base electrode.

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Bitz) were purified by recrystallization from boiling absolute alcohol. The infrared spectra of these tetrazoles appear in Appendix I as Figures 52 and 53 respectively.

B. Potentiometric Results.--1,3-bis(5-tetrazolyl)-n-propane and 1,4-bis(5-tetrazolyl)-n-butane were titrated in methanol with a standard glass electrode and sleeve calomel electrode as the reference. The titrant was tetrabutylammonium hydroxide in methanol, standardized with purified benzoic acid.

Since only one equivalence point is noted in the potentiometric titration curves of the respective bitetrazoles (Figure 7), it is apparent that acidity constants of the two protons on the bitetrazole molecule are within 2 pK units of each other. The calculated equivalent weights of 1,3-bis(5-tetrazolyl)-n-propane and 1,4-bis(5-tetrazolyl)-n-butane are 91 and 97 respectively. The theoretical equivalent weights for the respective propane and butane bitetrazoles are 90 and 99.

Although the overall dissociation constants of these bitetrazoles have not been determined, it appears that they should be of the same order of magnitude as the acidic proton of tetrazole, i.e., $K_a = 1.3 \times 10^{-5}$ (108).

C. Preparation of the Respective Transition Metal Complexes.--The complexes were prepared by the following procedures. The respective bitetrazole (0.02 mole) was

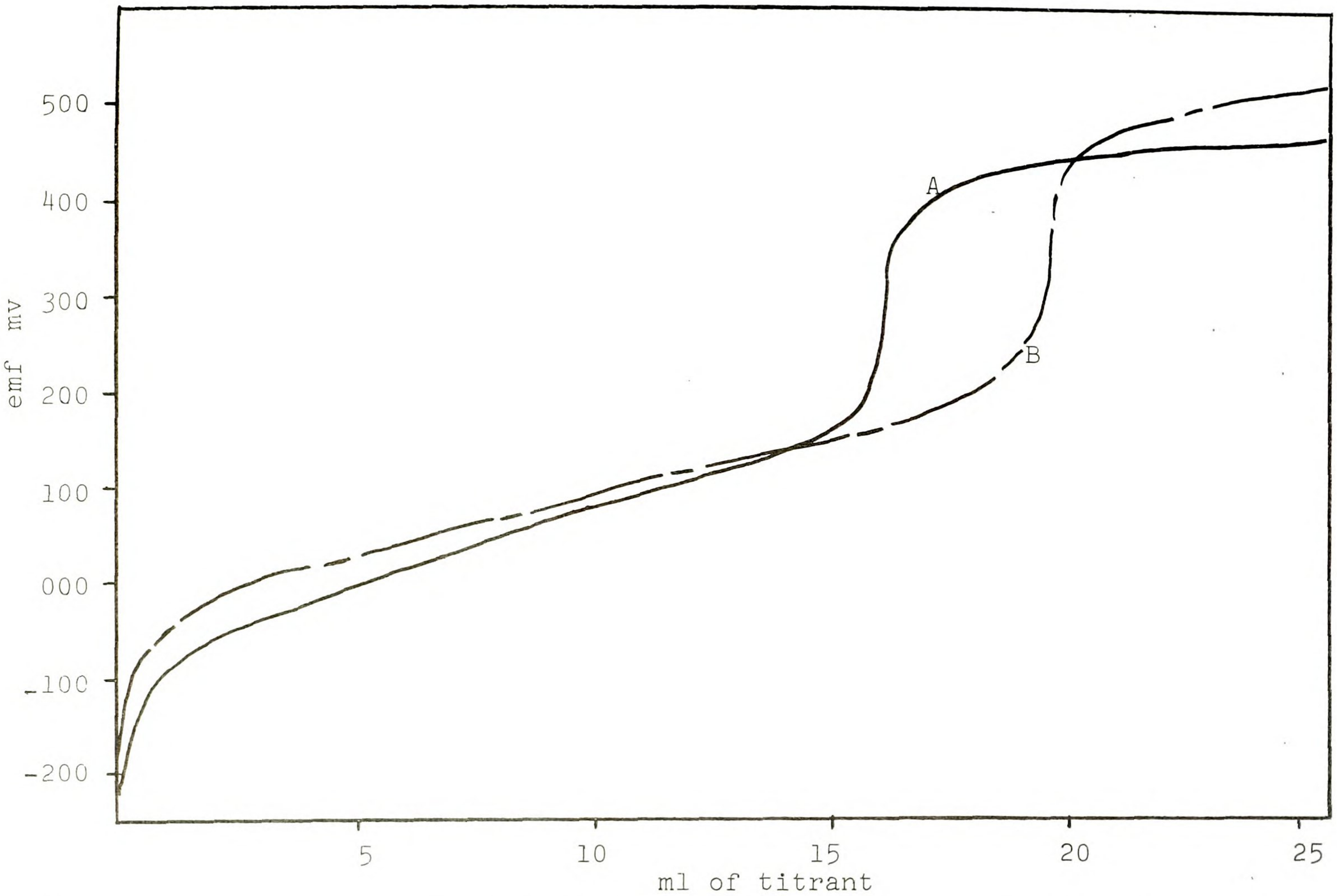

Figure 7.--The potentiometric titration curves of A, 1,3-bis(5-tetrazolyl)-n-propane and B,1,4-bis(5-tetrazolyl)-n-butane with tetrabutylammonium hychoxide in methanol.

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dissolved in 50 ml of absolute ethanol to which was added dropwise an absolute ethanol solution of the hydrated transition metal perchlorate (0.01 mole). The respective transition metal complex of either 1,3-bis(5-tetrazolyl)-n-propane or 1,4-bis(5-tetrazolyl)-n-butane immediately precipitated out of solution. The complexes were then filtered, extracted with ethanol for approximately 12 hours in a Soxhlet extractor in order to remove any unreacted bitetrazole and dried at 110°.

The cobalt(II), nickel(II), copper(II), and zinc(II) complexes of propane and butane bitetrazole were prepared. They are all nonhydroscopic microcrystalline, shock sensitive powders which have decomposition temperatures in excess of 250° and are insoluble in polar and nonpolar solvents.

The results of the elemental analyses performed on these complexes are listed in Table XII and indicate that the most probable composition is M^{II}(Bitz). The results of the analyses are rather poor, indicating a moderate degree of contamination.

D. Magnetic Susceptibilities.--The magnetic moments of the complexes were determined by the Gouy method previously described (13) and are listed in Table XIII. The magnetic moments obtained were much lower than the expected values which again indicates the impurity of the complexes.

TABLE XII--Elemental Analyses of Some Transition Metal Complexes with 1,3-Bis(5-tetrazolyl)-n-propane and 1,4-Bis(5-tetrazolyl)-n-butane.

Most Probable Composition	mol wt	Calculated					Found		
		%M	%C	%H	%N	%M	%C	%H	%N
1,3-bis(5-tetrazolyl)-n-propane	180.16	---	33.33	4.48	62.20	---	33.31	4.50	62.21
Co(PBT)	237.08	24.86	25.33	2.55	47.27	18.39	28.20	3.90	35.29
Ni(PBT)	236.86	24.79	25.36	2.55	47.31	19.53	26.47	3.11	44.10
Cu(PBT)	241.68	26.29	24.85	2.50	46.36	23.10	23.44	2.87	39.65
1,4-bis(5-tetrazolyl)-n-butane	194.19	---	37.11	5.19	56.60	---	37.10	5.25	57.90
Co(BBT)	251.11	23.47	28.70	3.21	44.62	16.90	25.74	3.66	36.74
Ni(BBT)	250.89	23.40	28.72	3.21	44.66	15.02	25.25	3.37	36.62
Cu(BBT)	255.72	24.85	28.18	3.15	43.82	21.10	28.38	3.54	40.00
						---	22.27	3.43	32.38

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| Most
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|---|
| Co(PBT) |
| Ni(PBT) |
| Cu(PBT) |
| Zn(PBT) |
| Co(BBT) |
| Ni(BBT) |
| Cu(BBT) |
| Zn(BBT) |

TABLE XIII-Calculated Magnetic Moments and Unpaired Spins of some Transition Metal Complexes with 1,3-Bis(5-Tetrazolyl)-n-propane and 1,4-Bis(5-tetrazolyl)-n-butane..

Most Probable Composition	X_M Exp $X10^3$	X_M Corr. $X10^3$	n obs.	μ_{eff} BM
Co(PBT)	5.36584	5.46479	2.77	3.64
Ni(PBT)	1.60913	1.71015	1.27	2.03
Cu(PBT)	0.96518	1.06334	0.89	1.62
Zn(PBT)	0.08945	0.00939	0.01	0.15
Co(BBT)	5.45371	5.57384	2.81	3.68
Ni(BBT)	1.53605	1.64940	1.23	2.01
Cu(BBT)	0.45781	0.57036	0.54	1.18
Zn(BBT)	0.09399	0.01935	0.03	0.20

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E. X-Ray Powder Pattern.--The samples were first ground to the consistency of fine powder and then packed into 0.5 mm thin-walled glass capillary tubes. The attempt to compare the crystal character of the above complexes was unsuccessful because the respective complex crystal size was too small to permit satisfactory powder diffraction diagrams to be obtained. This same condition was noted for other types of tetrazole complexes (109, 110). Grinding these complexes is not recommended because of their shock sensitive nature.

F. Spectral Measurements.

1. Infrared Spectra: The spectra in the 5000-680 cm^{-1} region were obtained with the samples dispersed in Nujol. The infrared spectra of the transition metal complexes of the type M^{II}(PBT) were essentially identical as were the spectra of the M^{II}(BBT) type complexes. A representative spectrum of each type of complex appears in Appendix I as Figures 54 and 55. The strong perchlorate band at ~1100 cm^{-1} was absent in all of the spectra indicating that the complexes do not contain the perchlorate group as the counter ion. However, one obtains a positive test for the perchlorate ion when tetraphenylarsonium chloride is used, indicating the presence of some occluded perchlorate ion.

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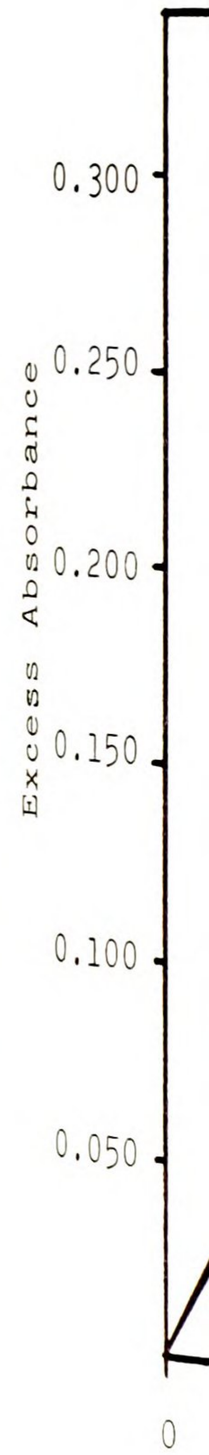
2. Visible and Near Infrared Spectra of the Copper-Bitetrazole Complexes in Ethanol.

a. Method of continuous variation: The bitetrazole complexes were investigated with the method of continuous variation (III) in which the total analytical concentration of Copper(II) perchlorate hexahydrate and the respective bitetrazole was 2.0×10^{-3} in purified ethanol (Figure 8). Maxima were obtained at a ligand mole fraction of 0.5, which clearly shows that the stoichiometry of the copper(II) complexes of 1,3-bis(5-tetrazolyl)-n-propane and 1,4-bis(5-tetrazolyl)-n-butane is given by Cu(Bitz). The measurements were carried out at four different wavelengths, and a small shift of the maxima in the plot of absorbance vs. mole fraction of ligand was noted. This shift may be due to the formation of a colloidal precipitate of the respective complex.

b. Mole-ratio study: A mole-ratio study of the 1,3-bis(5-tetrazolyl)-n-propane and 1,4-bis(5-tetrazolyl)-n-butane with copper(II) perchlorate hexahydrate in purified ethanol is shown in Figure 9. These data confirm the results obtained with the continuous variations study. The formation constants of the complexes were calculated from spectrophotometric data (112) and the values varied from 6.63 to 14.90×10^{4} depending on the wavelength at which the measurements were obtained. The relatively large variation in the results is probably due to



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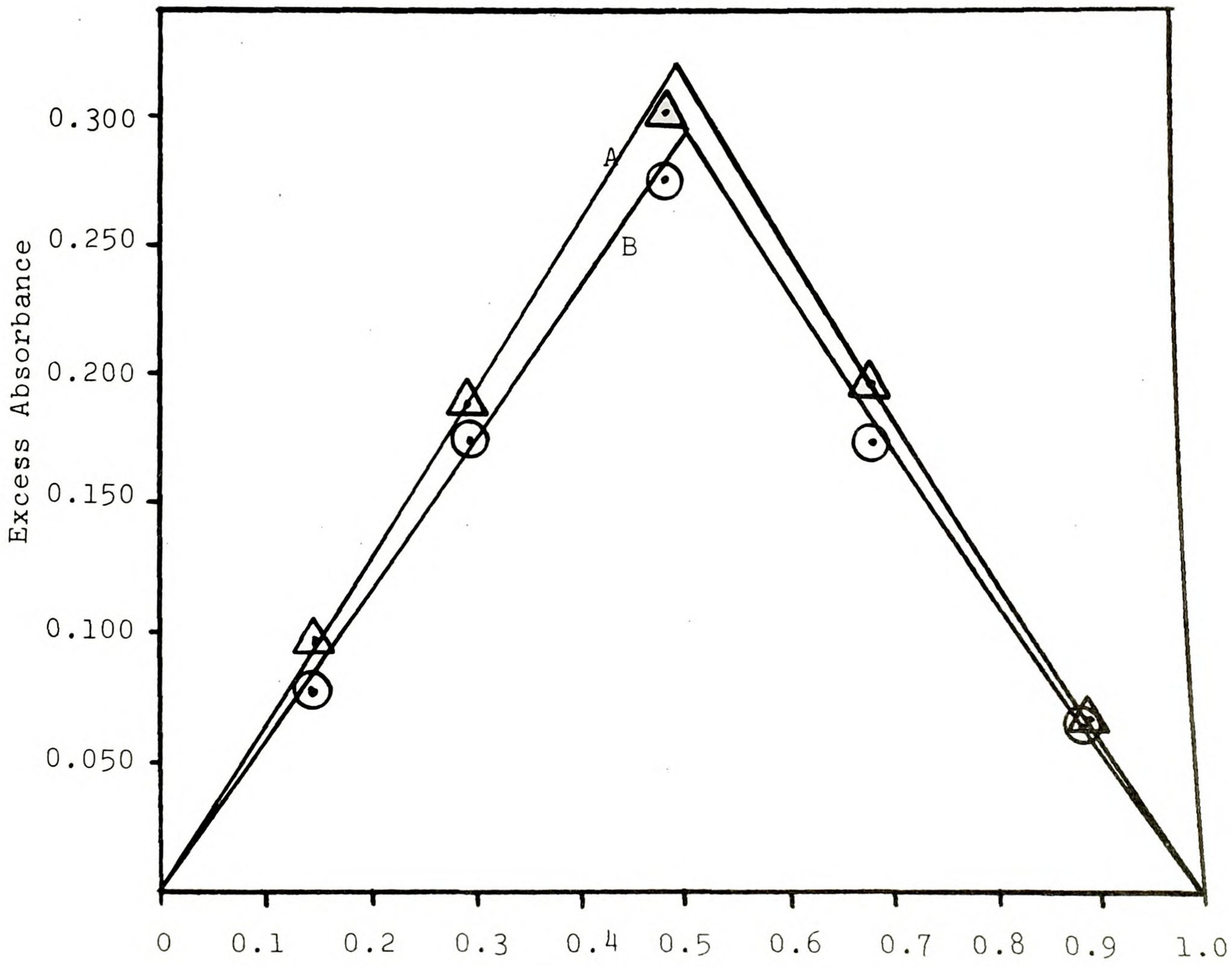

Figure 8.--A continuous variations study at 680 mμ of copper (II) perchlorate hexahydrate with A,1,3-bis(5-tetrazolyl)-n-propane and B,1,4-bis(5-tetrazolyl)-n-butane in purified ethanol. The total analytical concentration of copper (II) ion and ligand is 2.0×10^{-3} M.

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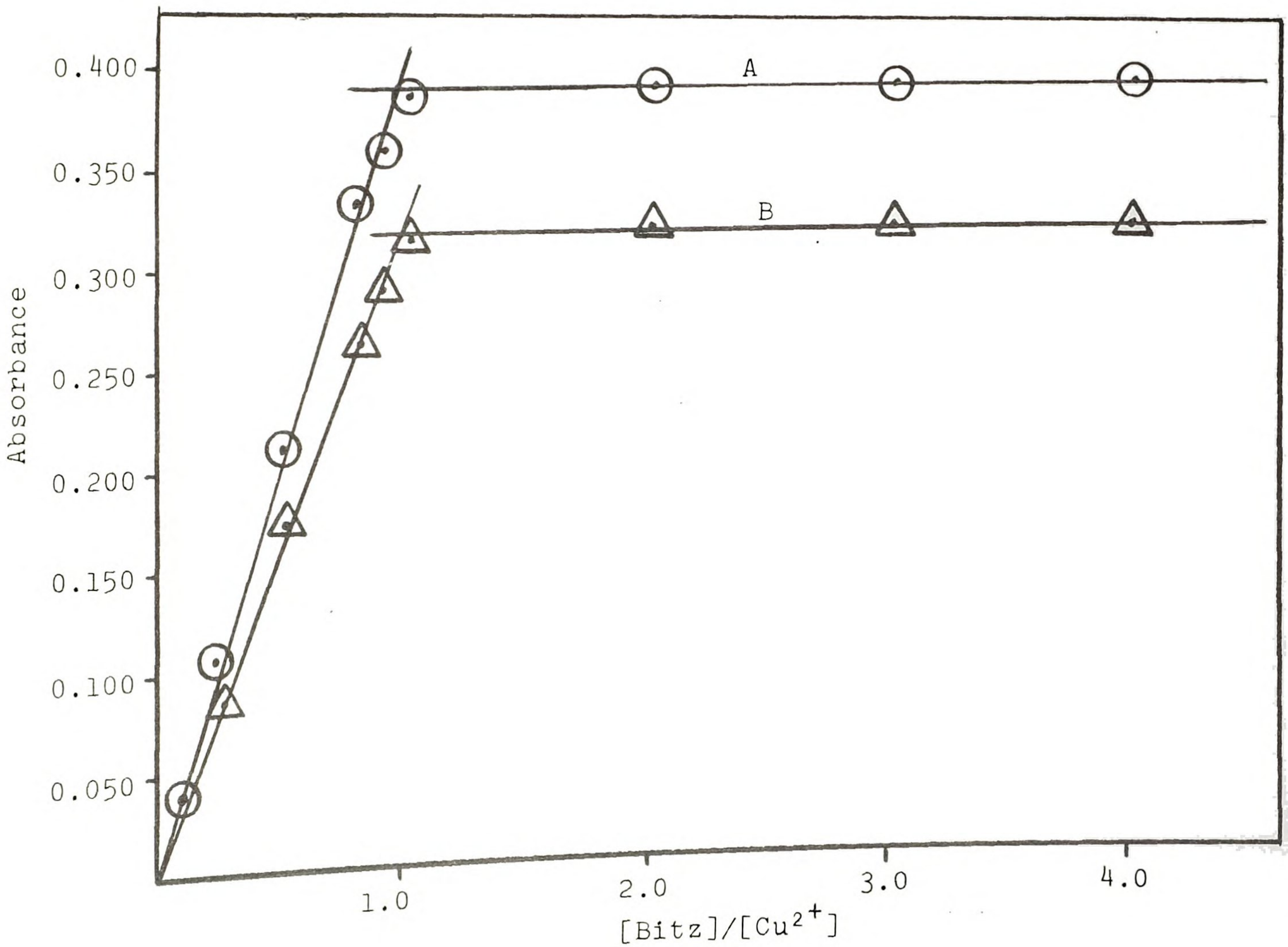

Figure 9.--Molar ratio study of 1 x 10^{-3} M copper (II) perchlorate hexahydrate with A,1,4-bis(5-tetrazolyl)-n-butane and B,1,3-bis(5-tetrazolyl)-n-propane in purified ethanol at 670 mμ.

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a colloidal precipitate observed in the solution by the Tyndall effect. Complex concentrations as low as 4×10^{-4} M were tried in various solvents such as methanol, ethanol, n-butanol and nitromethane; however, a colloidal precipitate of the complex always formed.

G. Reflectance Spectra.--The electronic spectra of the transition metal bitetrazole complexes (Figures 10 and 11) were recorded on a Beckman model DK-2, spectrophotometer equipped with a diffuse reflectance attachment. The absorbance values are given in Table XIV.

TABLE XIV.—Electronic Absorption Spectra (cm^{-1}) of the Transition Metal Complexes of 1,3-Bis(5-tetrazolyl)-n-propane and 1,4-Bis(5-tetrazolyl)-n-butane.

Complex	ν_{max}
Ni(BBT)	10,000, 18,200, 28,100
Ni(PBT)	10,200, 18,200, 28,600
Co(BBT)	9,530, 21,100
Co(PBT)	9,530, 20,800
Cu(BBT)	13,500
Cu(PBT)	14,700

The reflectance spectra are essentially those expected for the respective transition metal ions in octahedral configurations, and the absorption maxima appear

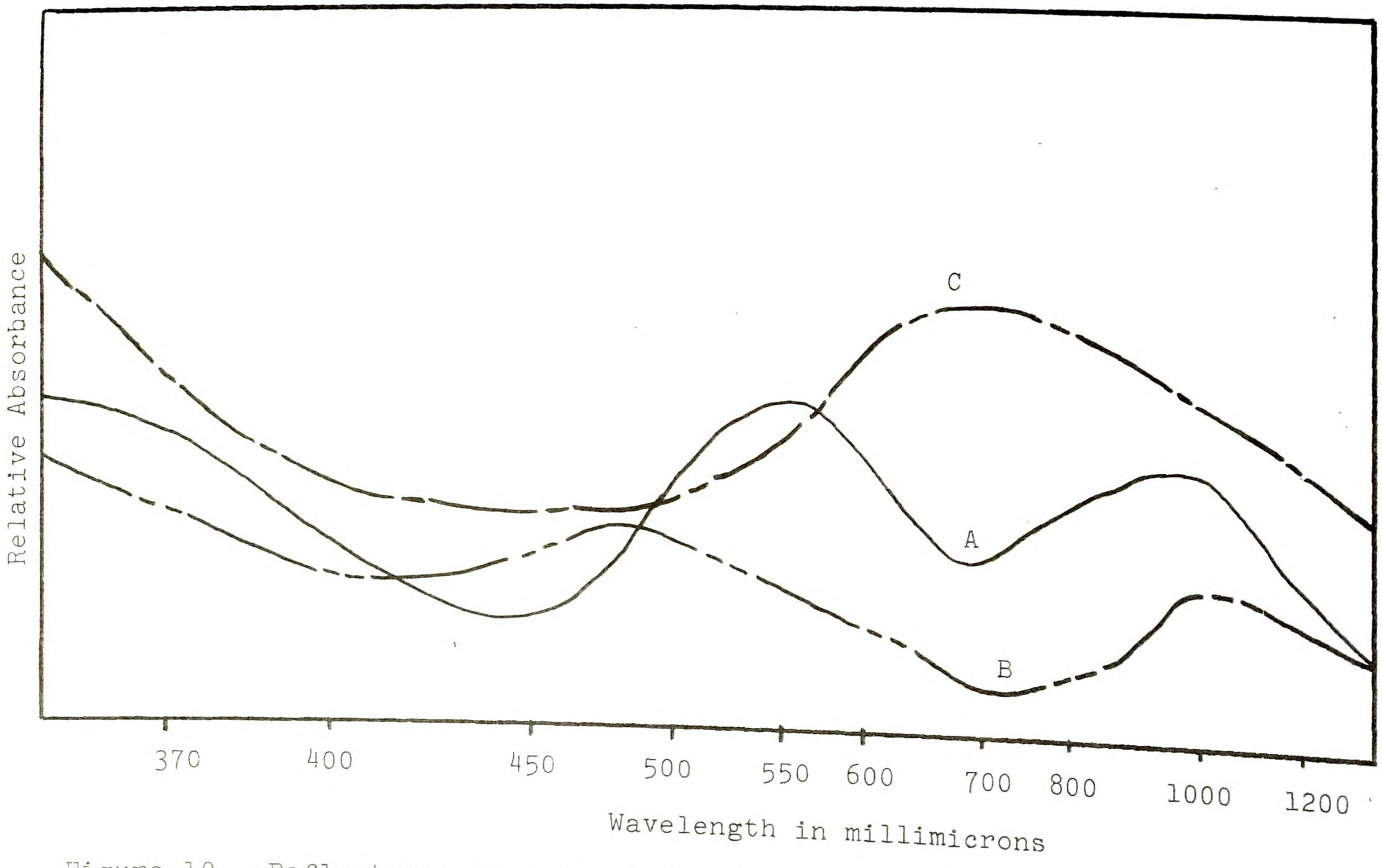

Figure 10.--Reflectance spectra of the respective (A) nickel (II), (B)cobalt (II), and (C)copper (II) perchlorate complexes with 1,3-bis(5-tetrazolyl)-n-propane.

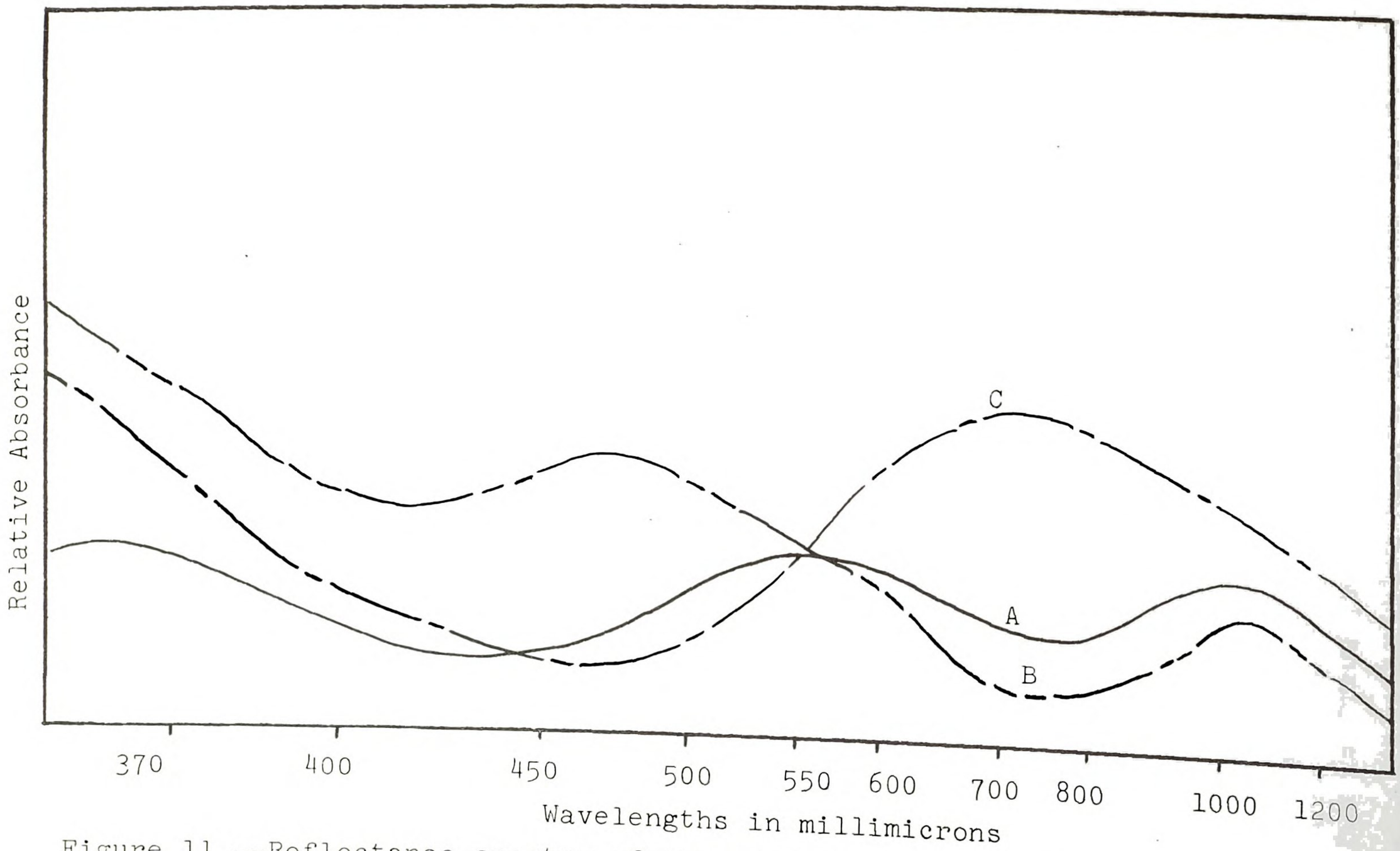

Figure 11.--Reflectance spectra of the respective (A) nickel (II), (B) cobalt (II), and (C) copper (II) perchlorate complexes with 1,4-bis(5-tetrazolyl)-n-butane.

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to be independent of the ligand. These results are in conflict with the proposed elemental analyses and the spectrophotometric study which indicates a one to one salt-like complex. Therefore, it is difficult to visualize the central transition metal ion in an octahedral environment. Because of the obviously non-stoichiometric and explosive nature of these complexes, this work was discontinued.

XVIII. Preparation of Bis(trimethylenetetrazole)silver(I) and Bis(tetramethylenetetrazole)silver(I) Nitrate

A. Bis(trimethylenetetrazole)silver(I) Nitrate.-- A solution containing 8.50 grams (0.05 mole) of silver(I) nitrate in 100 ml of water was added to a solution containing 12 grams of trimethylenetetrazole (0.11 mole) in 100 ml of water. The solution was concentrated to a very viscous liquid by air evaporation in a hood over a period of two weeks. Crystals were very difficult to obtain, and the covered syrup residue was allowed to remain in the hood. After approximately thirty days crystals appeared in the syrup. They were allowed to grow for an additional two weeks until they were approximately 3 mm x 15 mm. The larger single crystals were then removed from the syrup residue and quickly washed with cold water to remove the remaining syrup residue. The crystals were then dried with tissue paper. The melting point of the complex was

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58-60°. All efforts to purify the complex by recrystallization with seeding from various solvents were unsuccessful because syrup resulted when the solvent was removed. The infrared spectrum appears in Appendix I as Figure 56.

<u>Anal</u>. Calcd for $Ag(C_3MT)_2NO_3$: C, 24.63%; H, 3.10%; N, 32.31%.

Found: C, 23.80%; H, 2.90%; N, 31.60%.

B. <u>Bis(tetramethylenetetrazole)silver(I) Nitrate</u>.--This complex was prepared from 13 grams of tetramethylenetetrazole (0.105 mole) in the manner previously described for bis(trimethylenetetrazole)silver(I) nitrate. The same procedure was followed to obtain and purify the complex which has a melting point of 108°. The infrared spectrum of this complex appears in Appendix I as Figure 57.

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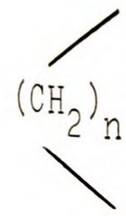

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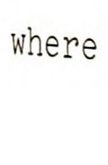
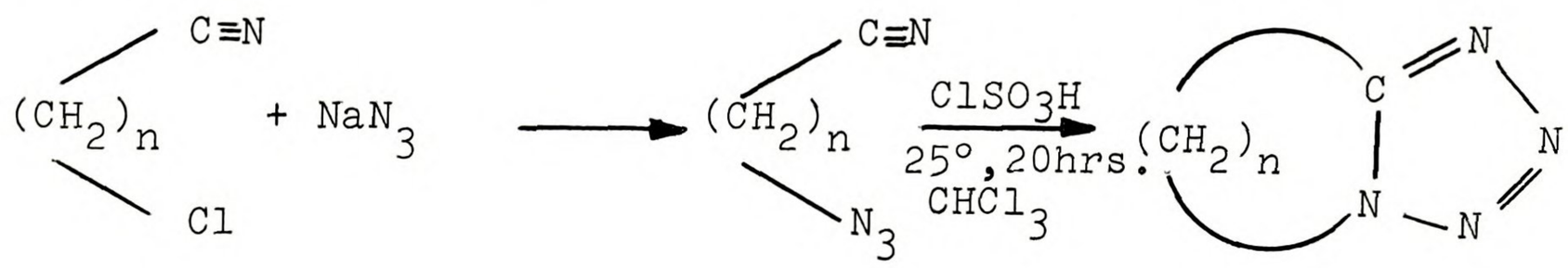


RESULTS AND DISCUSSION

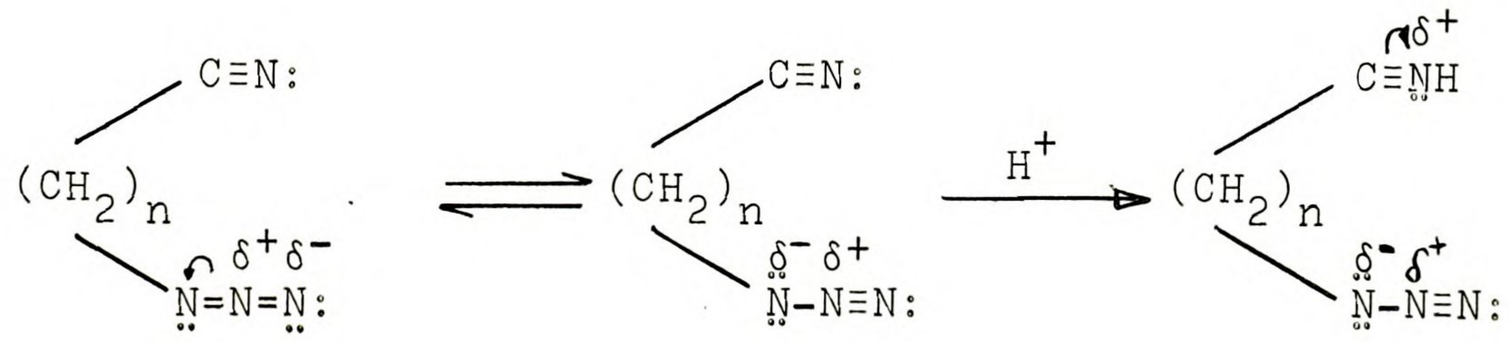
I. The Mechanism of the Intramolecular Rearrangement of ω-Azidoalkanenitriles in the Preparation of Tri- and Tetramethylenetetrazole

Von Kereszty's work describes the acid-catalyzed cyclization of 4-azidobutyronitrile and 5-azidovaleronitrile to form the respective bicyclictetrazoles (29). The synthesis takes place according to the following equation.



where n = 3, 4

The following mechanism involving acid-catalyzed intramolecular condensation is proposed. In the highly acidic chlorosulfonic acid-chloroform mixture, the nitrile nitrogen is protonated (I) causing a polarization of the nitrile triple bond and the



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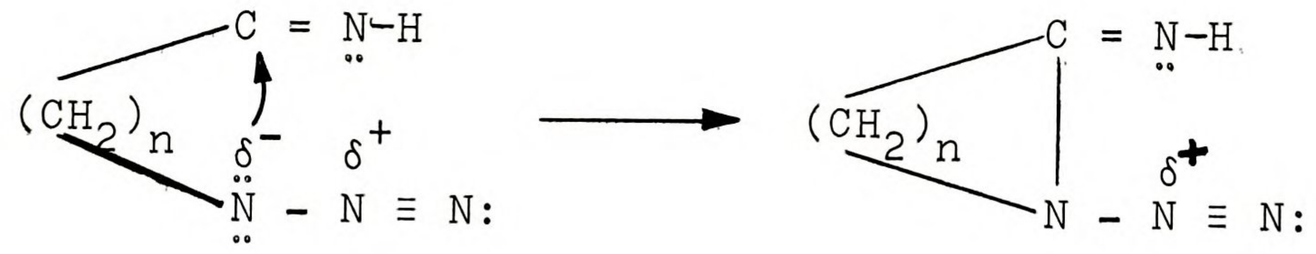
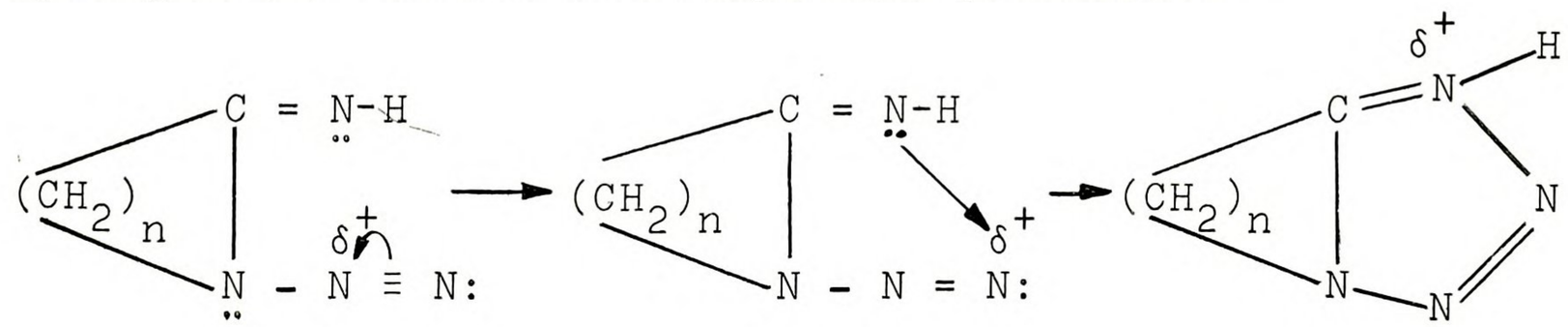
shifting of a pair of electrons toward the protonated nitrogen, leaving the nitrile carbon electron deficient (II). The next step involves a nucleophilic attack of the electron deficient carbon atom by the electron rich nitrogen attached to the methylene chain (III).



(II) (III)

The tetrazole ring closure could take place when a pair of electrons are shifted from the azide triple bond to the electron deficient center nitrogen (IV). This shift causes the terminal azide nitrogen to be electron deficient, and ring closure may take place through a nucleophilic attack by the nitrogen atom which is attached to the hydrogen (V) to form the respective protonated



(IV) (V) (VI)

cyclopolymethylenetetrazole (VI) which then loses a proton to give the desired product (VII).

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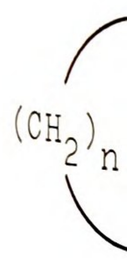

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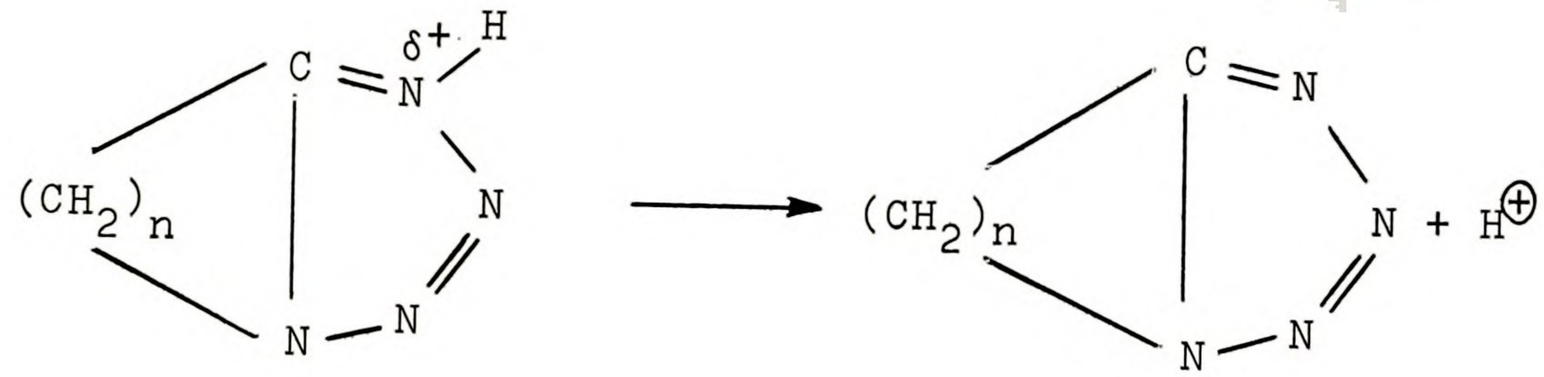
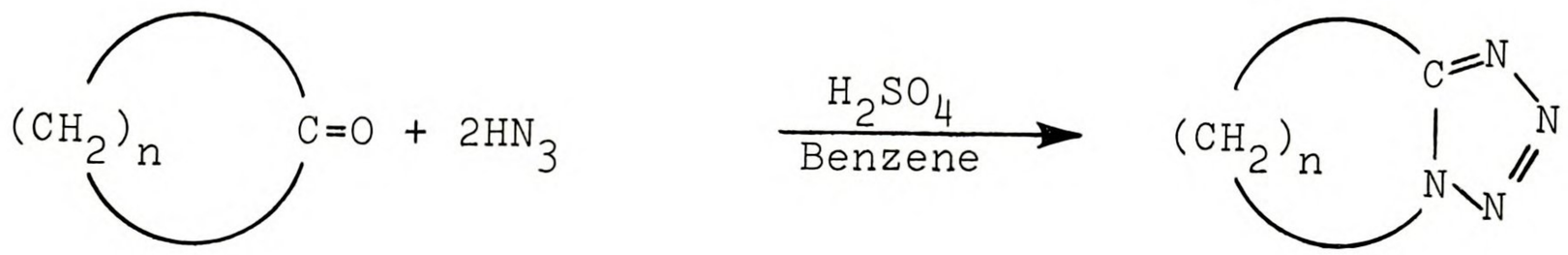


(VI) (VII)

II. The Mechanism of the Schmidt Reaction in the Preparation of the 1,5-Cyclopolymethylene-tetrazoles

The stoichiometry of the preparation of tetrazoles with hydrazoic acid, present in great excess in a highly acidic medium, is represented by the following equation.



By analogy with the mechanisms which have been proposed for the Schmidt reaction, it is possible to postulate the following mechanism for the above reaction.

The concentrated sulfuric acid transforms the hydrazoic acid(I) to its active form (II), and, at the same time, the carbonyl oxygen becomes protonated, thus converting the cyclic ketone(III) into a hydroxycarbonium ion (IV).

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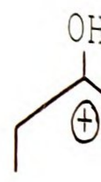

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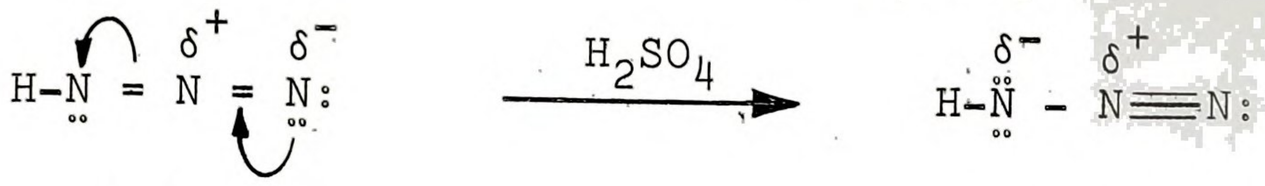

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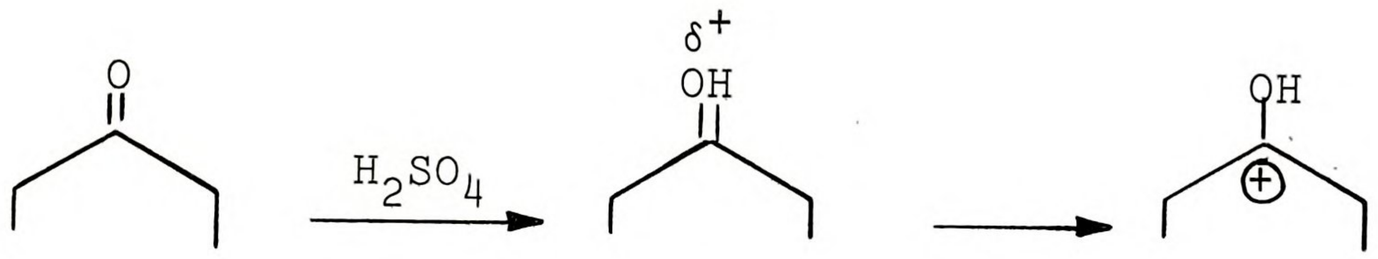

(III) (IV)

The general mechanism for the reaction appears to be a nucleophilic attack on the cyclic hydroxycarbonium ion (IV) by the activated hydrazoic acid molecule to form a transitory intermediate (V).

(IV) (V)

The intermediate compound loses one mole of nitrogen and undergoes a Beckmann type rearrangement which results in ring expansion and the formation of a second hydroxy-carbonium ion (VI).

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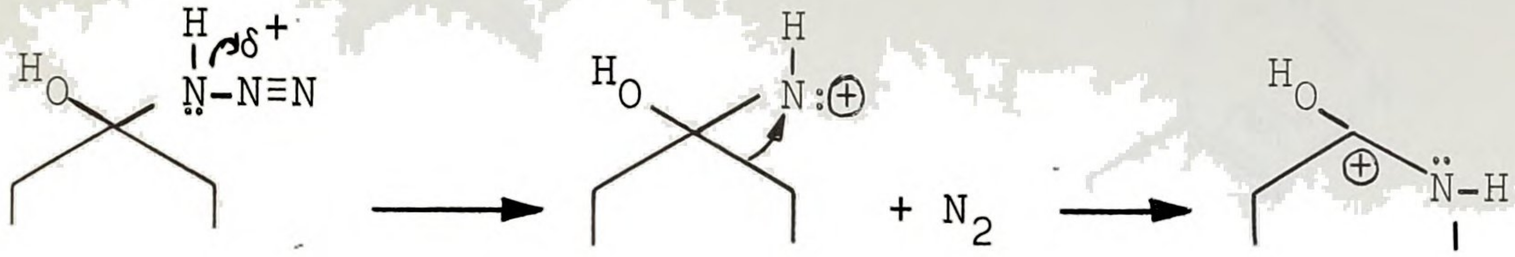
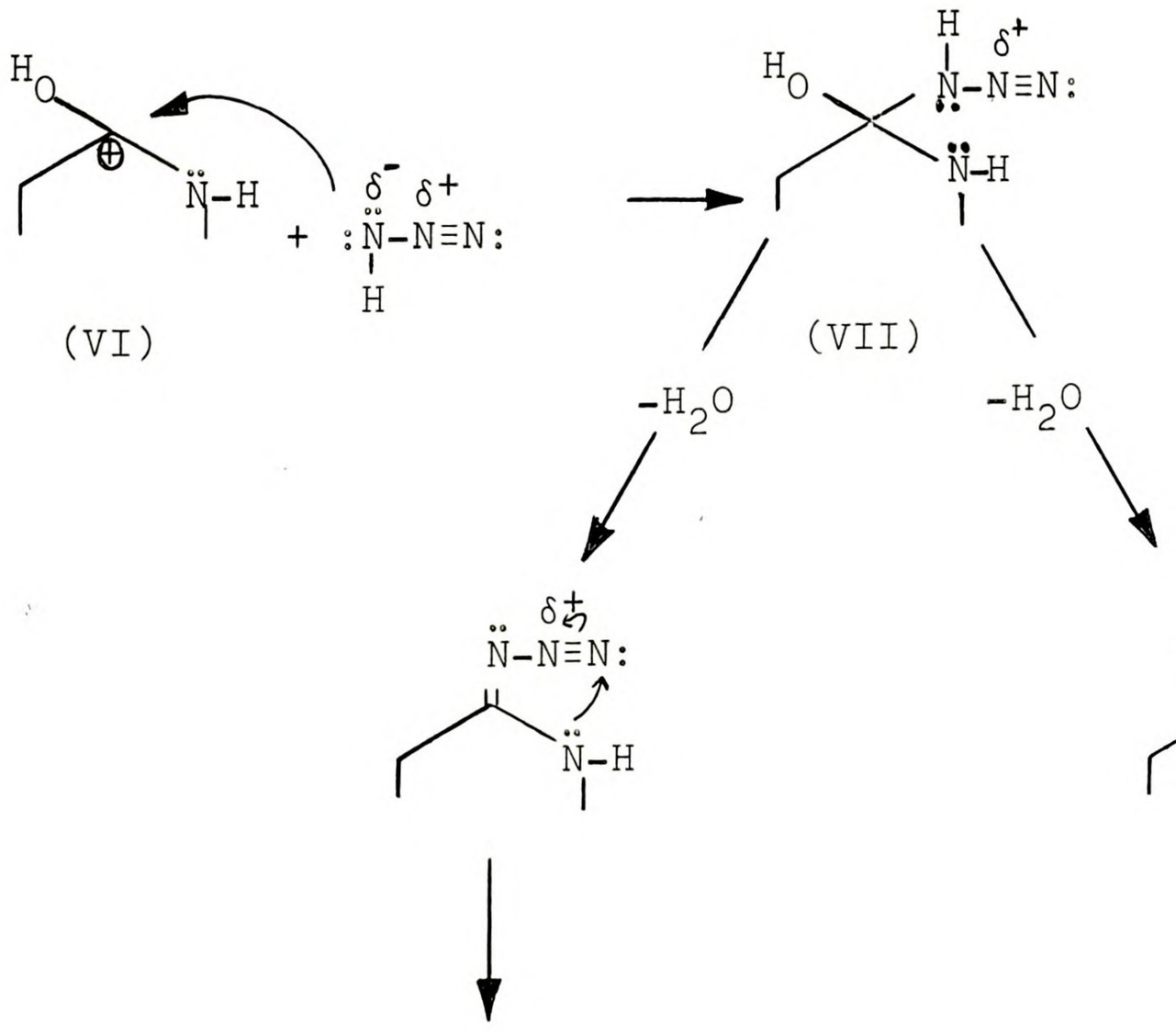


(V) (VI)

A second nucleophilic attack of hydrazoic acid on the Beckmann transient adduct (VI) produces intermediate (VII) which loses a mole of water to give two possible intermediates. Each of these, on ring closure and ejection of a proton, yields the respective cyclopolymethylenetetrazole (VIII).



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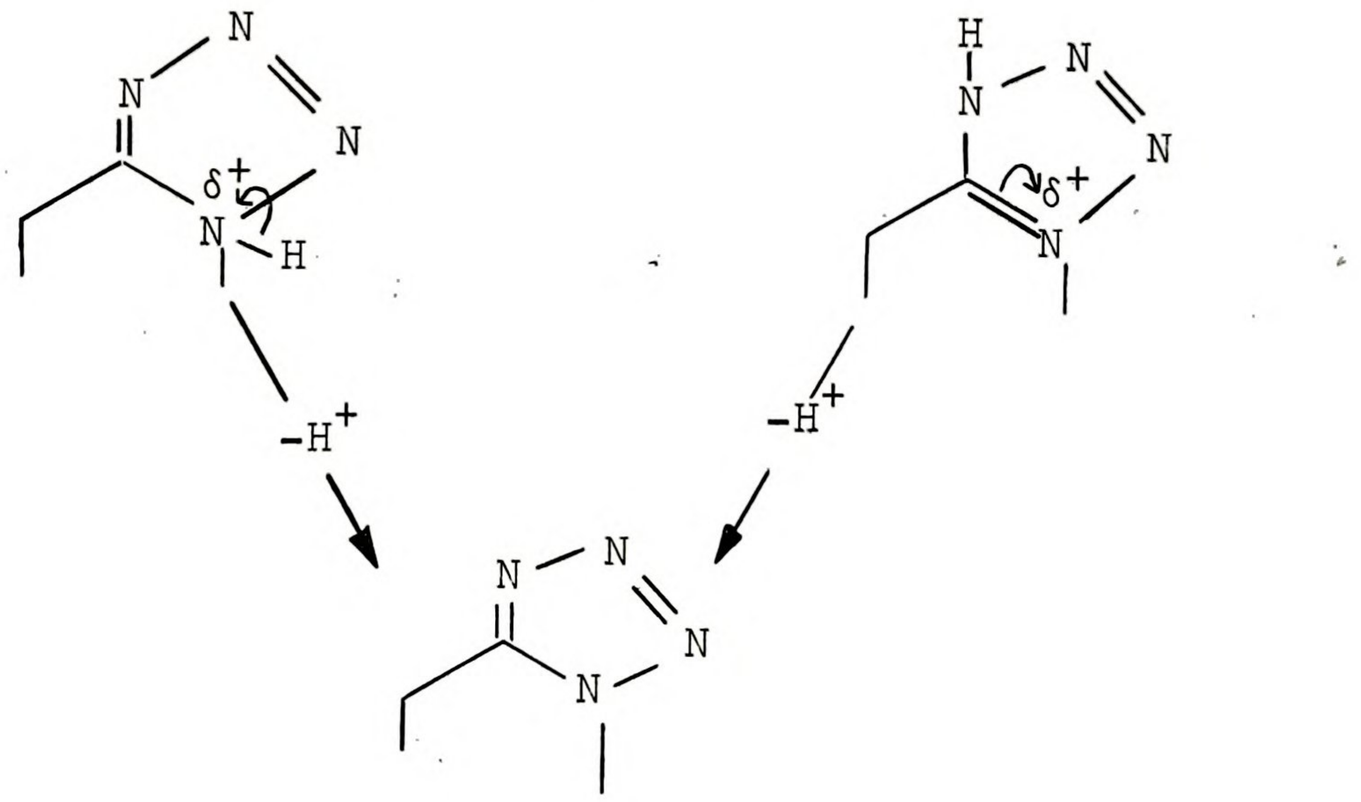

(VIII)

III. Evaluation of the Nuclear Magnetic Resonance, Infrared, and Mass Spectra of the Various 1,5-Cyclopolymethylene-tetrazoles

A. Nuclear Magnetic Resonance Spectra.--The proton magnetic resonance spectra of the cyclopolymethylene-tetrazoles are essentially the same with the exception of trimethylenetetrazole which shows a more complex spectra due to spin-spin splitting. A typical spectrum of the remaining cyclopolymethylenetetrazoles has two triplets of unit area at about 5.5 and 6.9 τ respectively and a third or fourth complex peak, depending on the cyclopoly-methylenetetrazole, at about 8.0 and 8.6 τ respectively which are integer values of the first two peaks.

The assignments of the cyclopolymethylenetetrazole resonance peaks were based on the nmr of 1-methyl,

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5-methyl, and 1,5-dimethyltetrazole. The $N-CH_3$ resonance peak for 1-methyltetrazole was observed at 5.7 τ, and the $C-CH_3$ resonance peak for 5-methyltetrazole was observed at 7.4 τ. Proton nmr spectra obtained for 1,5-dimethyltetrazole showed two sharp peaks in the ratio of 1:1 with the $N-CH_3$ resonance at 5.95 τ and the $C-CH_3$ resonance at 7.42 τ (113). Therefore, the 5.5 τ triplet of each cyclopolymethylenetetrazole was assigned to the methylene protons adjacent to the 1-nitrogen of the tetrazole ring and the 6.9 τ triplet to the methylene protons adjacent to the 5-carbon atom. The single peak that was obtained in the spectra of tetra- and pentamethylenetetrazole at about 8.0 τ arose from the remainder of the methylene protons. As the number of methylene groups in the ring were increased beyond five, two bands became discerible in the regions of 7.9 and 8.75 τ. The resonance peak at about 7.9 τ with twice the unit area was due to the almost equivalent methylene protons adjacent to the methylene groups which gave rise to the two triplets. The resonance peak in the 8.6 τ region was due to the remaining methylene protons. Since these protons are most distant from the tetrazole ring, their chemical shift approached the position expected for methylene protons of a hydrocarbon.

The nmr spectra of the respective 6,6-dihalocyclopolymethylenetetrazoles show essentially the same patterns with complex triplets in the regions of 5.3 and 7.0 τ which are

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assigned to the methylene protons adjacent to the 1-nitrogen and 5-carbon atoms respectively. The remainder of the methylene protons of each cyclopolymethylenetetrazole give rise to a very complex singlet in the region of 7.4 to 8.0 τ. This singlet is split into two peaks in the case of 6,6-dichlorohexamethylenetetrazole as described above.

B. Infrared Spectra.--The infrared spectra of the various 1,5-cyclopolymethylenetetrazoles, 6,6-dihalocyclopolymethylenetetrazoles, and bitetrazoles were determined in the 5000-670 cm^{-1} region. The absorption bands characteristic of the tetrazole ring were observed in all the compounds (55,56). The spectra of the various 1,5-cyclopolymethylenetetrazoles are very similar except for slight shifts and variance of intensities of some absorptions bands. The spectral features of the 1,5-cyclopolymethylenetetrazoles are retained in the corresponding 6,6-dihalocyclopolymethylenetetrazoles but with slight positional shifts and changes in the intensities of the absorption bands. A new band appears in the region of 760-780 cm^{-1} in the spectra of the 6,6-dichlorocyclopolymethylenetetrazoles which is attributed to the C-Cl stretching frequency.

A direct correlation of the various tetrazole bands was not attempted because weaker bands may not be discernible in poorly defined spectra, and the inability of the spectrometer to resolve closely spaced absorptions must also be taken into account.

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C. Mass Spectra.--The mass spectra fragmentation patterns of the various cyclopolymethylenetetrazoles are essentially the same with the most common fragments corresponding to C_2H_5, CH_2N, CH_2N_2, and N_2. The relative abundance of each of these fragments varies and depends on the respective cyclopolymethylenetetrazole. The parent peak of the respective cyclopolymethylenetetrazole is either very weak or absent. All the spectra were corrected for instrument background.

IV. Spectrophotometric Study of the Coordination Ability of the 1,5-Cyclopolymethylenetetrazoles

The results obtained in the spectrophotometric part of this investigation are shown in Table VII. It has been noted previously that the donor properties of the cyclopolymethylenetetrazoles are rather weak and the formation constant values for the iodine complexes in 1,2-dichloroethane at 25° ranged from 1.42 to 2.64 liter $mole^{-1}$. The formation constant for the pentamethylenetetrazole-iodine complex was reported as 7.5 in a previous publication (64). However, that work was done in carbon tetrachloride solutions. Keefer and Andrews (114) determined that the formation constant of the benzene-iodine complex in carbon tetrachloride solutions at 25° was 1.55 liter $mole^{-1}$. Therefore, toward iodine the donor properties of the tetrazole ring are of the same order of magnitude as those of the benzene ring.

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A study of the charge-transfer complexes of mono- and disubstituted tetrazoles with π-electron acceptors has shown that, while such complexes do exist in solution, they are extremely unstable and are largely dissociated even in concentrated solutions (70). The formation constants of the benzene-tetracyanoethylene and pentamethylene-tetrazole-tetracyanoethylene complexes are comparable, but the formation constant of iodine monochloride with pentamethylenetetrazole is larger by three orders of magnitude than that of the benzene-iodine monochloride complex (64). Moreover, it has been recently shown that in the solid pentamethylenetetrazole-iodine monochloride complex the bonding occurs through one of the nitrogen atoms (71).

Therefore, it appears that the tetrazole-iodine interaction involves σ type bonding. Under these conditions, the inductive effect of the polymethylene ring would not be too significant. The formation constants seem to increase with the increasing length of the hydrocarbon chain with the exception of pentamethylenetetrazole which does not fit into the series. This irregularity may be due to difference in the solvation of pentamethylene-tetrazole as compared with the other homologues since this compound is, by far, the most soluble of the series, both in water and in nonaqueous solvents. Physicochemical properties of other cyclopolymethylenetetrazoles are

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practically unknown at this time and will have to be investigated more thoroughly before possible reasons for the discrepancy can be advanced.

V. Spectrophotometric Study of the Coordination Ability of the Various Bitetrazoles

The following studies include the preliminary spectrophotometric determinations of the complexing ability of bitetrazoles.

A. 1,1'-Diphenyl-5,5'-bitetrazole.--Continuous variation studies of the reaction of 1,1'-diphenyl-5,5'-bitetrazole with copper(II) perchlorate in nitromethane or iodine in 1,2-dichloroethane indicate that no reaction occurred between the bitetrazole and the respective Lewis acid. These results suggest a deactivation of the coordination ability of the tetrazole ring. Because solid complexes of 1,5-dialkyl-substituted tetrazoles have been prepared (13), it would appear that the phenyl rings may be responsible for this deactivation.

Transition metal complexes with 5-aryltetrazoles have been isolated as crystalline solids (51-53). However, analytical results and infrared spectra indicate that the 5-substituted tetrazoles coordinate as anions and not through the tetrazole ring electrons as must be the case in 1,5-dialkyl-substituted tetrazoles.

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Gilbert and Brubaker (54) prepared the respective crystalline complexes of 1-methyl, 1-cyclohexyl, and 1-phenyltetrazole with nickel(II), zinc(II), and platinum(II) chlorides. Stability constant measurements of the 1-phenyltetrazole nickel complex in tetrahydrofuran were calculated to be of the order of 10^4. However, since some of the data were rejected, the authors feel that these results may not be significant. Nevertheless, since solid complexes of 1-phenyltetrazole can be isolated, a significant interaction occurs between 1-phenyltetrazole and the transition metal ions in ethanol or tetrahydrofuran. In a later study Garber and Brubaker (56) prepared bis(1-methyl-5-tetrazolyl)nickel(II) and bis(1-cyclohexyl-5-tetrazolyl)nickel(II) complexes containing nickel-carbon bonding by reacting 1-substituted-5-tetrazolyllithium intermediate prepared in situ in tetrahydrofuran with dichlorobis(triethylphosphine)nickel(II). When the same conditions were used to prepare the corresponding bis(1-phenyl-5-tetrazolyl)nickel(II) complex, the 1-phenyl-5-tetrazolyllithium intermediate was recovered unchanged.

It is clear that the coordination ability of 1,1'-diphenyl-5,5'-bitetrazole was deactivated. It is unlikely that the phenyl groups caused this deactivation because they tend to increase the Lewis basicity of the tetrazole rings. Also, complexes with 1-phenyltetrazole have been prepared (54). A more satisfactory explanation is that

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with two tetrazole rings adjacent to each other, the relatively large iodine molecule is unable to approach the active coordination site of the tetrazole ring to form a substantial bond. Therefore, the complex formed between the respective Lewis acid and the bitetrazole may have a very small formation constant (<1) and cannot be detected spectrophotometrically. A possibility also exists, however, that adjacent tetrazole rings may cause deactivation of both rings.

B. α,ω-Bis(5-tetrazolyl)-n-alkanes.--Continuous variation and molar ratio studies of 1,3-bis(5-tetrazolyl)-n-propane and 1,4-bis(5-tetrazolyl)-n-butane in ethanol with copper(II) perchlorate hexahydrate indicate the existence of a 1:1 copper-bitetrazole complex in solution. Although the elemental analyses of the solid complexes are poor, they indicate that the most probable composition corresponds to the 1:1 transition metal-bitetrazole species. The reflectance spectra of the corresponding nickel(II), copper(II) and cobalt(II) bitetrazole complexes are those expected for the respective transition metal ions in an octahedral environment. These results are in an apparent conflict with the proposed elemental analyses and the spectrophotometric study which indicates the formation of a one to one salt-like complex. A possible explanation seems to be that in view of their relatively acid protons,

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these bitetrazoles behave in a manner similar to the 5-substituted tetrazoles (51-53) and are coordinated as anions.

VI. Potentiometric Study of the Coordination Ability of the 1,5-Cyclopolymethylenetetrazoles

The silver(I) ion is usually considered to have a characteristic coordination number of two although occasionally complexes with coordination numbers of three and four have been reported (115-117). Usually, where successive stability constants have been determined, the first two monodentate ligands are strongly attached to the silver ion. In the few cases where additional ligand molecules are taken up by the silver ion, the ligand-metal bonds are quite weak. In the case of the cyclopolymethylenetetrazoles, the complex formation appears to be complete after two ligand molecules are added to the silver ion.

Bis(pentamethylenetetrazole)silver(I) nitrate was isolated by Popov and Holm (20) and bis(trimethylenetetrazole)silver(I) nitrate was prepared in this investigation. All calculations of the respective instability constants were made on the assumption that the complex formed in solution contained two molecules of the respective cyclopolymethylenetetrazole per silver ion. Because a large excess of the ligand was used in these

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studies, it can be assumed that only negligible amounts of the 1:1 complex were present.

The results obtained in the potentiometric part of this investigation are shown in Tables X and XI. The formation constant values at 25° ranged from 1070 to 1250 liter mole^{-1}.

The data show some reproducible differences in the pK_f values obtained with the three electrodes. For example, the values obtained with the Corning NAS 11-18 sodium ion electrode are ~0.1 higher than values obtained with the

TABLE XV.--The Average pK_f Values for the Reaction

$$Ag^+ + 2\ C_nMT \rightleftharpoons Ag(C_nMT)_2^+ .$$

Tetrazole	pK_f (0.1 M KNO_3)	pK_f (0.4 M KNO_3)
Trimethylenetetrazole	-3.01±0.01	-2.98±0.05
Tetramethylenetetrazole	-3.07±0.03	-3.03±0.03
Pentamethylenetetrazole	-3.05±0.04	-3.00±0.05
Hexamethylenetetrazole	-3.05±0.01	-2.98±0.03
Heptamethylenetetrazole	-3.08±0.04	-3.32±0.03

As shown on page 100, the pK_f values should not be influenced by the ionic strength if the Debye-Huckel limiting law is obeyed. At the higher ionic strengths

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used in this investigation, however, deviations from the Dèbye-Huckel limiting law may be significant. In order to check this, the measurements were carried out at two ionic strengths, 0.1 and 0.4. Tables X, XI, and XV show that the results for tri, tetra, penta, and hexamethylene-tetrazole were independent of the ionic strength. There is a difference of about 0.3 pK_f unit in the case of heptamethylenetetrazole.

From the data listed in Tables X and XI, no significant change is observed in the formation constants of the various 1,5-cyclopolymethylenetetrazoles; and, once again, no simple correlation appears to exist between the length of the hydrocarbon chain and the stability of the respective silver(I) nitrate complex.

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RECOMMENDATIONS FOR FUTURE STUDIES

I. The following substituted tetrazoles could be synthesized and their respective physicochemical properties investigated.

A. The syntheses of the 6,6-dichloro and 6,6-dibromocyclopolymethylenetetrazoles not already prepared in this investigation could be extended.

B. The synthesis of the corresponding 6,6-diiodocyclopolymethylenetetrazoles could be attempted starting with 2,2-diiodoazacycloheptane prepared by reacting 2,2-dibromoazocycloheptane with sodium iodide in a stainless steel reactor at 100° for 24 hours (84).

C. The synthesis of monochloropentamethylenetetrazole should be attempted starting with 2-chlorocyclohexanone. The method described in this thesis for hexamethylenetetrazole can be followed, and the final product may be either 6-chloropentamethylenetetrazole or 10-chloropentamethylenetetrazole depending on the result of the ring expansion step (i.e.)

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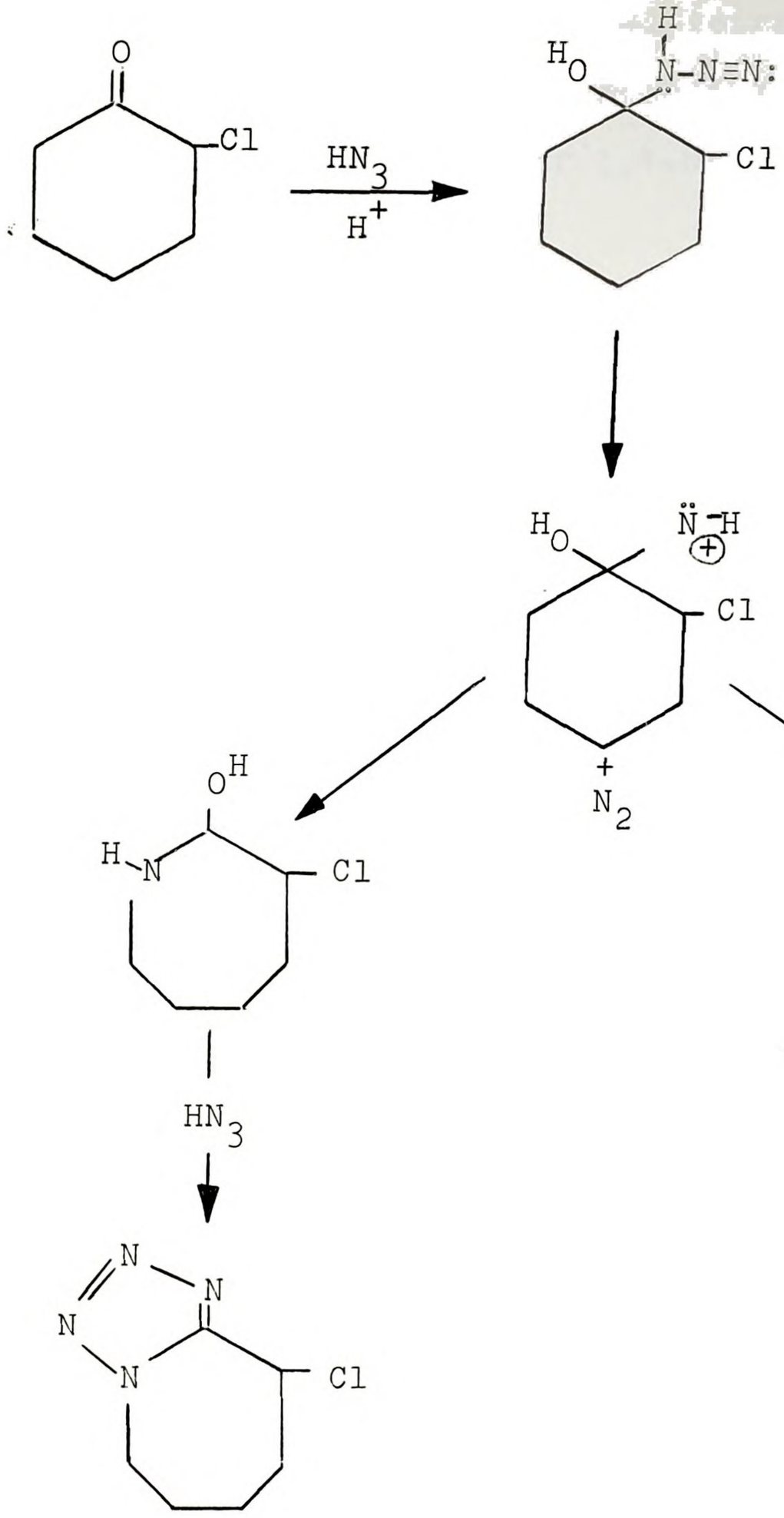

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D. Other α,ω-bis(5-phenyl-1-tetrazolyl)-n-alkanes could be synthesized with the method described in this thesis for the preparation of 1,4-bis(5-phenyl-1-tetrazolyl)-n-butane.

E. Various α,ω-bis(1-methyl-5-tetrazolyl)-n-alkanes could be synthesized by treating a warm aqueous solution of the sodium salt of the respective α,ω-bis(5-tetrazolyl)-n-alkane with dimethylsulfate as described by Cohen et al. (37).

II. A further investigation of the reasons why 1,1'-diphenyl-5,5'-bitetrazole does not complex Lewis acids should be initiated. The most logical reason for steric hindrance could be resolved by investigating the coordination ability of 5,5'-diphenyl-1,1'-bitetrazole, 1,4-bis (1-methyl-5-tetrazolyl)-n-butane, and 1,4-bis(5-phenyl-1-tetrazolyl)-n-butane which are presently available in this laboratory. The study could be extended further to include the α,ω-bis(5-phenyl-1-tetrazolyl)-n-alkanes and α,ω-bis (1-methyl-5-tetrazolyl)-n-alkane which could be synthesized as described above.

III. A study similar to that done with pentamethylenetetrazole (13, 15-17, 63) could be instituted to determine the complexing ability of the other 1,5-cyclopolymethylenetetrazoles prepared in this investigation with transition metal salts.

LITERATURE CITED

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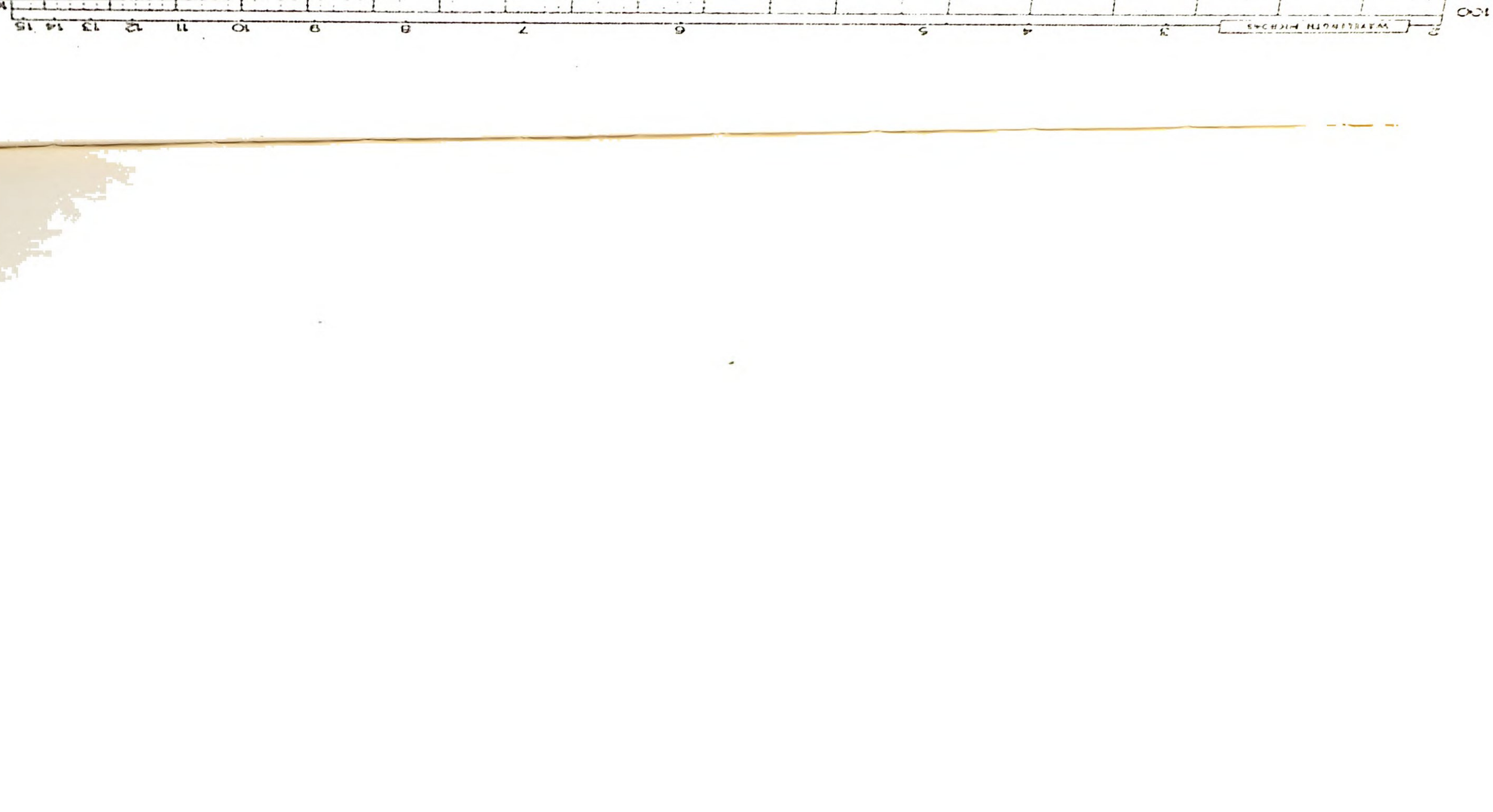
APPENDICES

APPENDIX I

SPECTRA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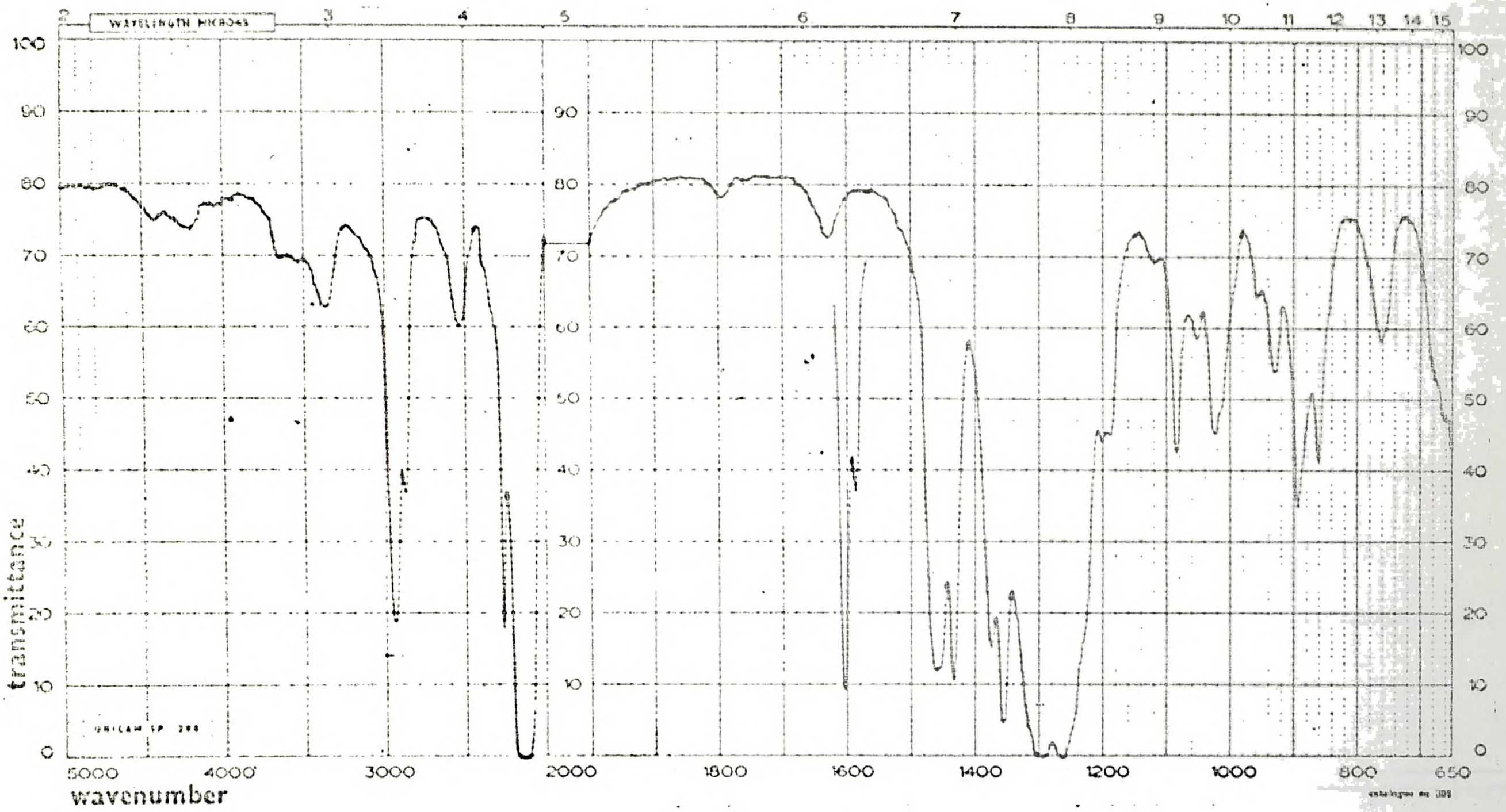

Figure 1. Infrared spectrum of 4-azidobutyronitrile (neat).

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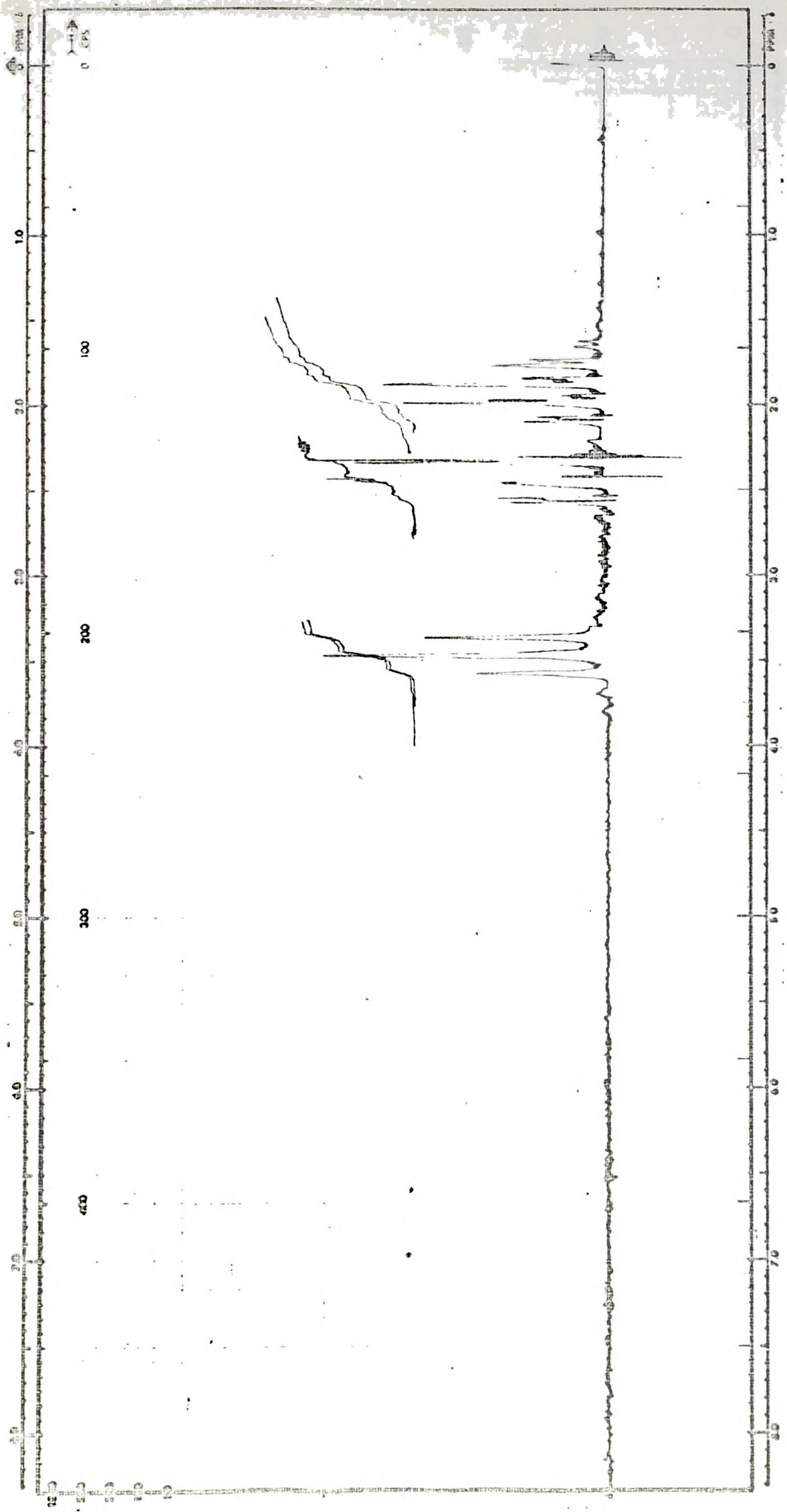


Figure 2. Nuclear magnetic resonance spectrum of 4-azidobutyronitrile (neat).

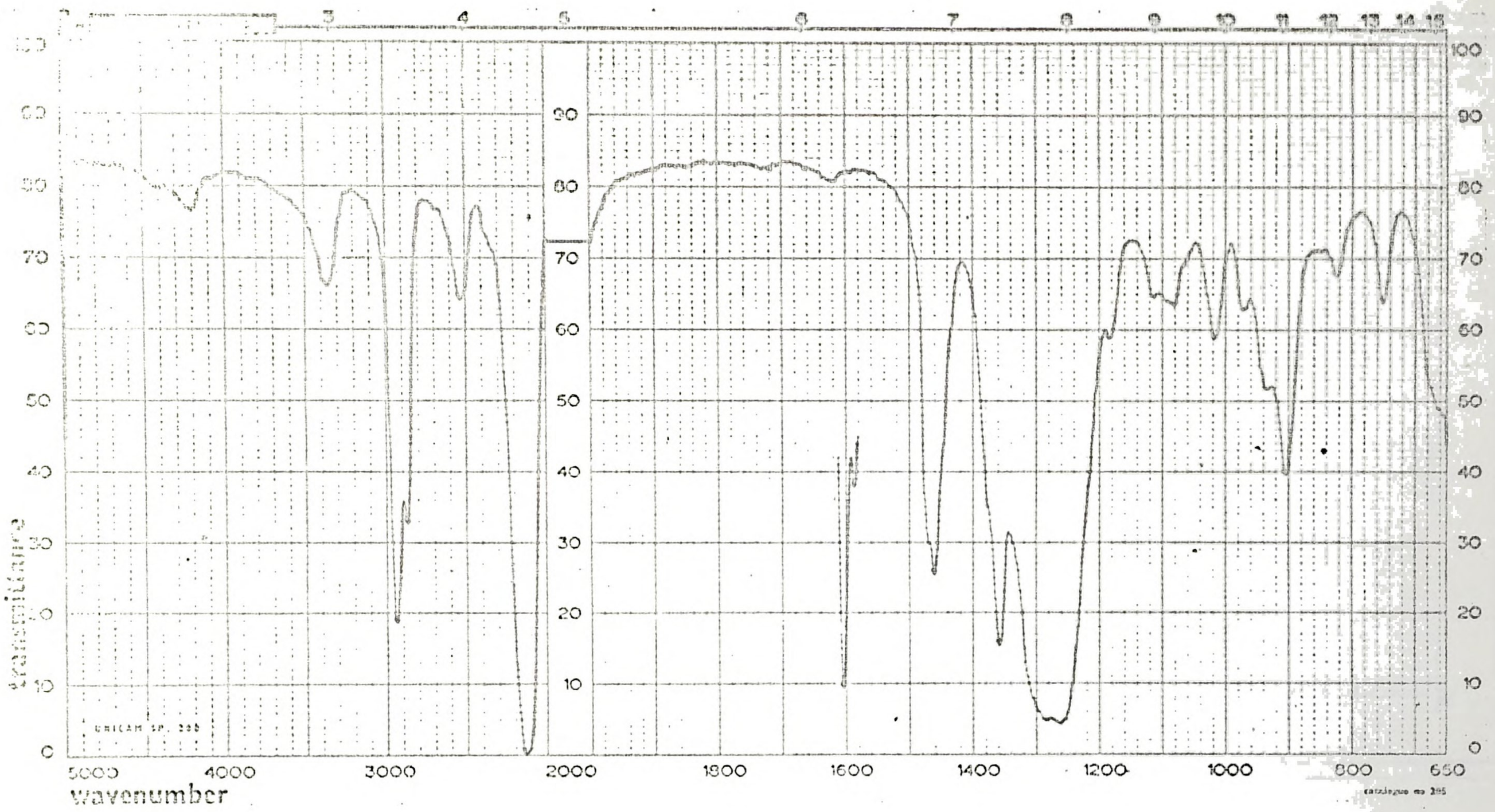
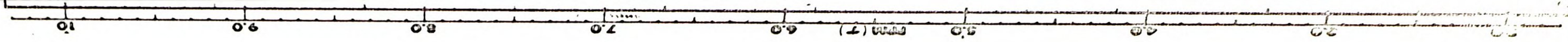


Figure 3. Infrared spectrum of 5-azidovaleronitrile (neat).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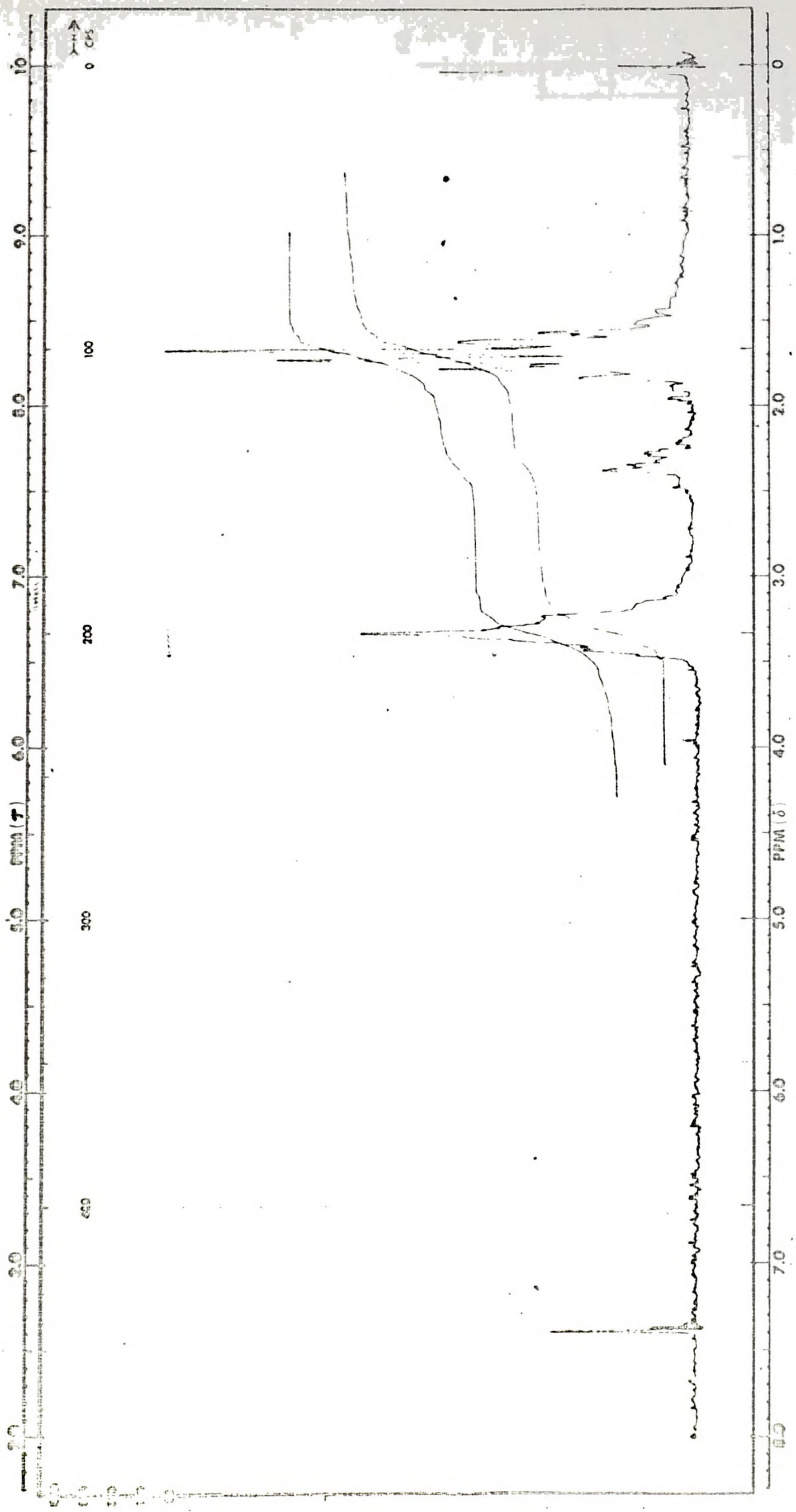


Figure 4. Nuclear magnetic resonance spectrum of 5-azidovaleronitrile (neat).

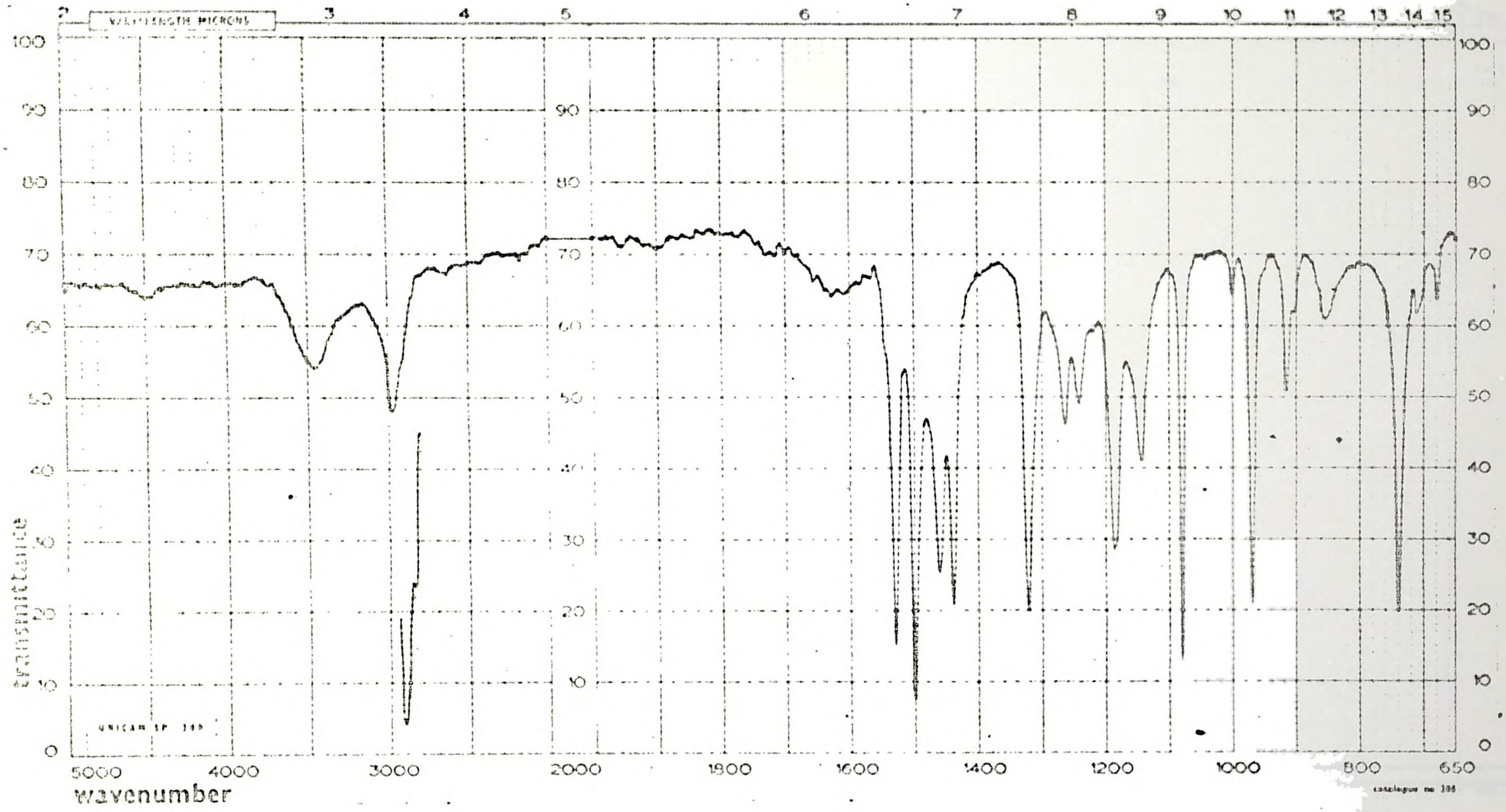


Figure 5. Infrared spectrum of trimethylenetetrazole (KBr).

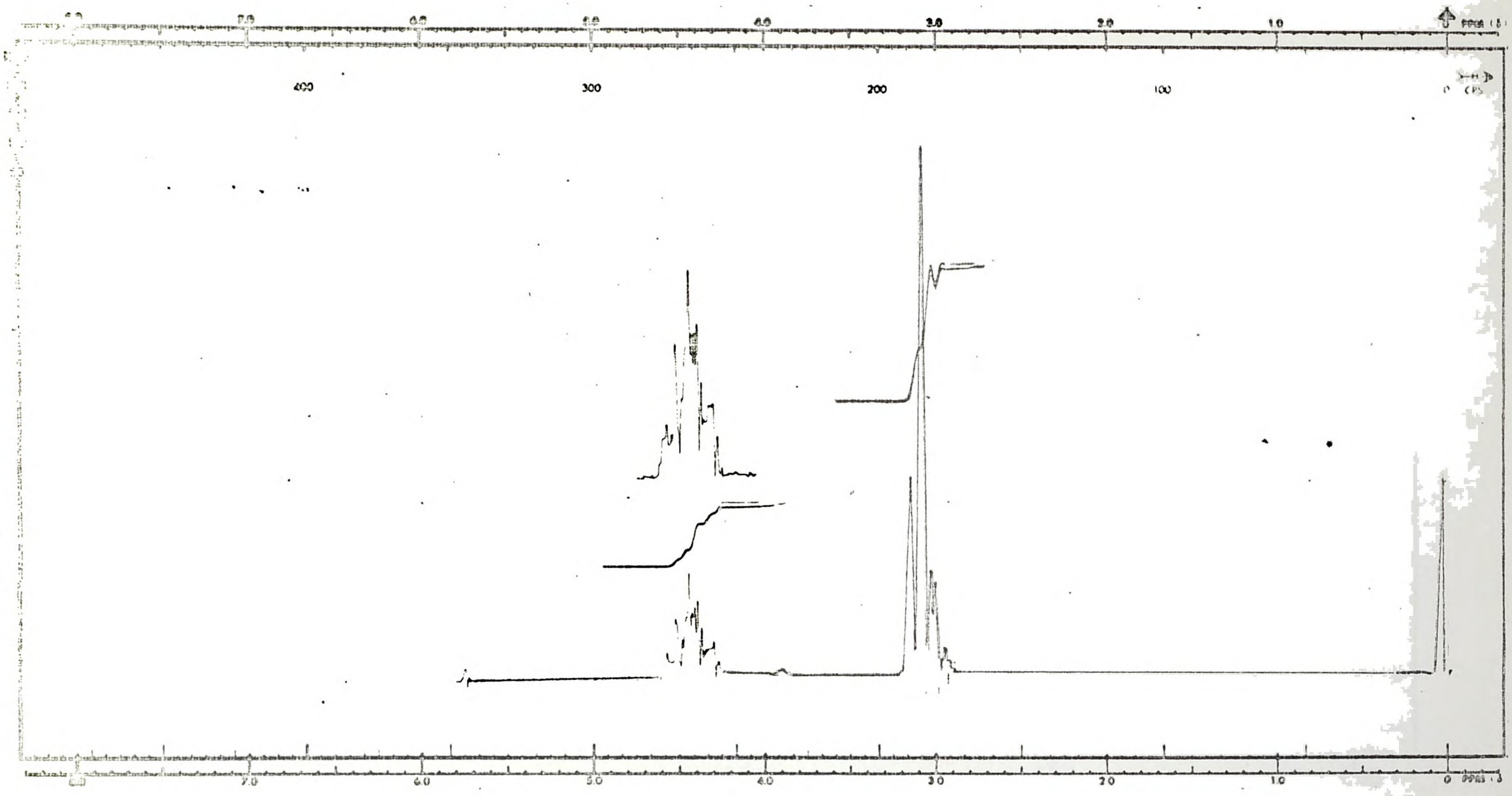


Figure 6. Nuclear magnetic resonance spectrum of trimethylenetetrazole ($CHCl_3$).

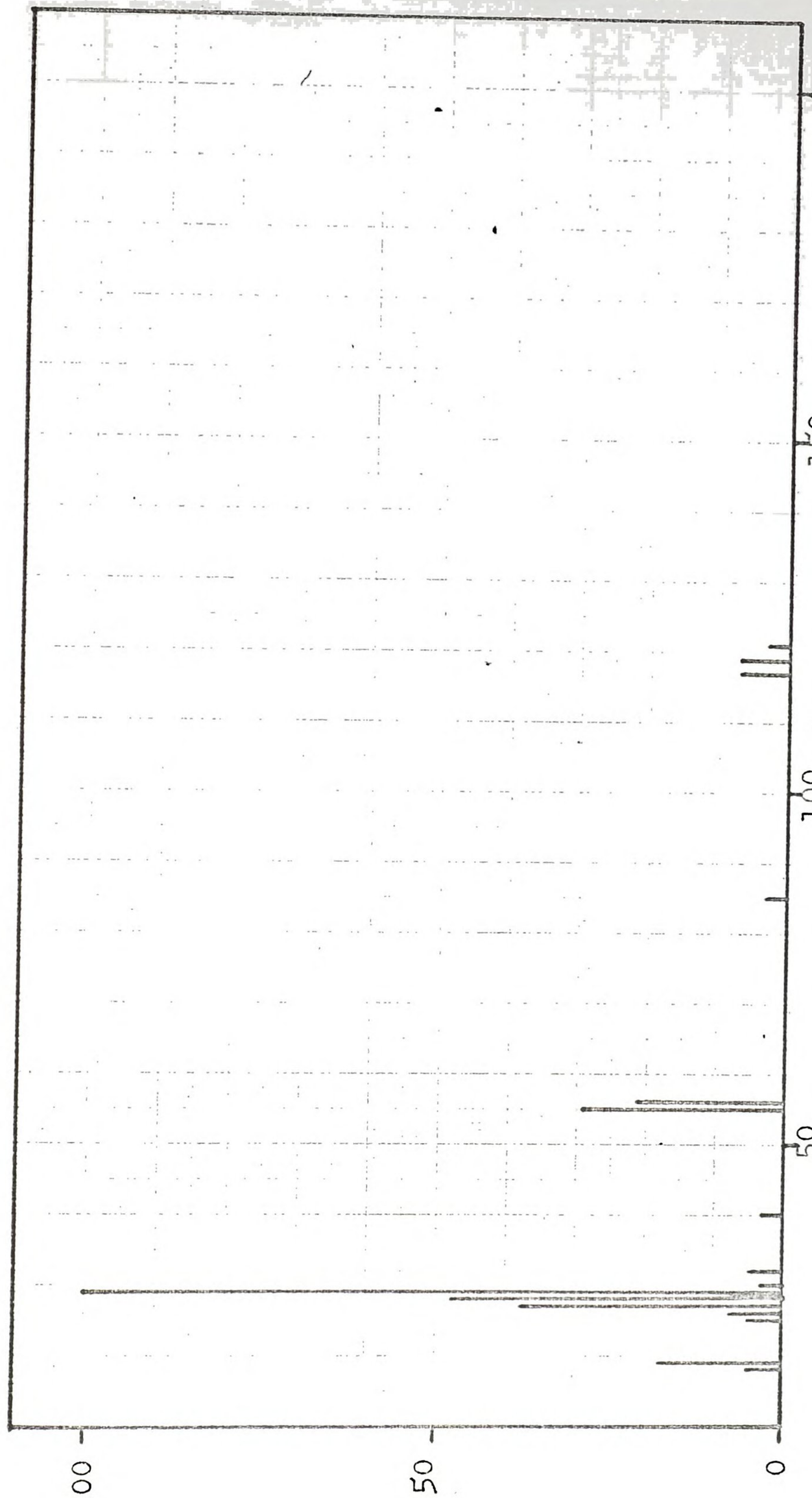


Figure 7. Mass spectrum of trimethylenetetrazole. (Fragments at m/e values of 117, 119 and 121 are due to chloroform impurity)

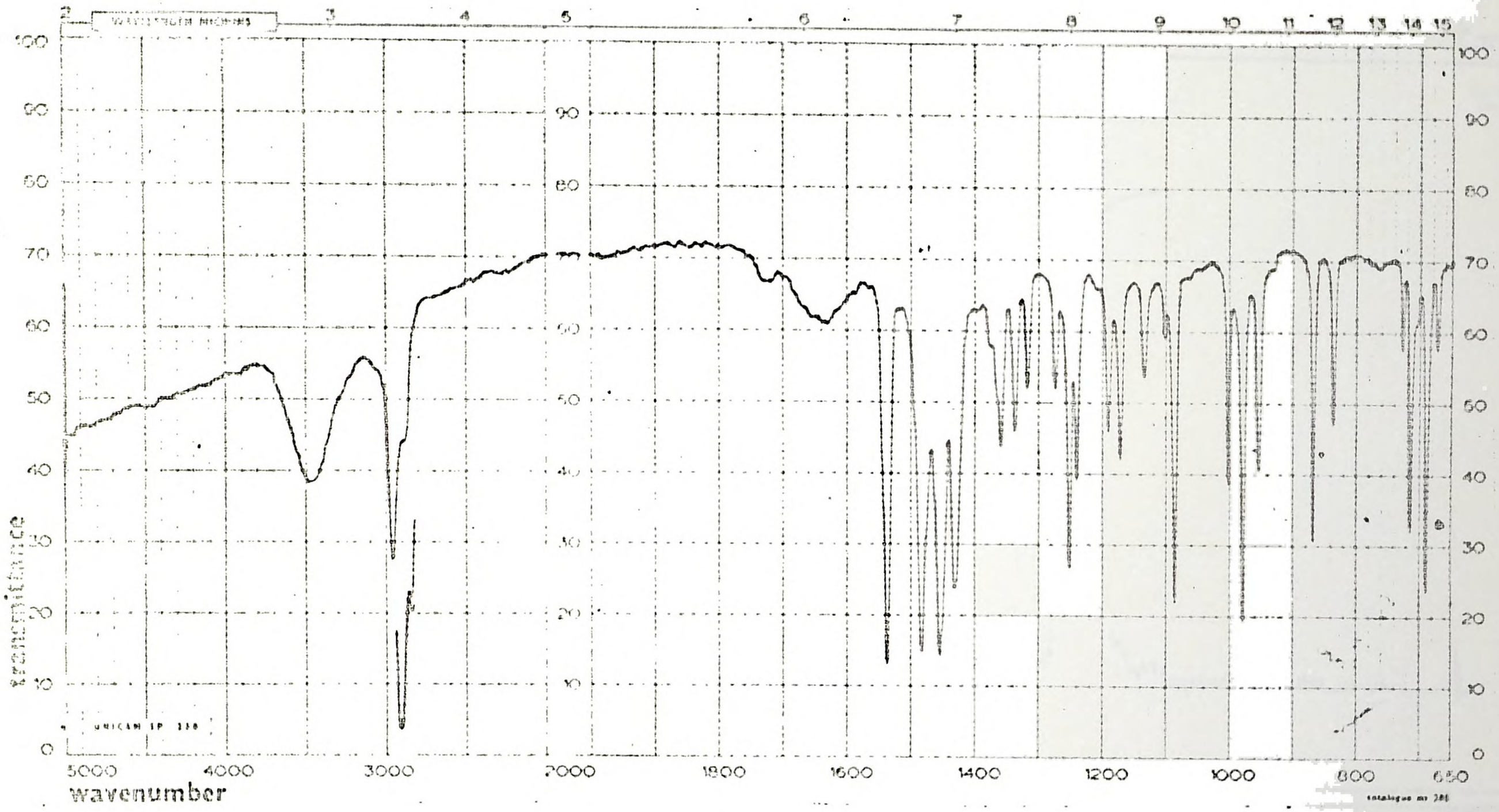


Figure 8. Infrared spectrum of tetramethylenetetrazole (KBr).

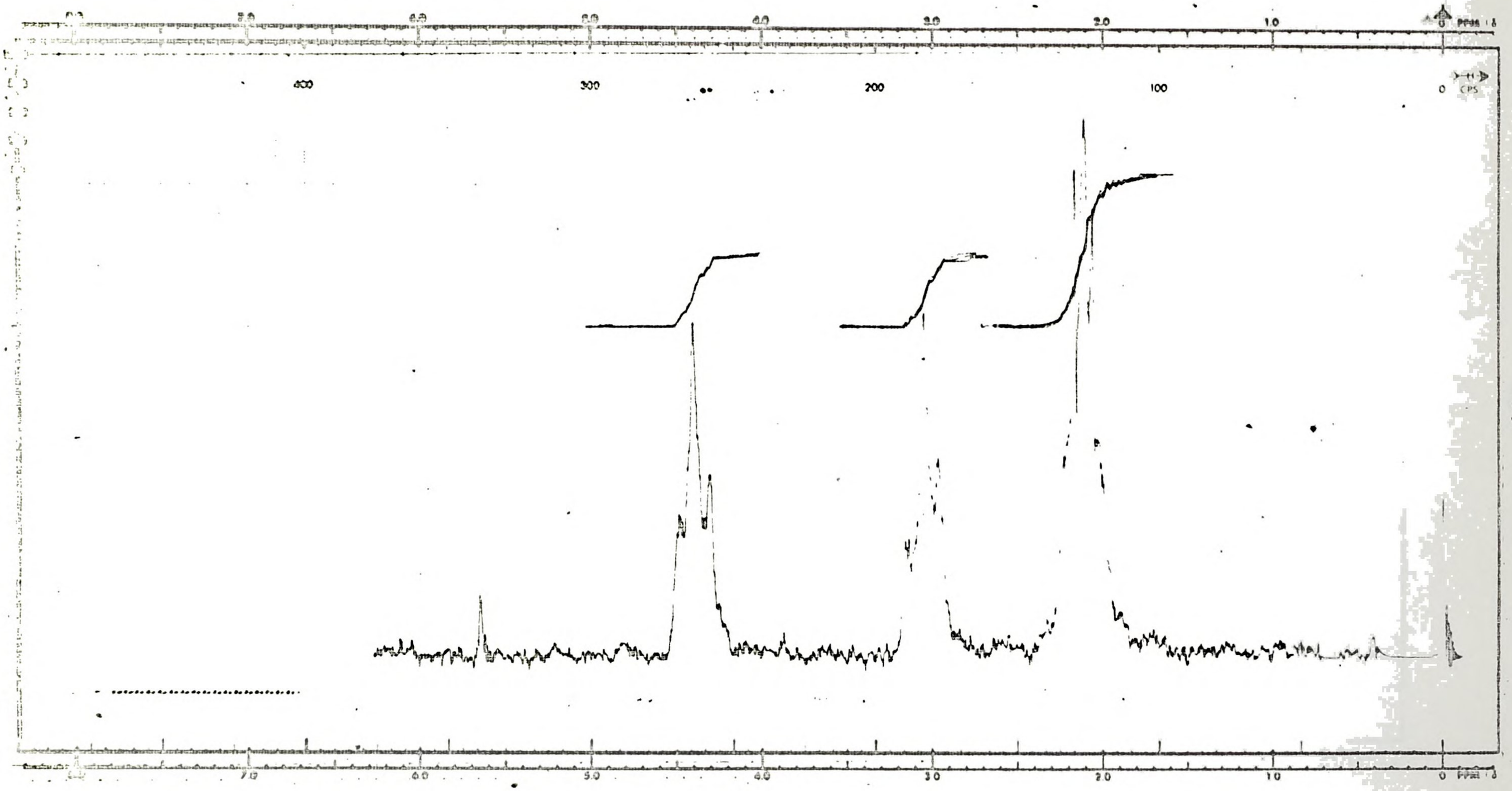


Figure 9. Nuclear magnetic resonance spectrum of tetramethylenetetrazole ($CHCl_3$).

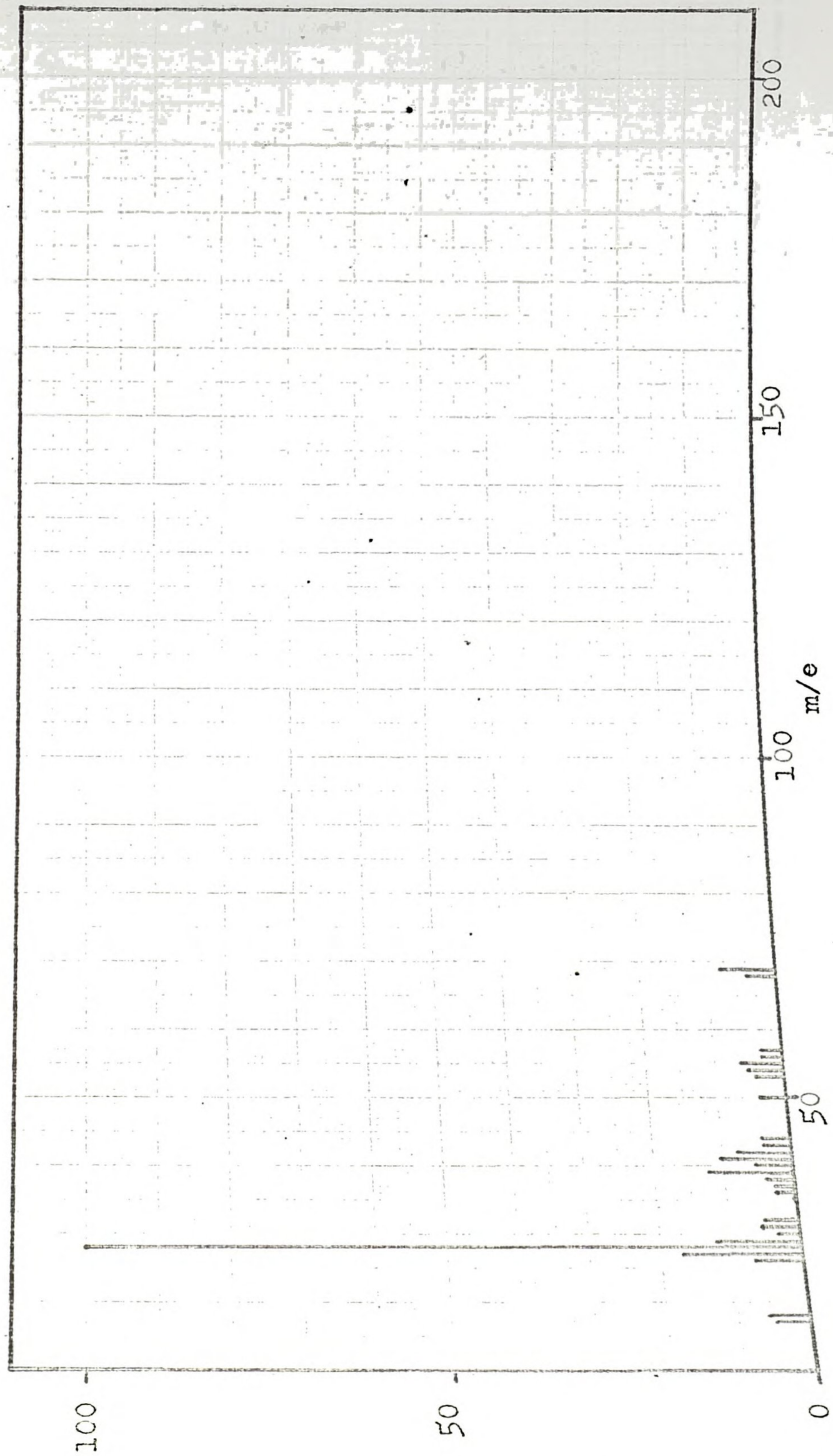


Figure 10. Mass spectrum of tetramethylenetetrazole.

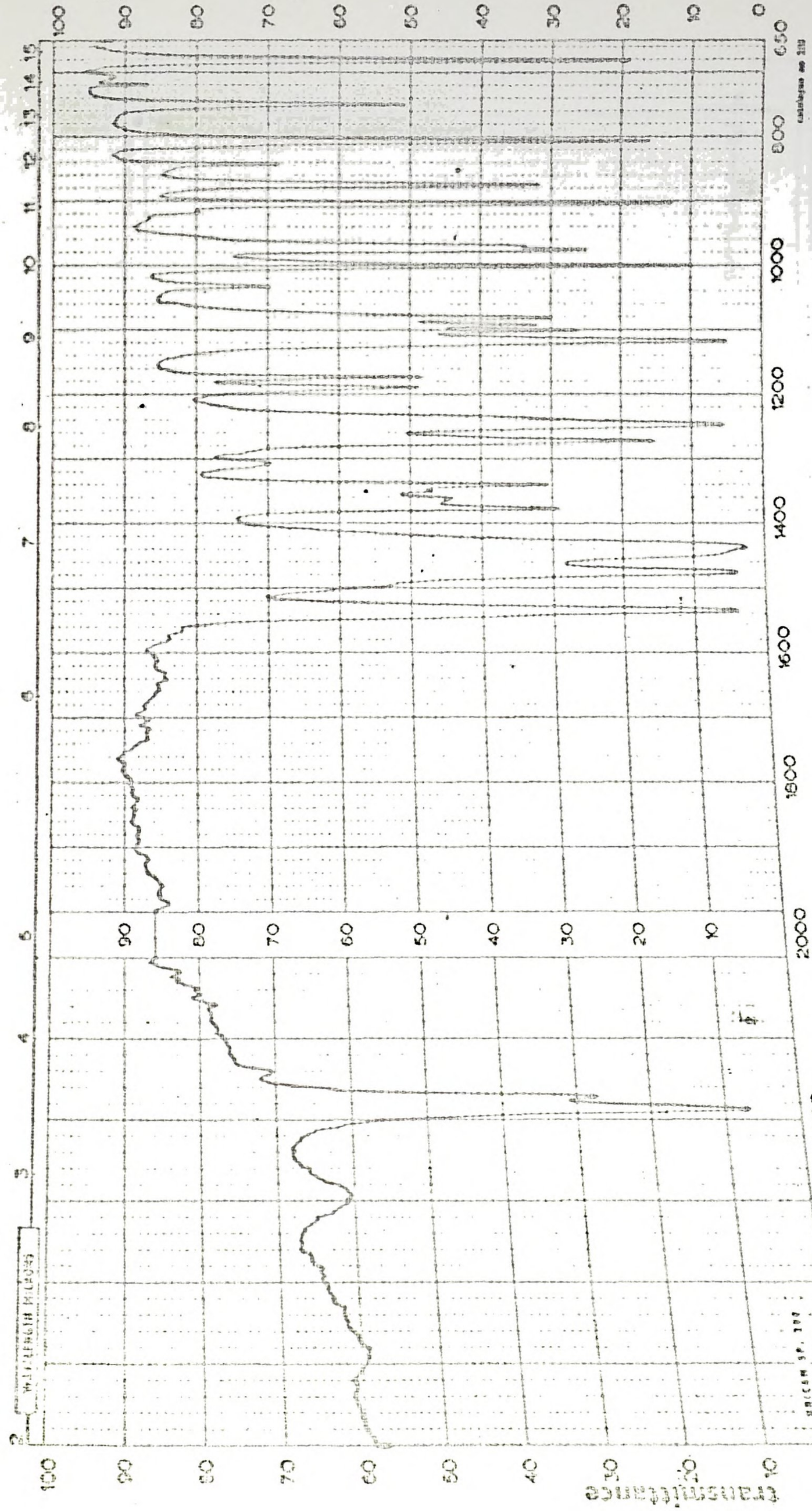


Figure 11. Infrared spectrum of pentamethylenetetrazole (KBr).

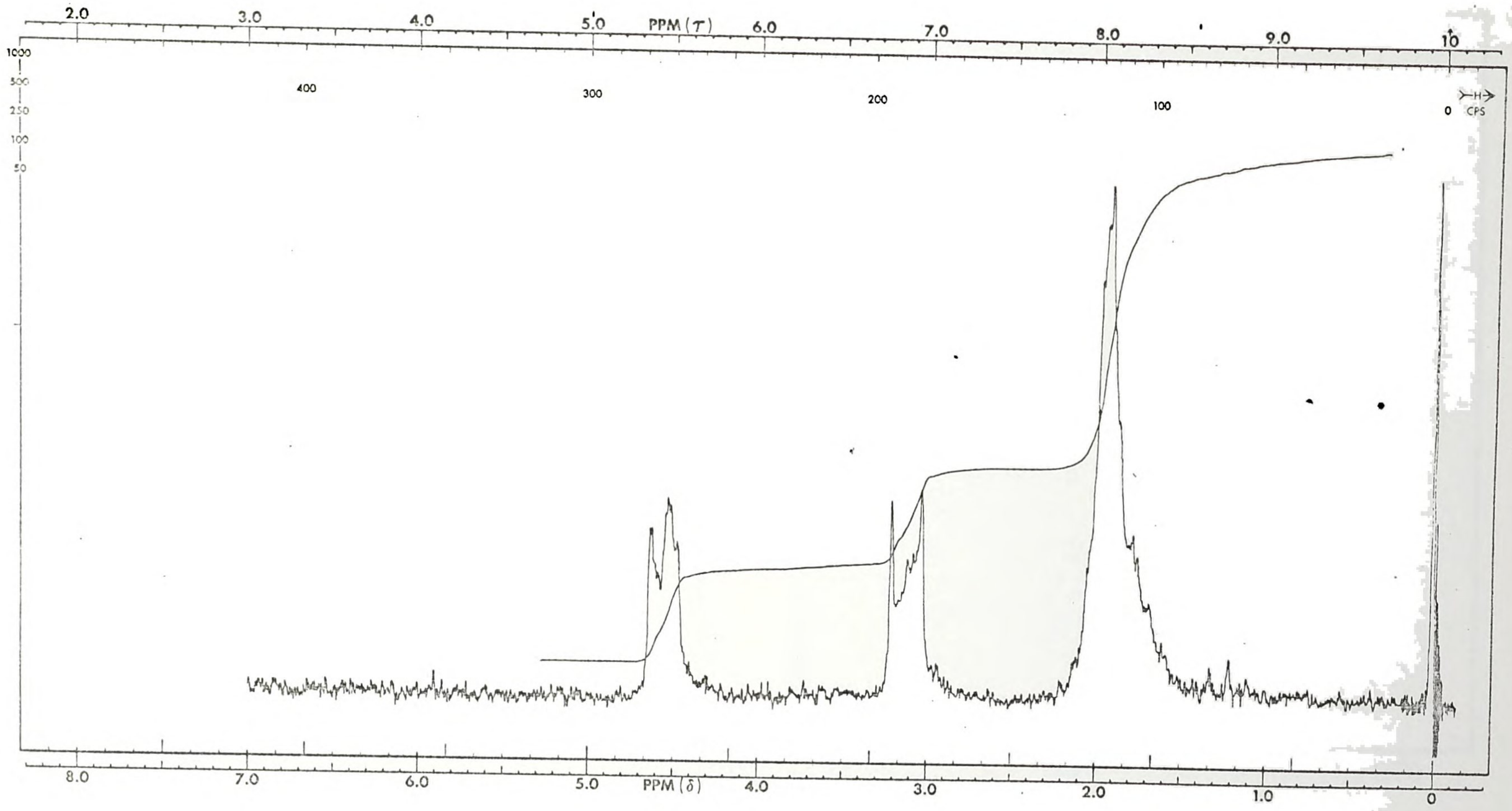


Figure 12. Nuclear magnetic resonance spectrum of pentamethylenetetrazole ($CHCl_3$).

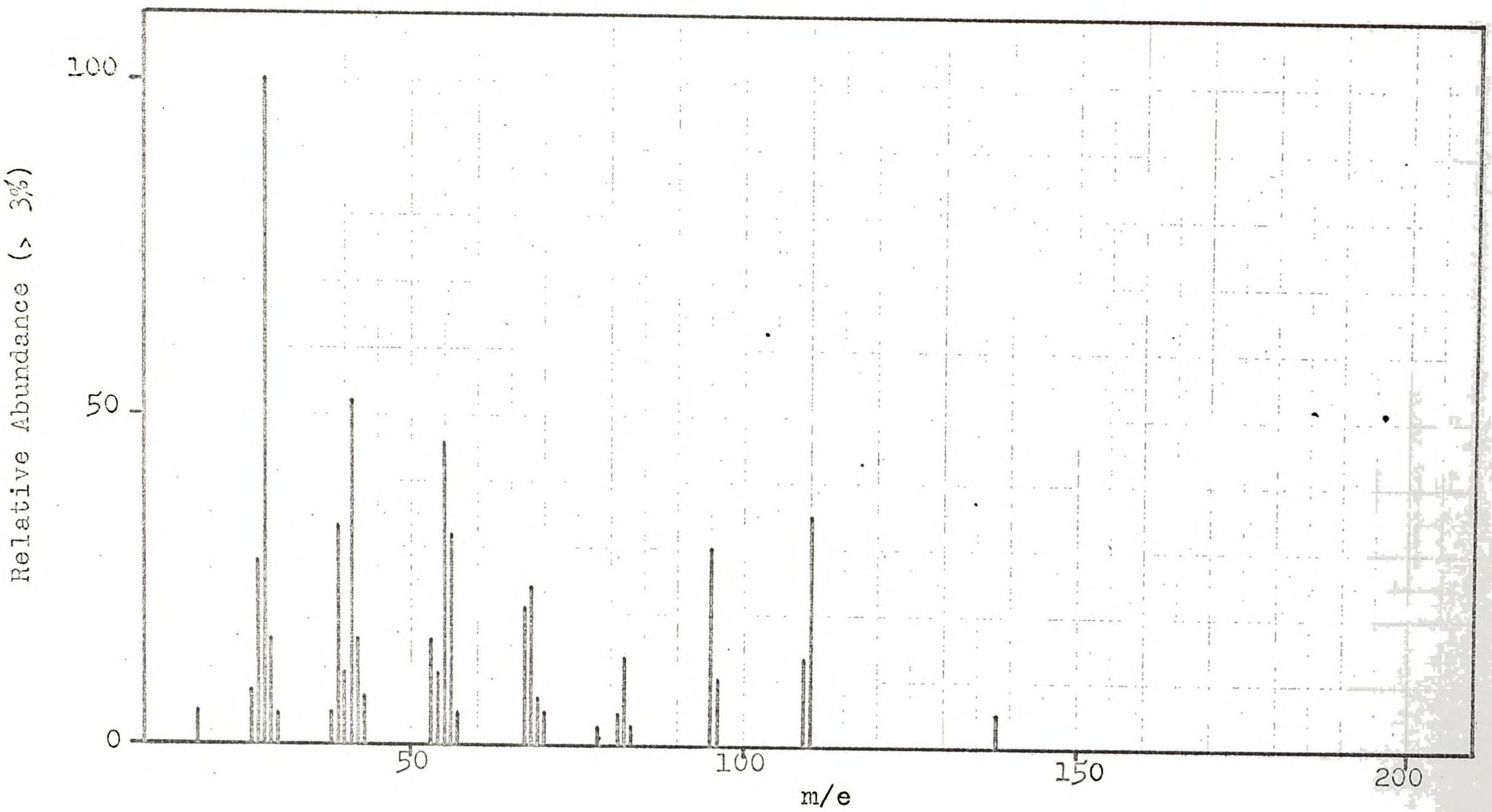


Figure 13. Mass spectra of pentamethylenetetrazole.

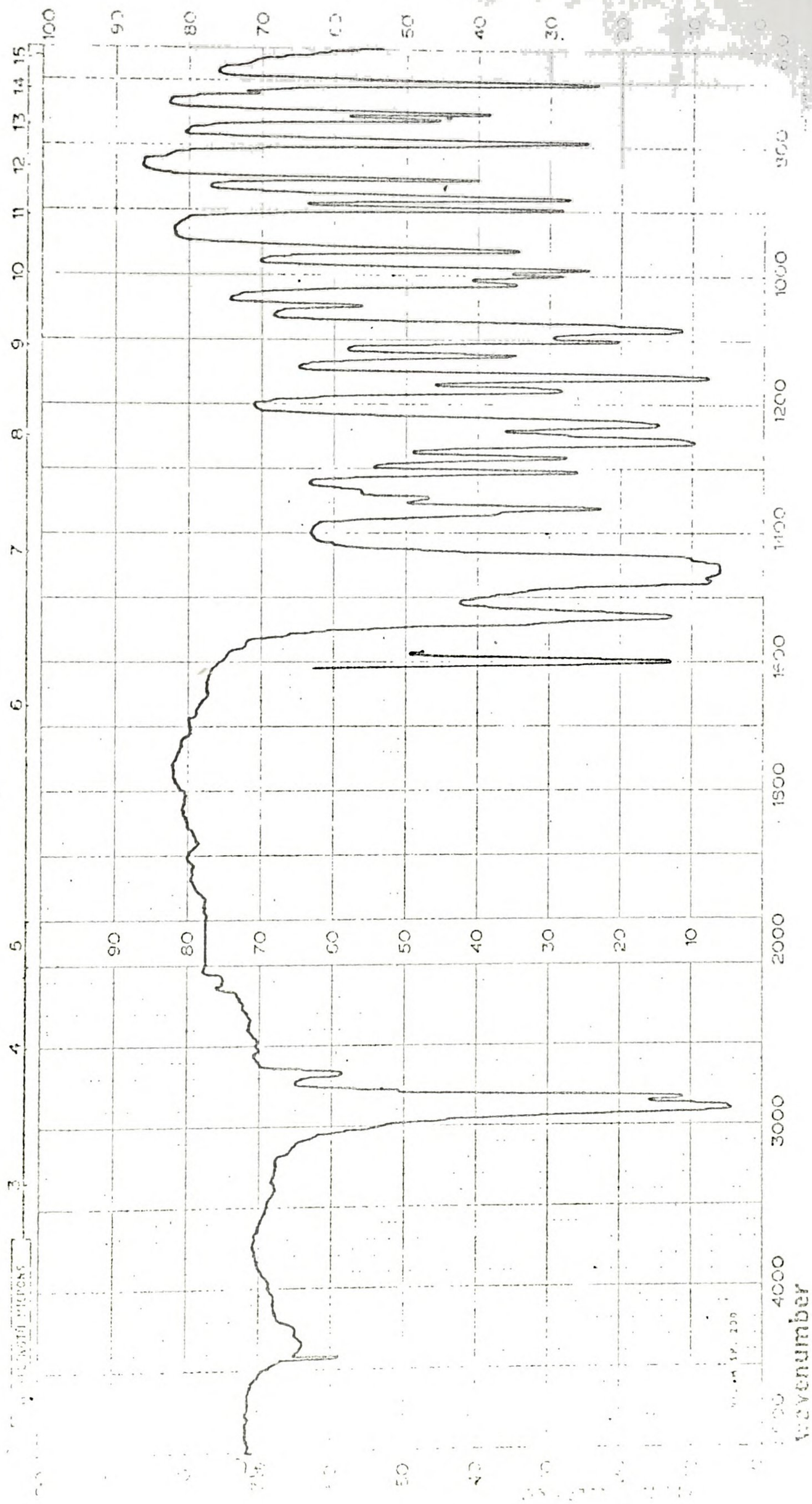
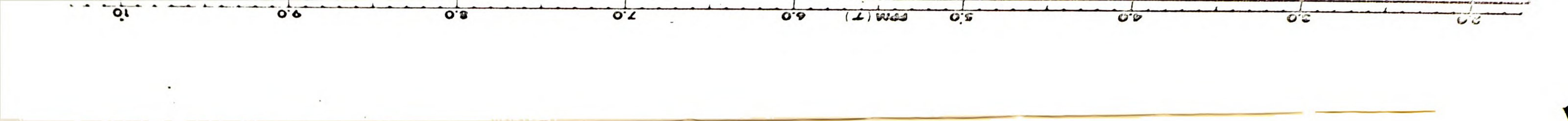


Figure 14. Infrared spectrum of hexamethylenetetrazole (KBr).


2.0
3.0
4.0
5.0
PPM (T)
6.0
7.0
8.0
9.0
10

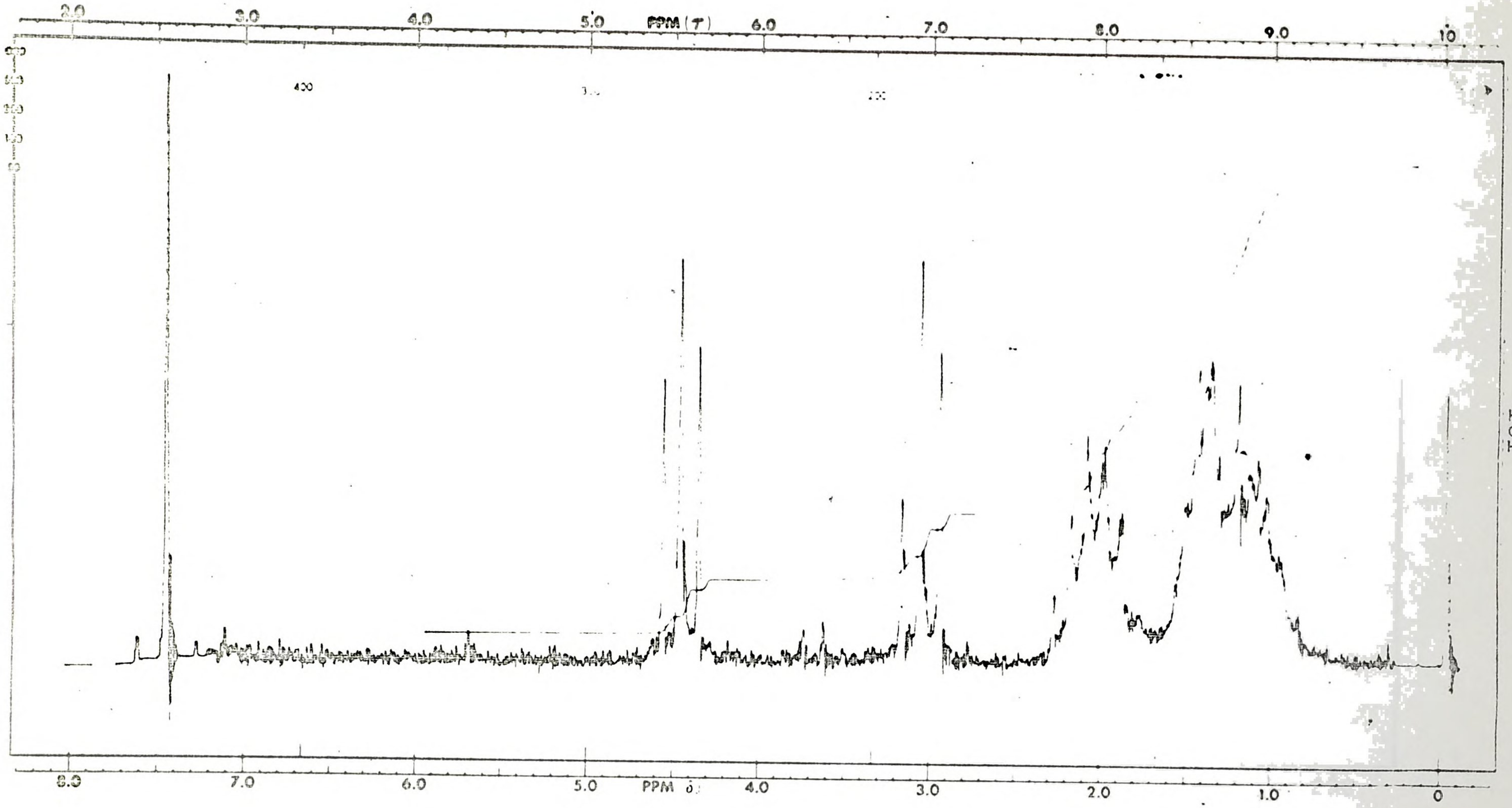


Figure 15. Nuclear magnetic resonance spectrum of hexamethylenetetrazole (CCl_4).

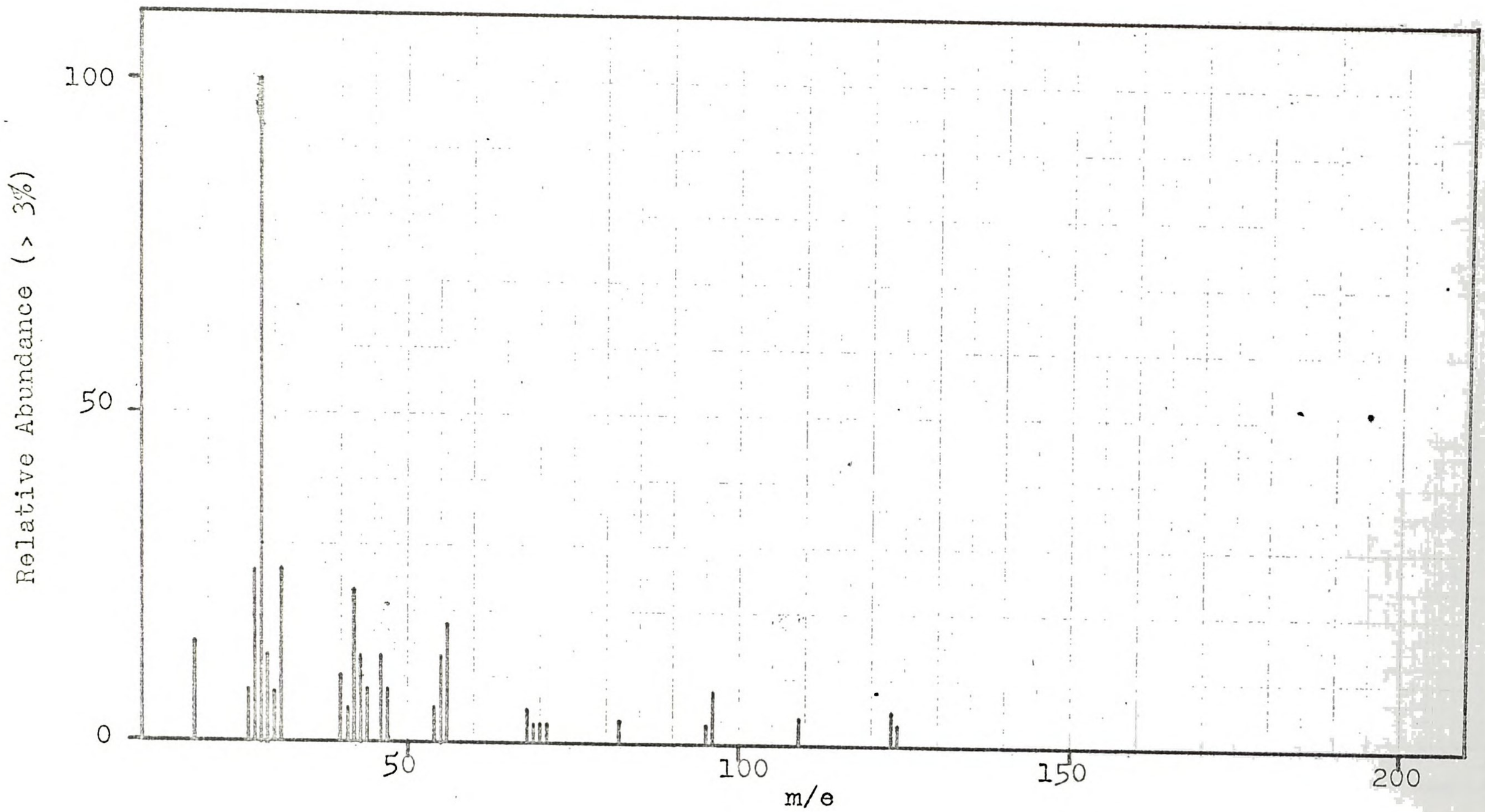


Figure 16. Mass spectrum of hexamethylenetetrazole.

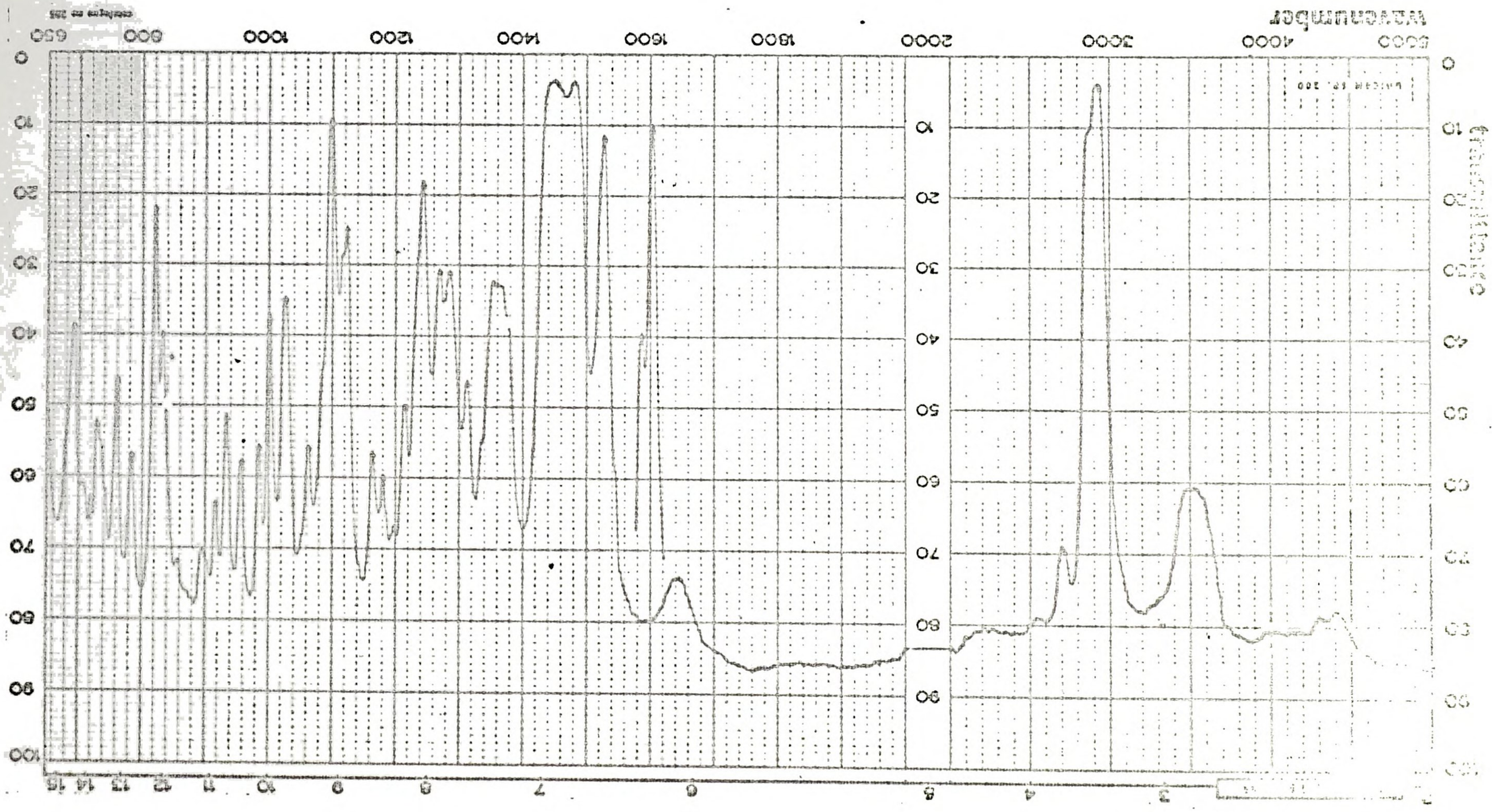


Figure 17. Infrared spectrum of heptamethylenetetrazole (KBr).

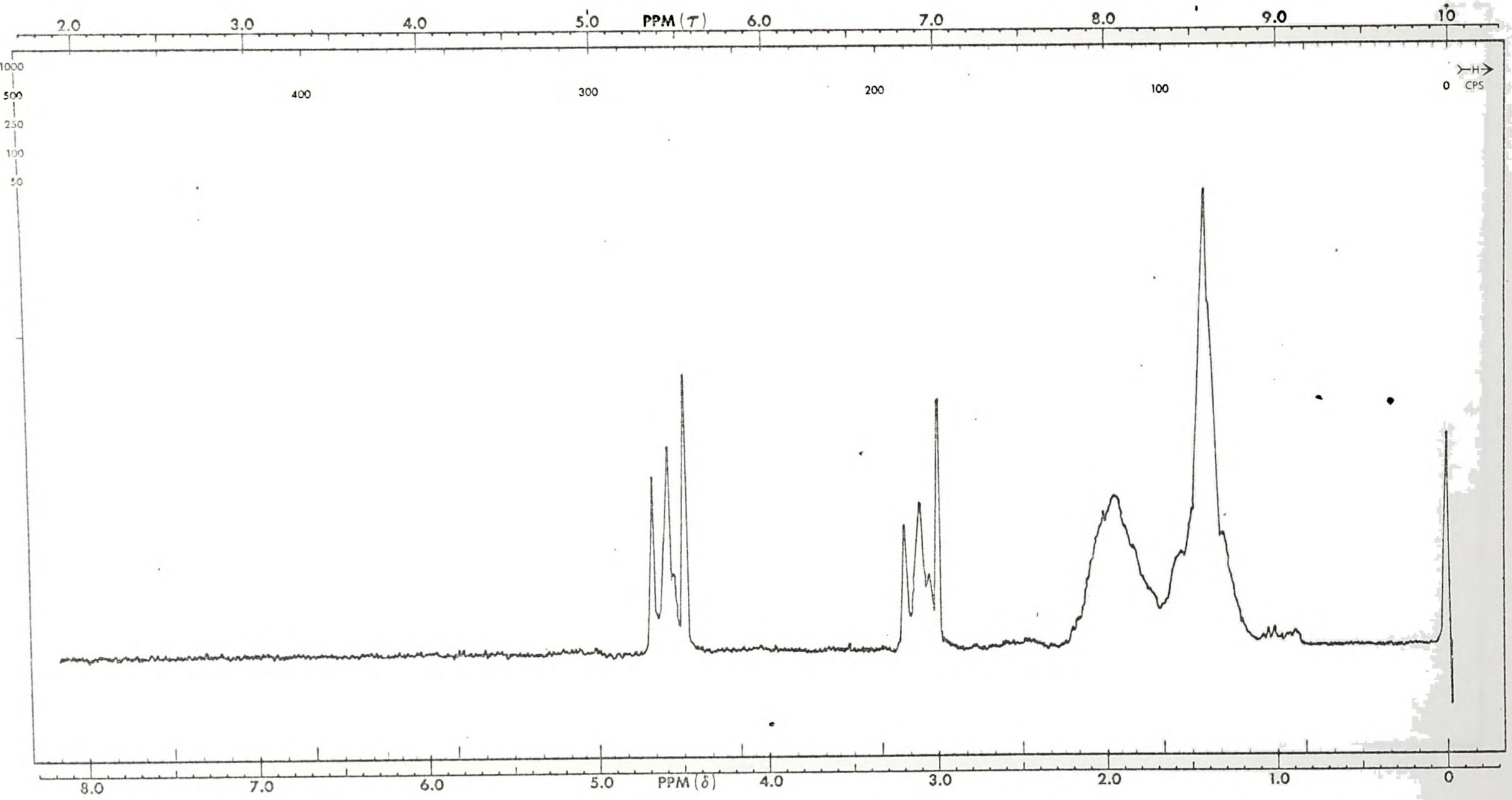


Figure 18. Nuclear magnetic resonance spectrum of heptamethylenetetrazole (CCl_4).

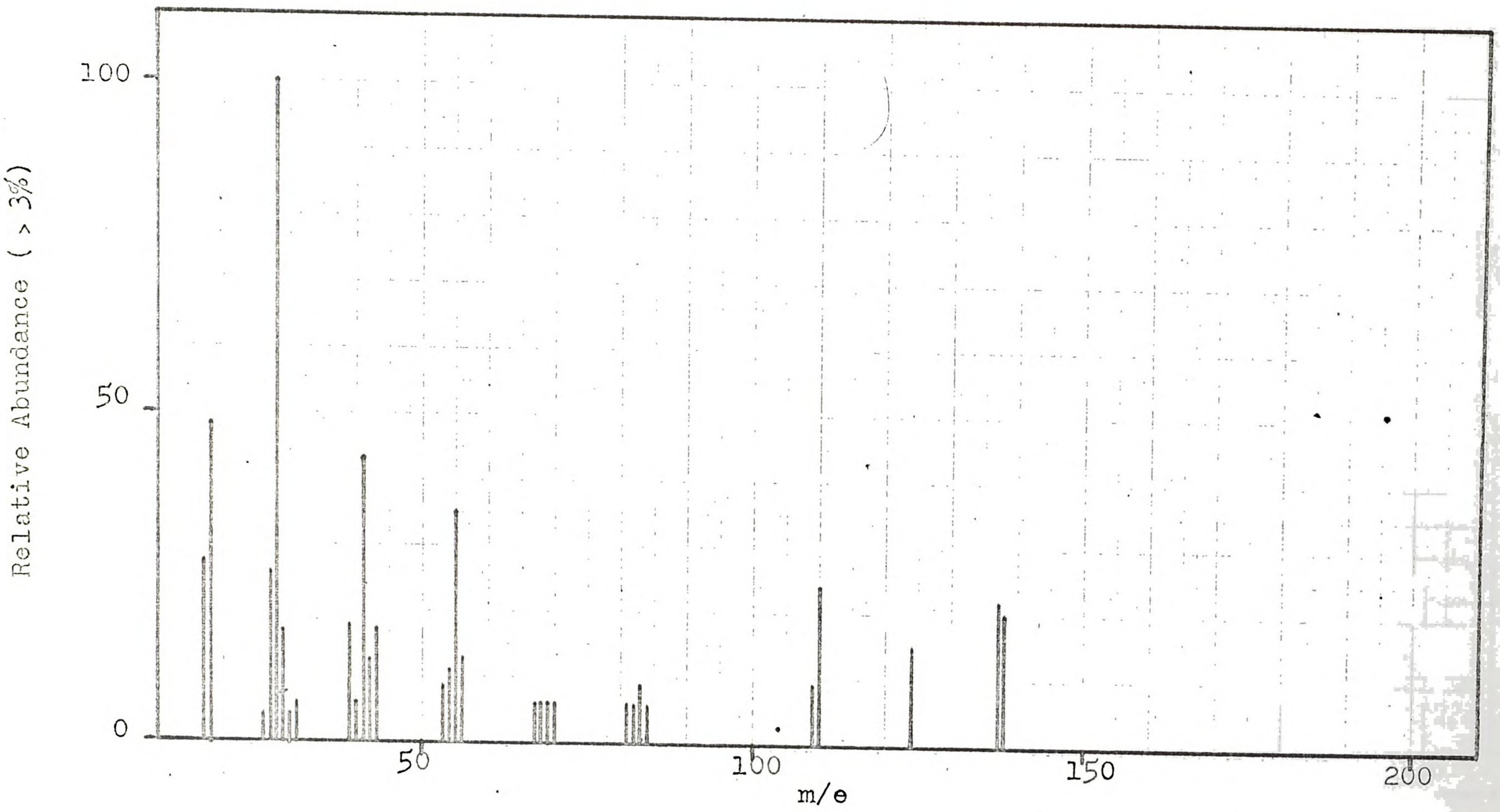


Figure 19. Mass spectrum of heptamethylenetetrazole.

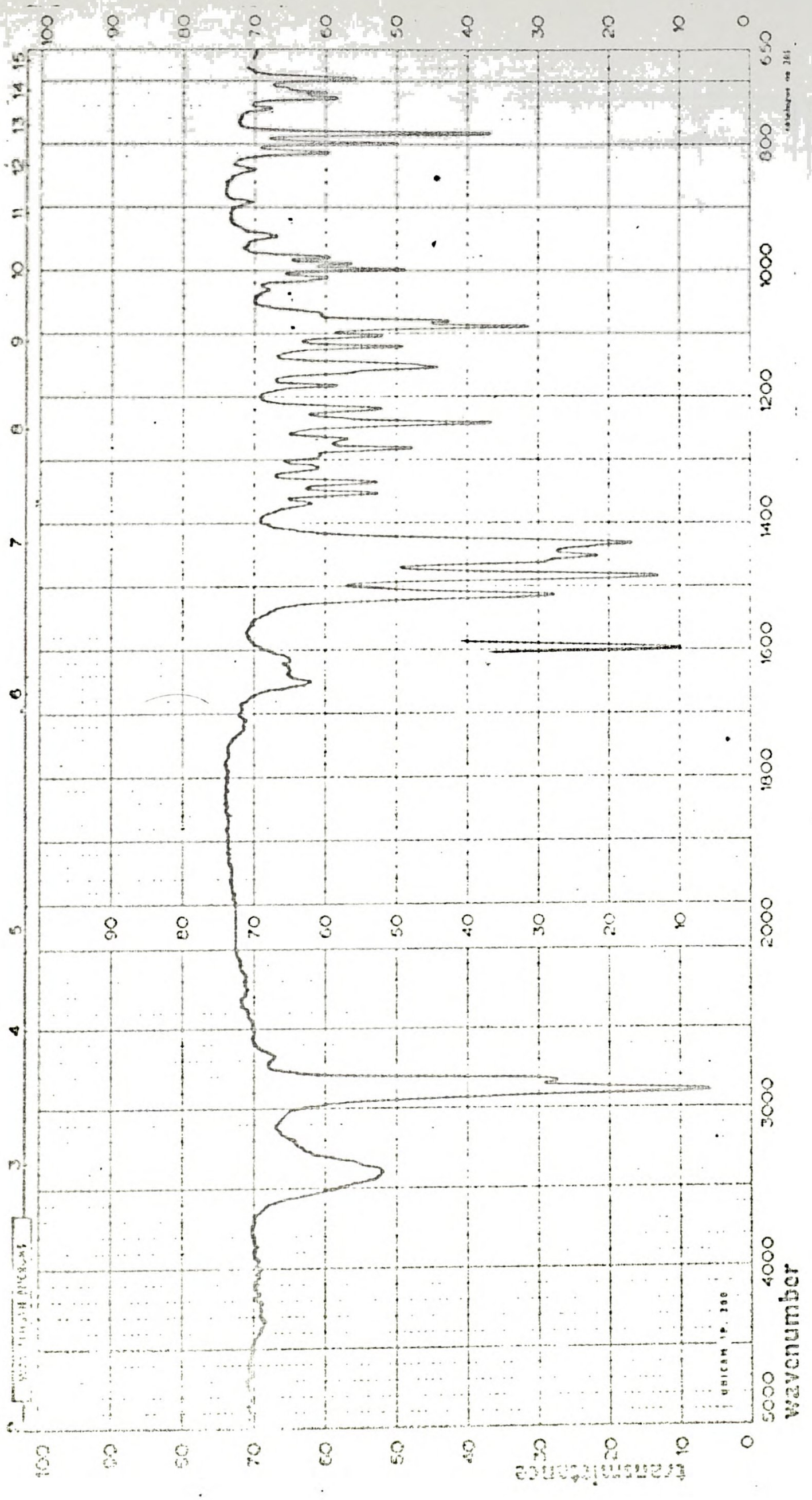


Figure 20. Infrared spectrum of octamethylenetetrazole (KBr).

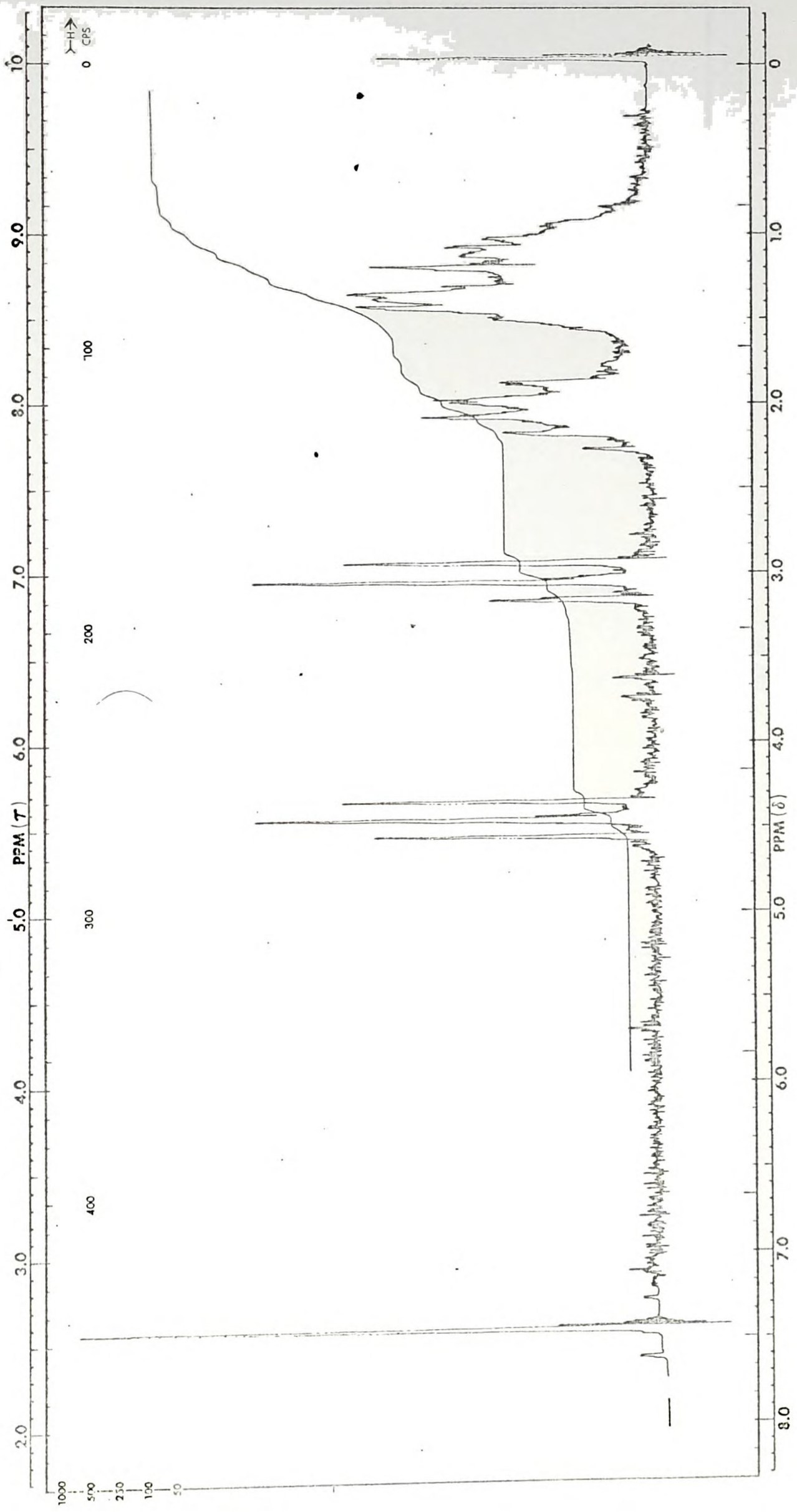


Figure 21. Nuclear magnetic resonance spectrum of octamethylenetetrazole ($CHCl_3$).

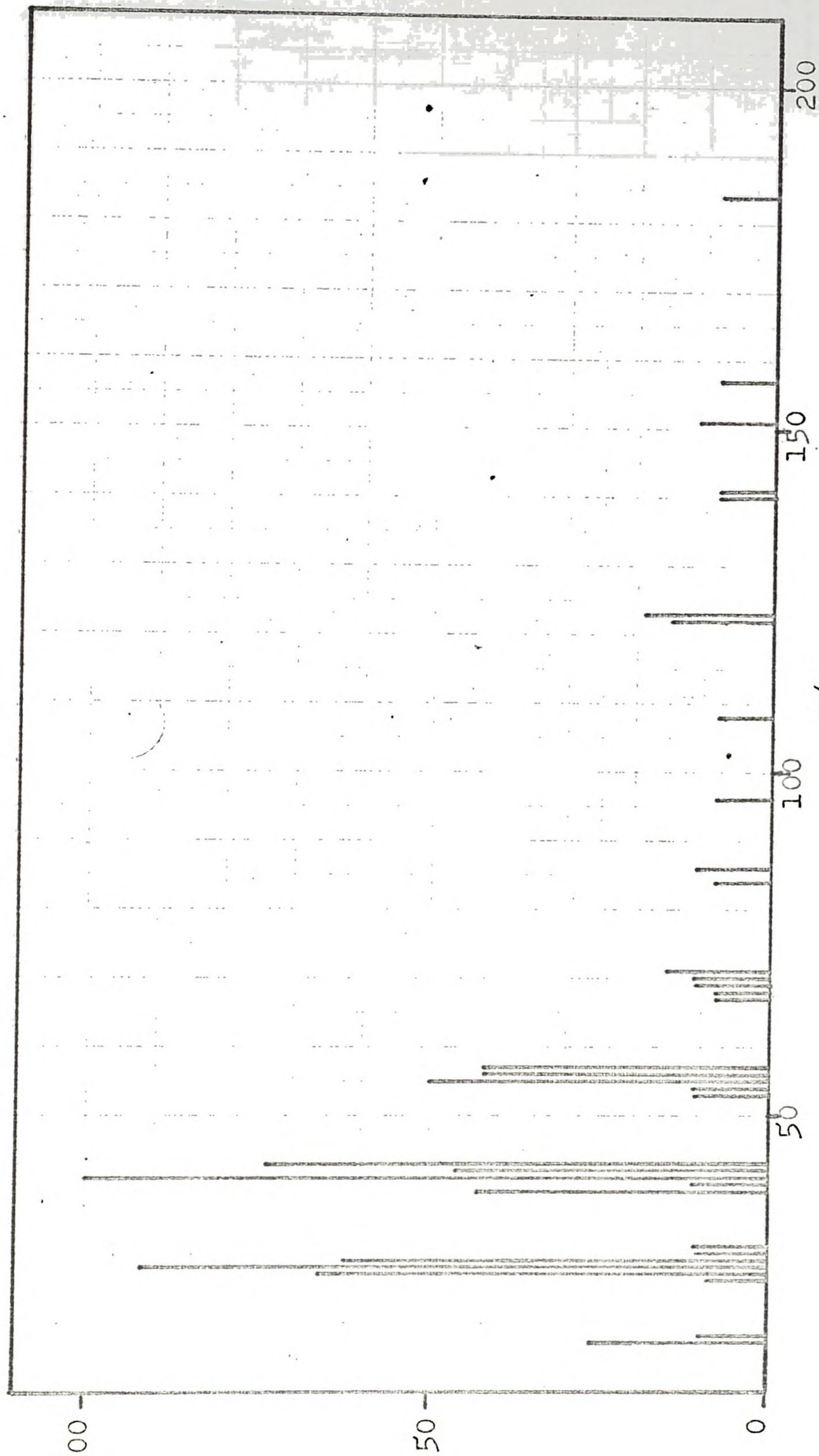


Figure 22. Mass spectrum of octamethylenetetrazole.

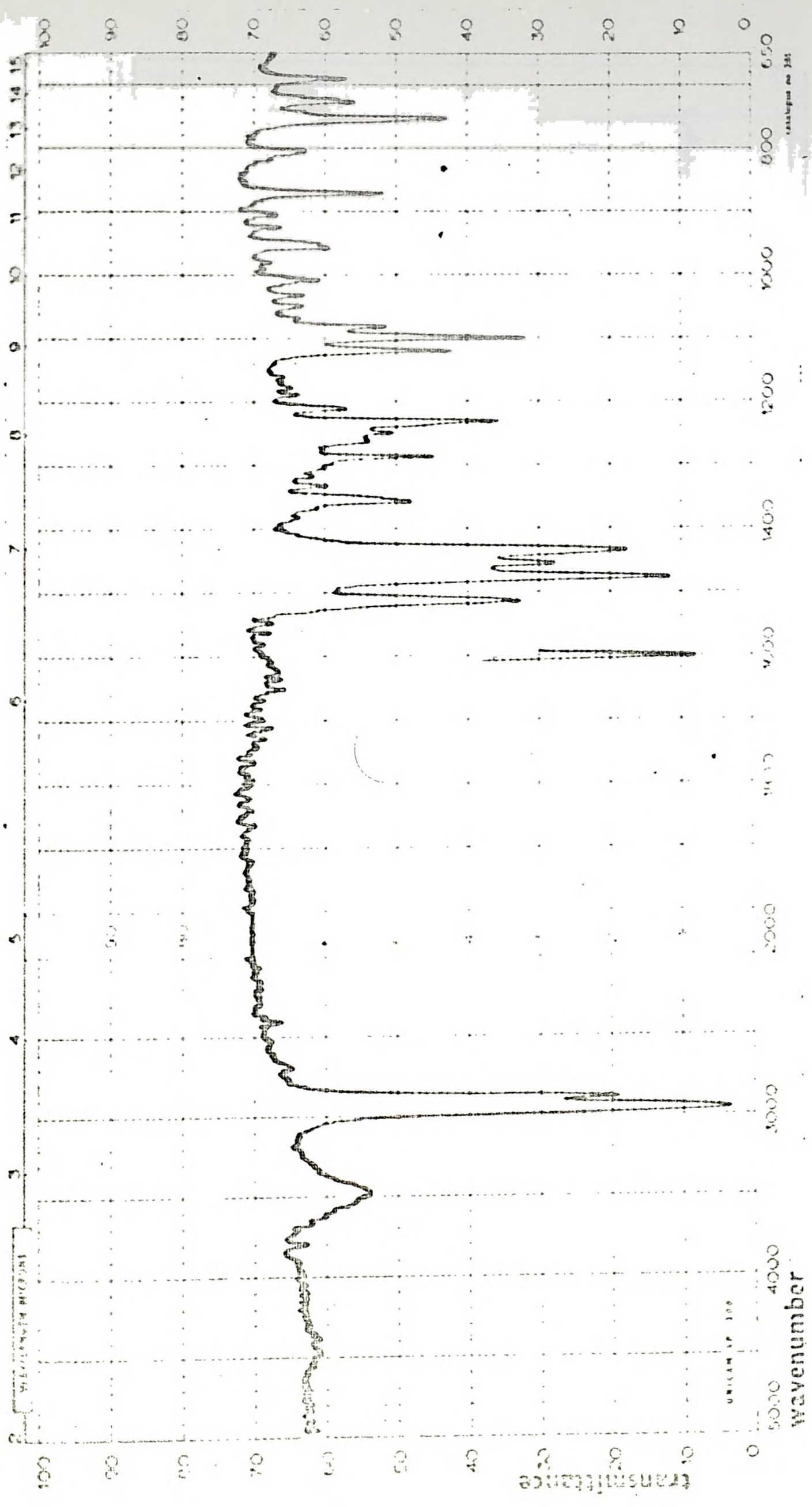


Figure 23. Infrared spectrum of nonamethylenetetrazole (KBr).

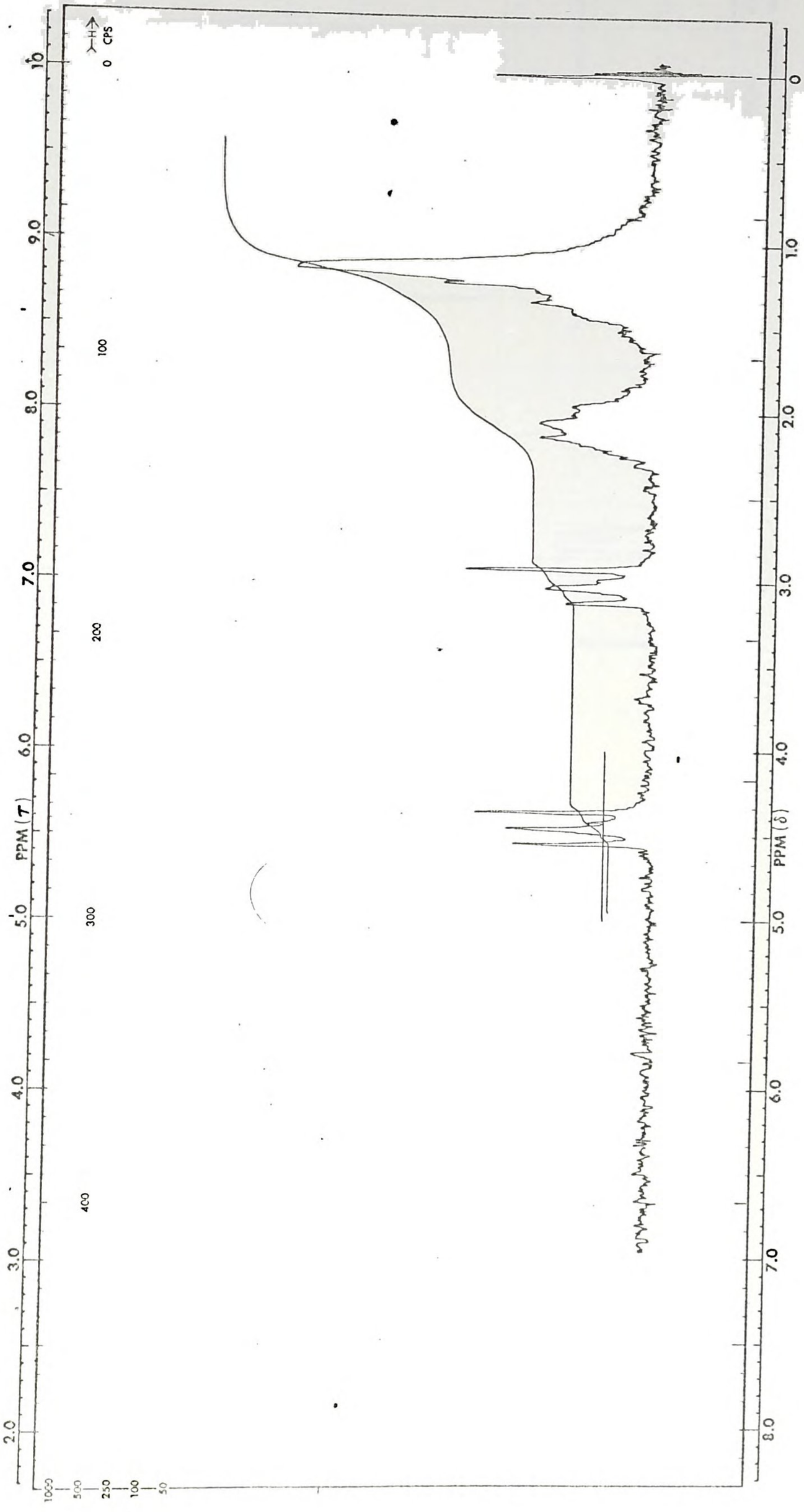


Figure 24. Nuclear magnetic resonance spectrum of nonamethylenetetrazole ($CHCl_3$).

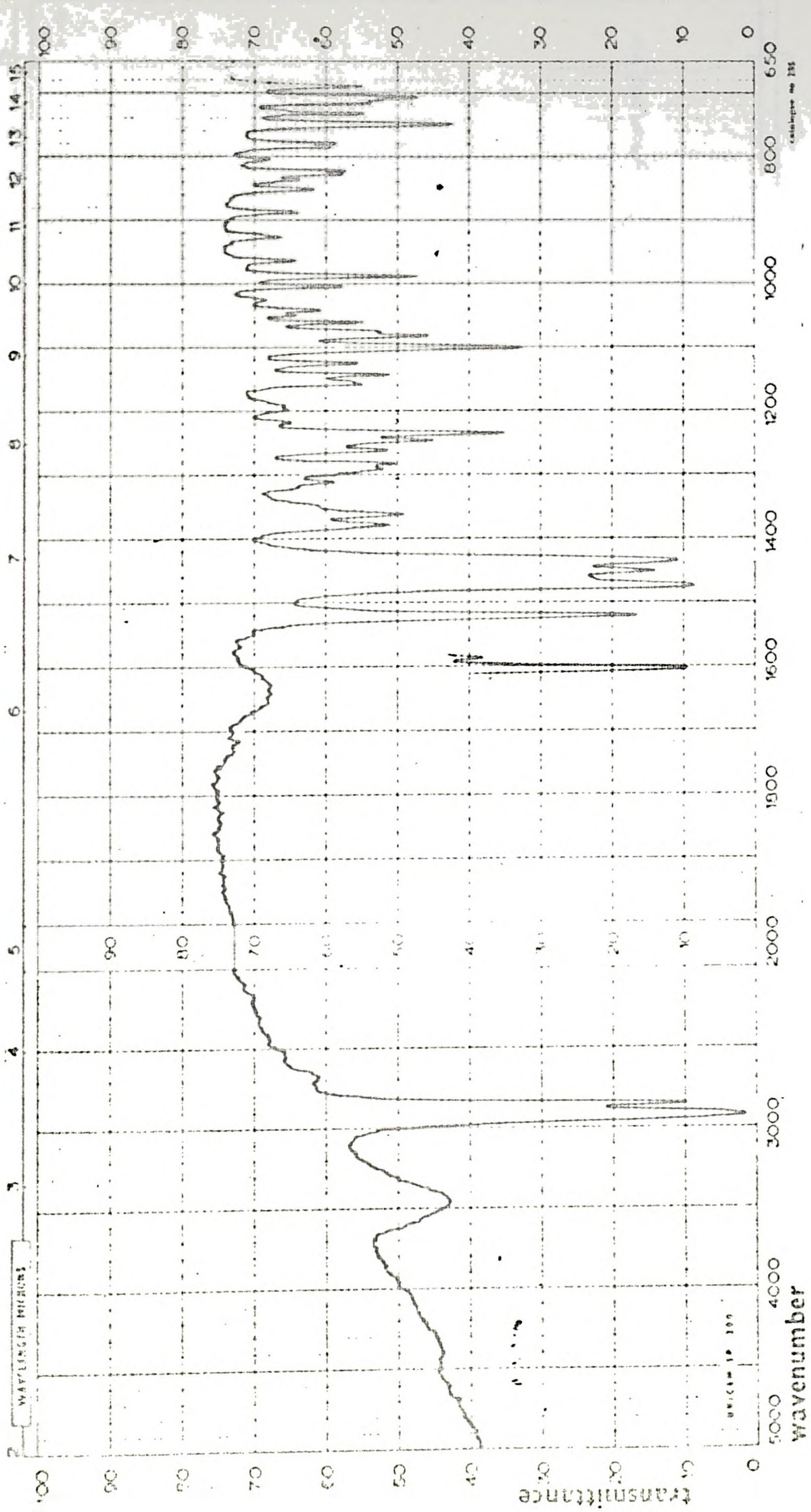


Figure 25. Infrared spectrum of undecamethylenetetrazole (KBr).

0.0
0.5
0.7
0.9
1.0

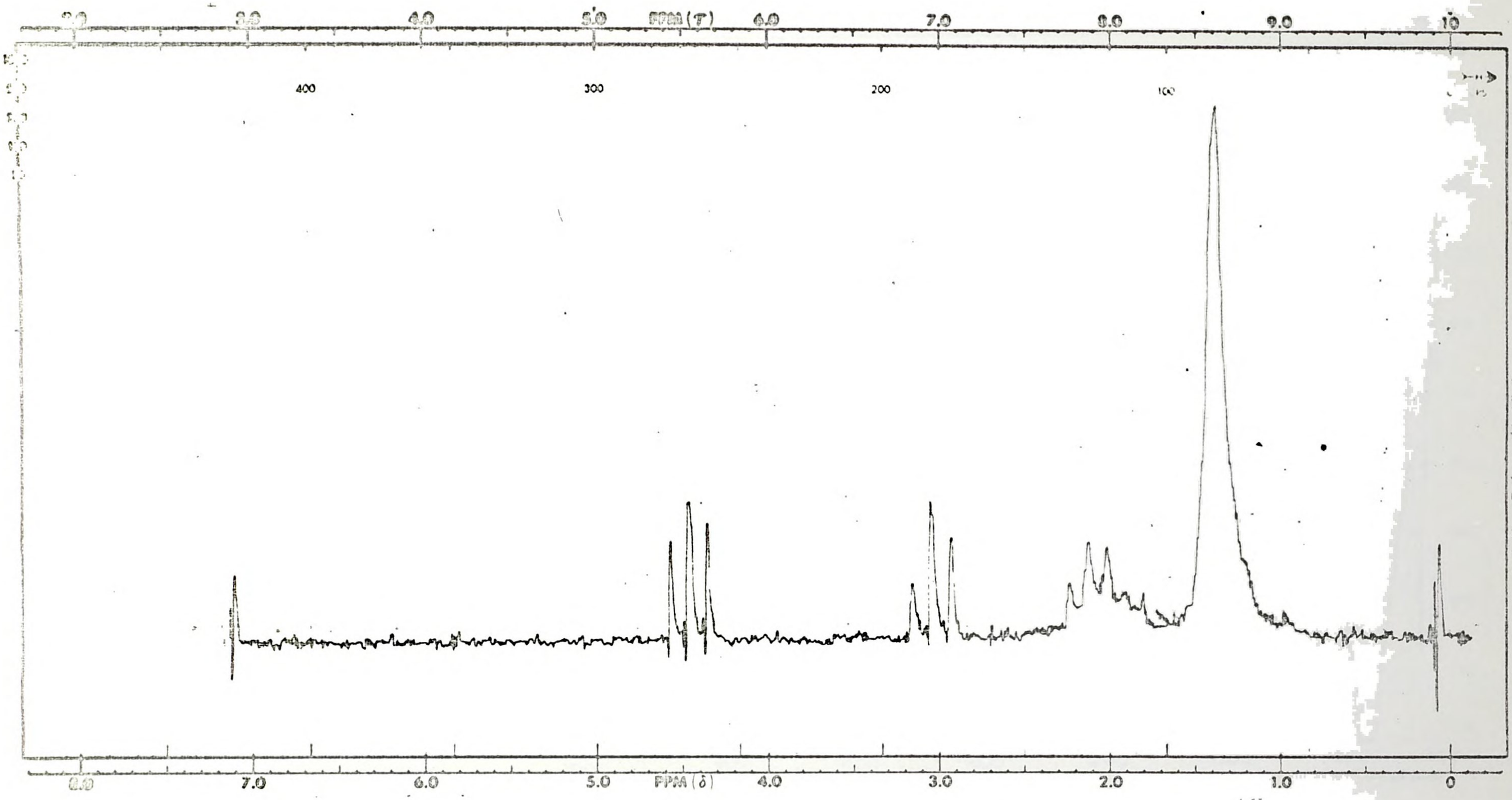


Figure 26. Nuclear magnetic resonance spectrum of undecamethylenetetrazole ($CHCl_3$).

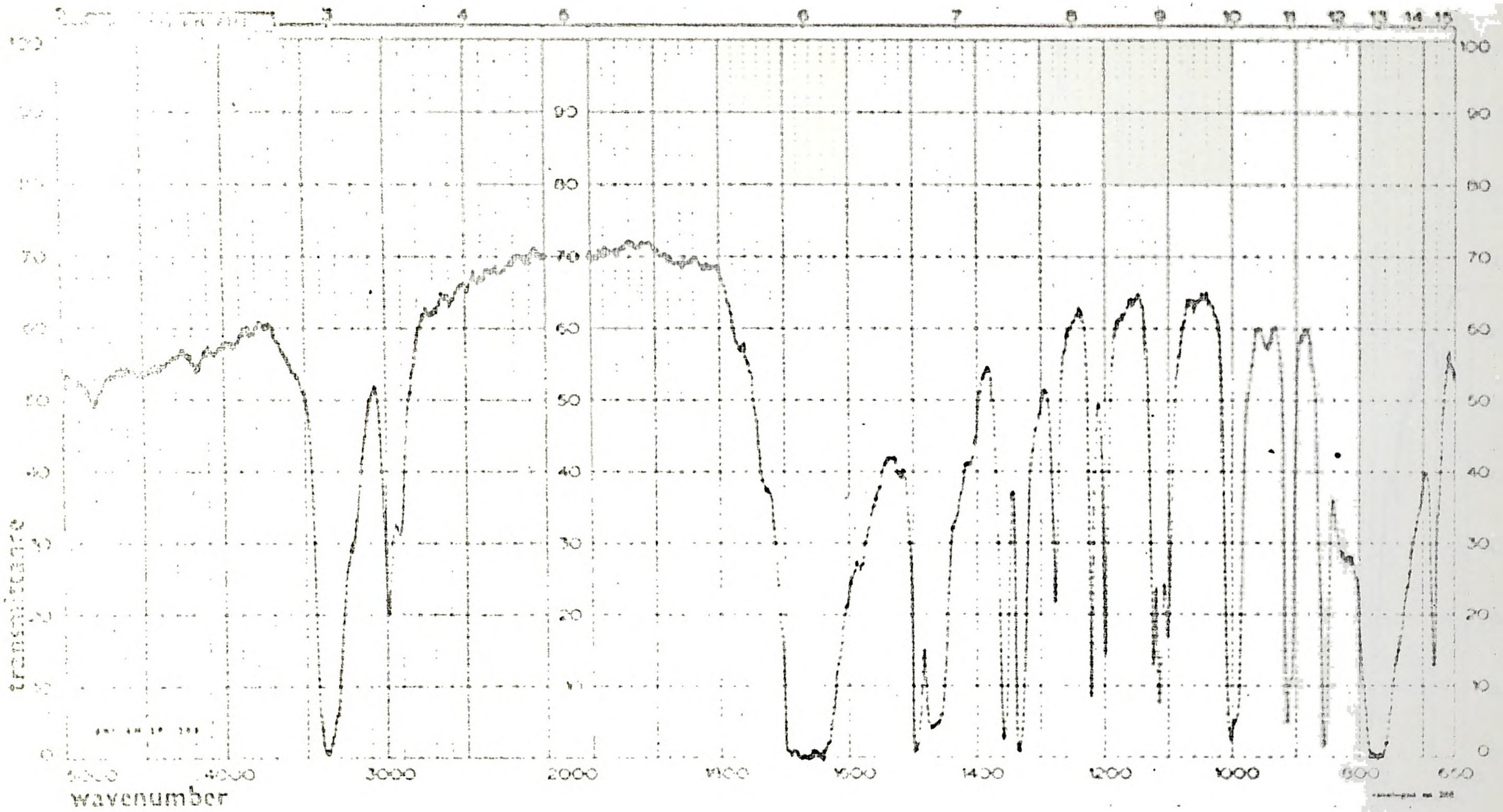


Figure 27. Infrared spectrum of 2,2-dichloro-6-azacyclo-hexanone (KBr).

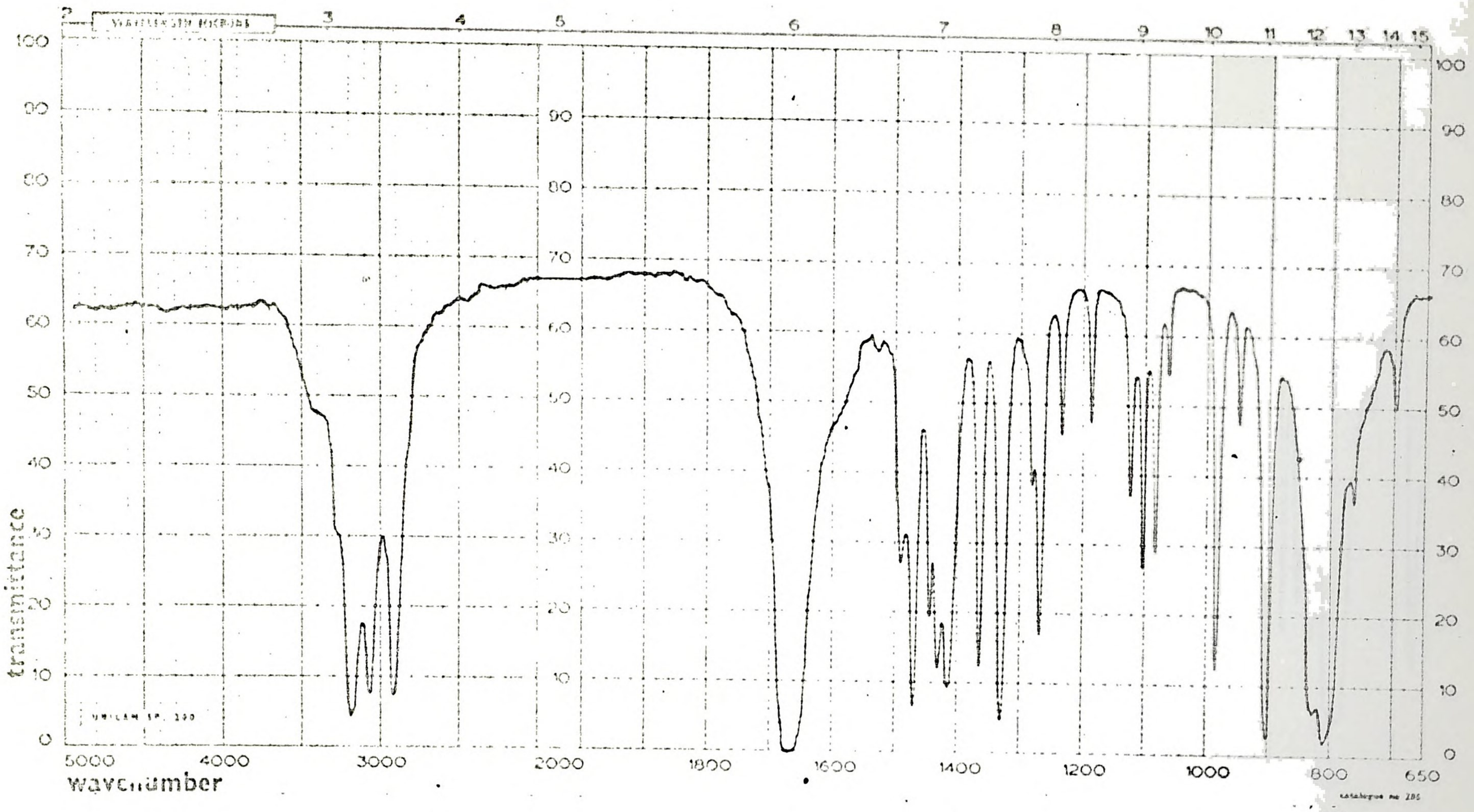


Figure 28. Infrared spectrum of 2,2-dichloro-7-azacycloheptanone (KBr).

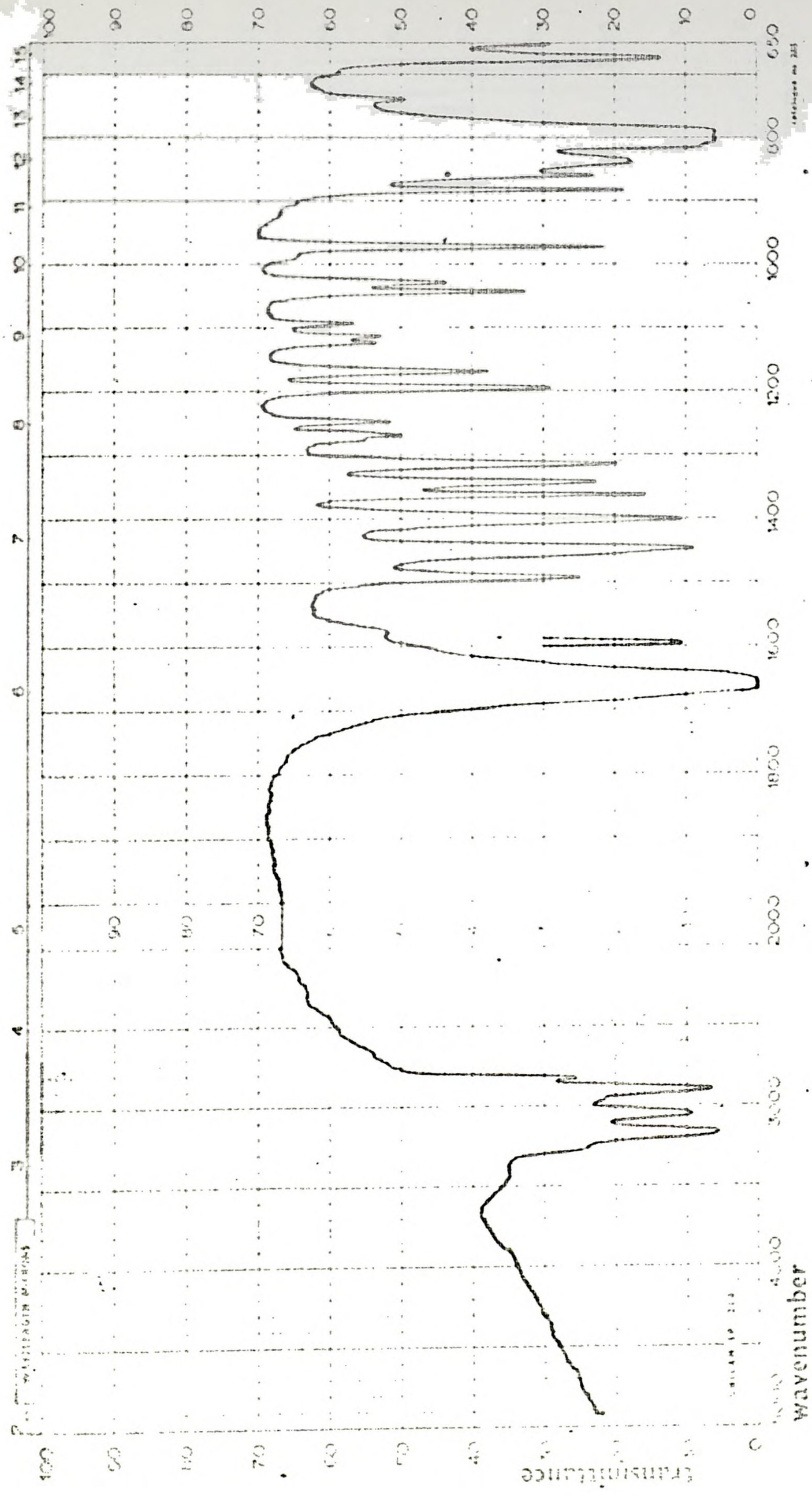


Figure 29. Infrared spectrum of 2,2-dichloro-8-azacyclooctanone (KBr).

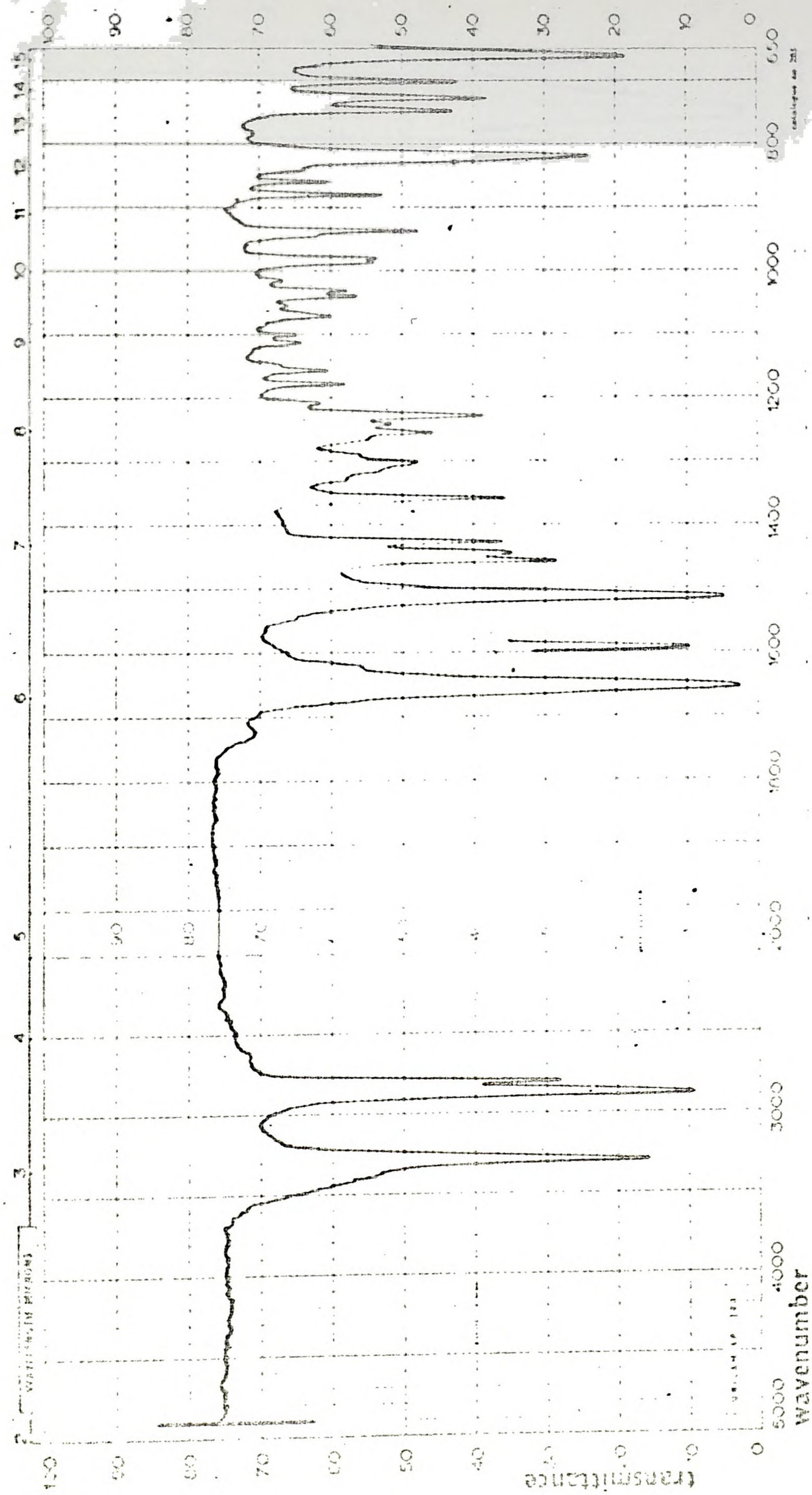


Figure 30. Infrared spectrum of 2,2-dichloro-13-azacyclotridecanone (KBr).

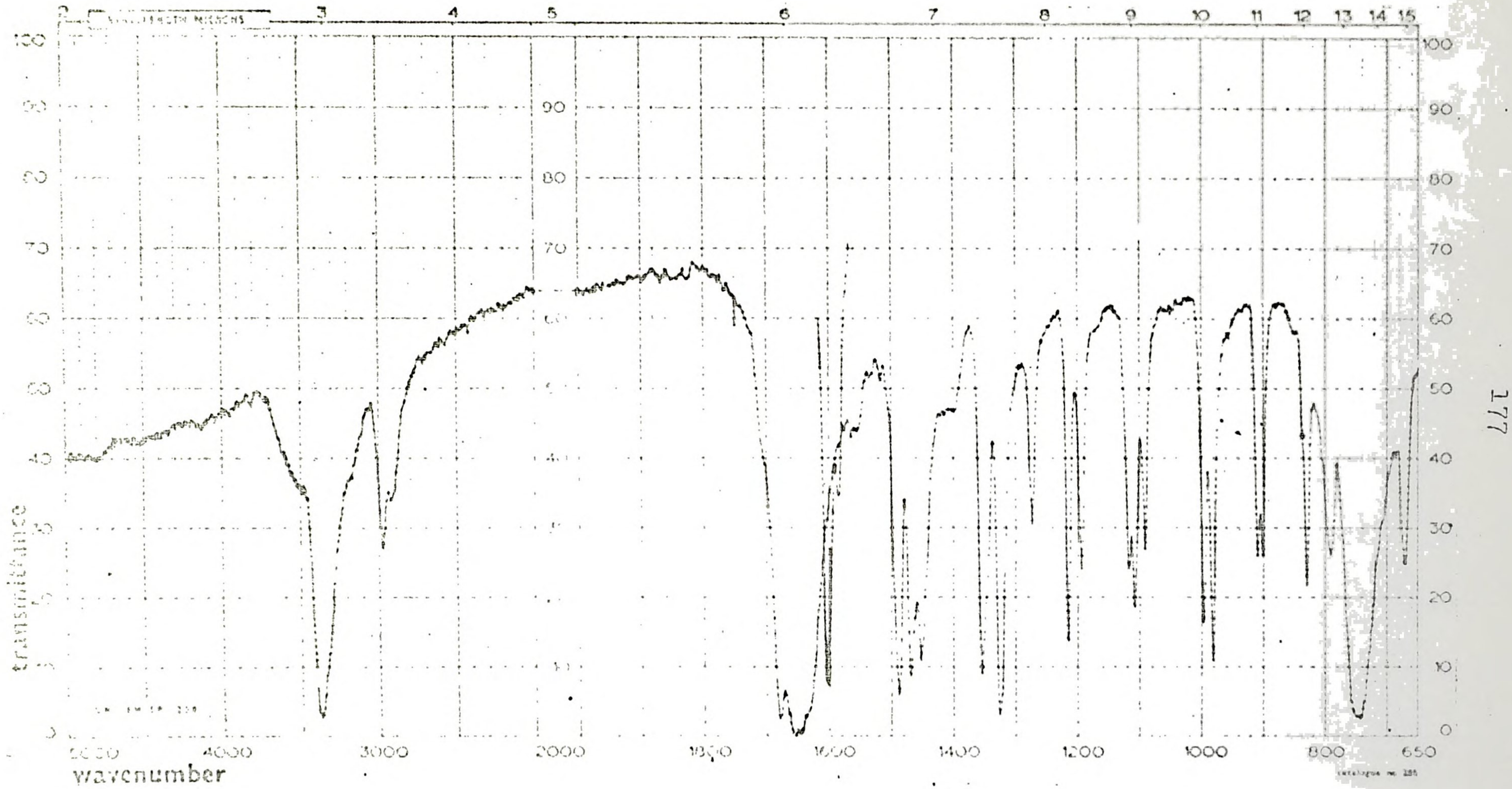


Figure 31. Infrared spectrum of 2,2-dibromo-6-azacyclohexanone (KBr).

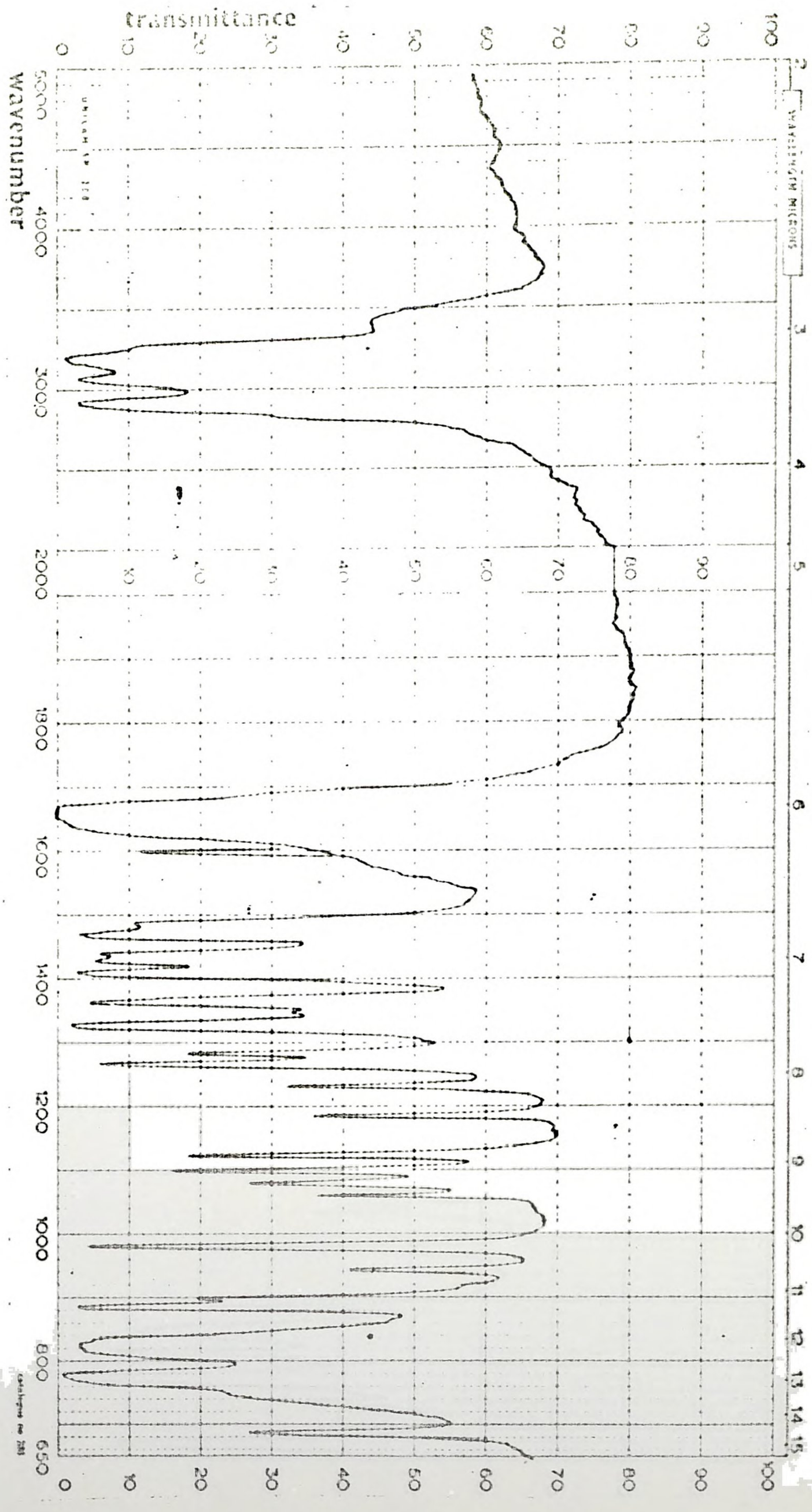


Figure 32. Infrared spectrum of 2,2-dibromo-7-azacycloheptanone (KBr).

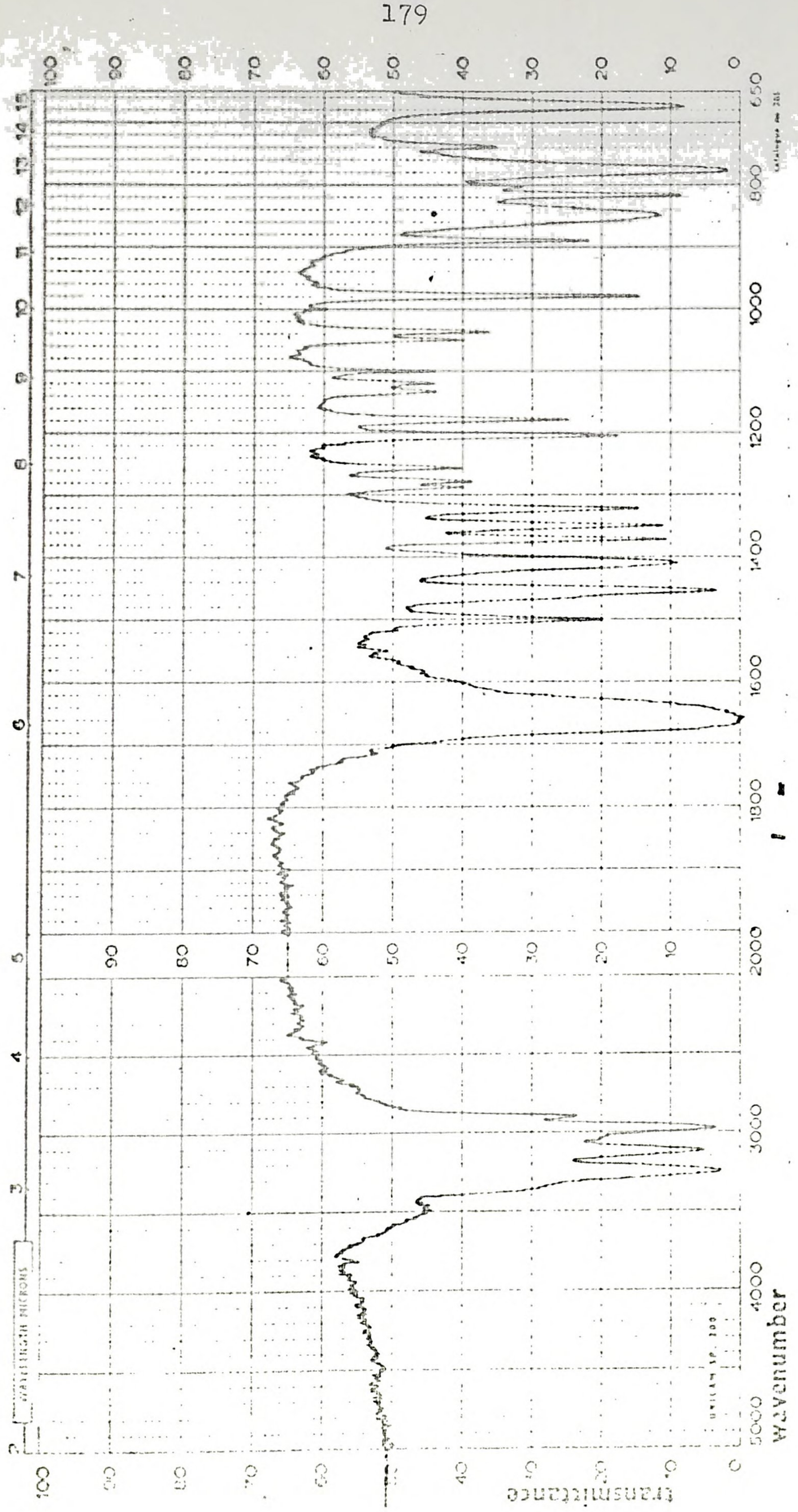


Figure 33. Infrared spectrum of 2,2-dibromo-8-azacyclooctanone (KBr).

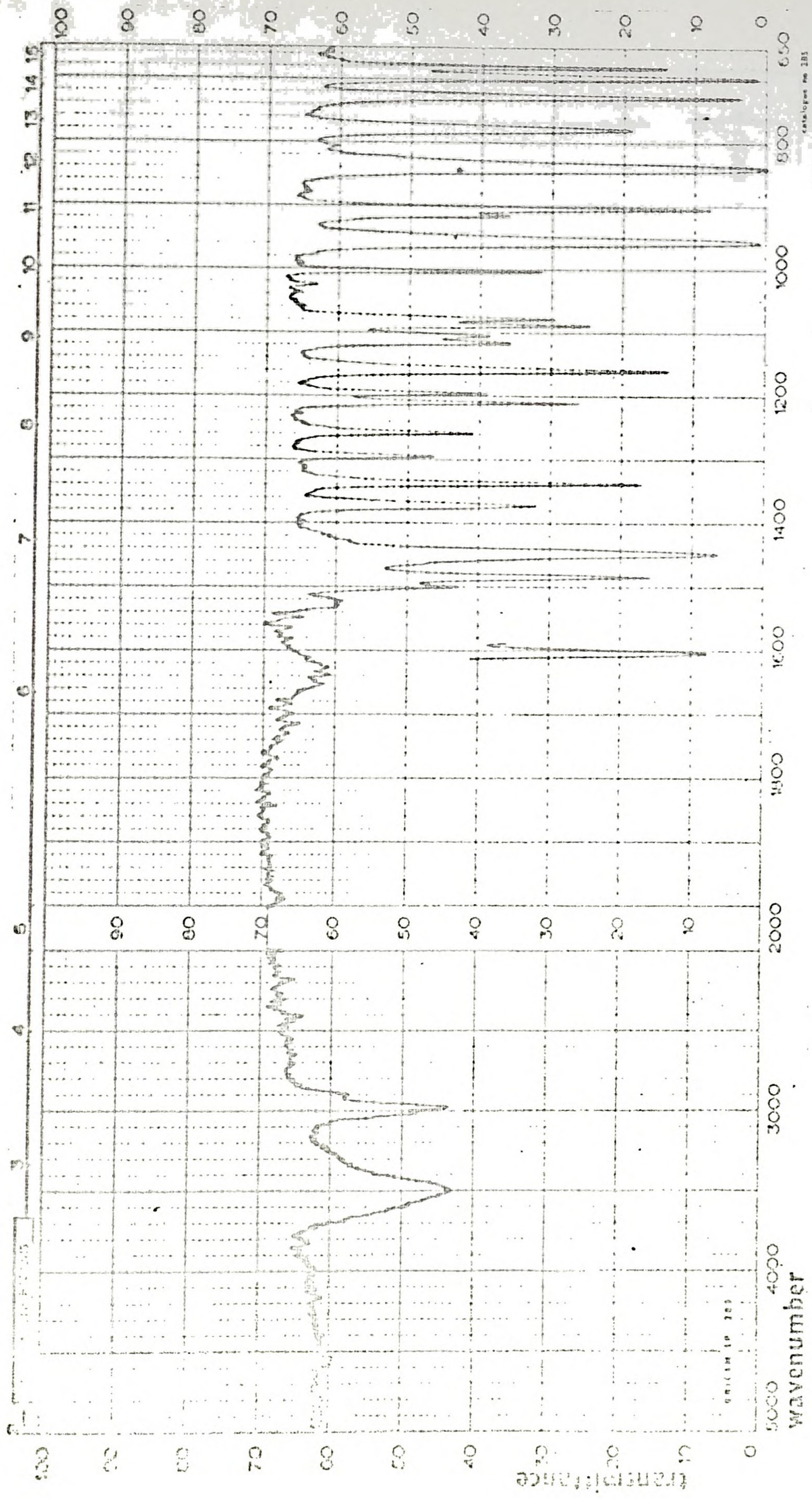


Figure 34. Infrared spectrum of 6,6-dichlorotetramethylenetetrazole (KBr).

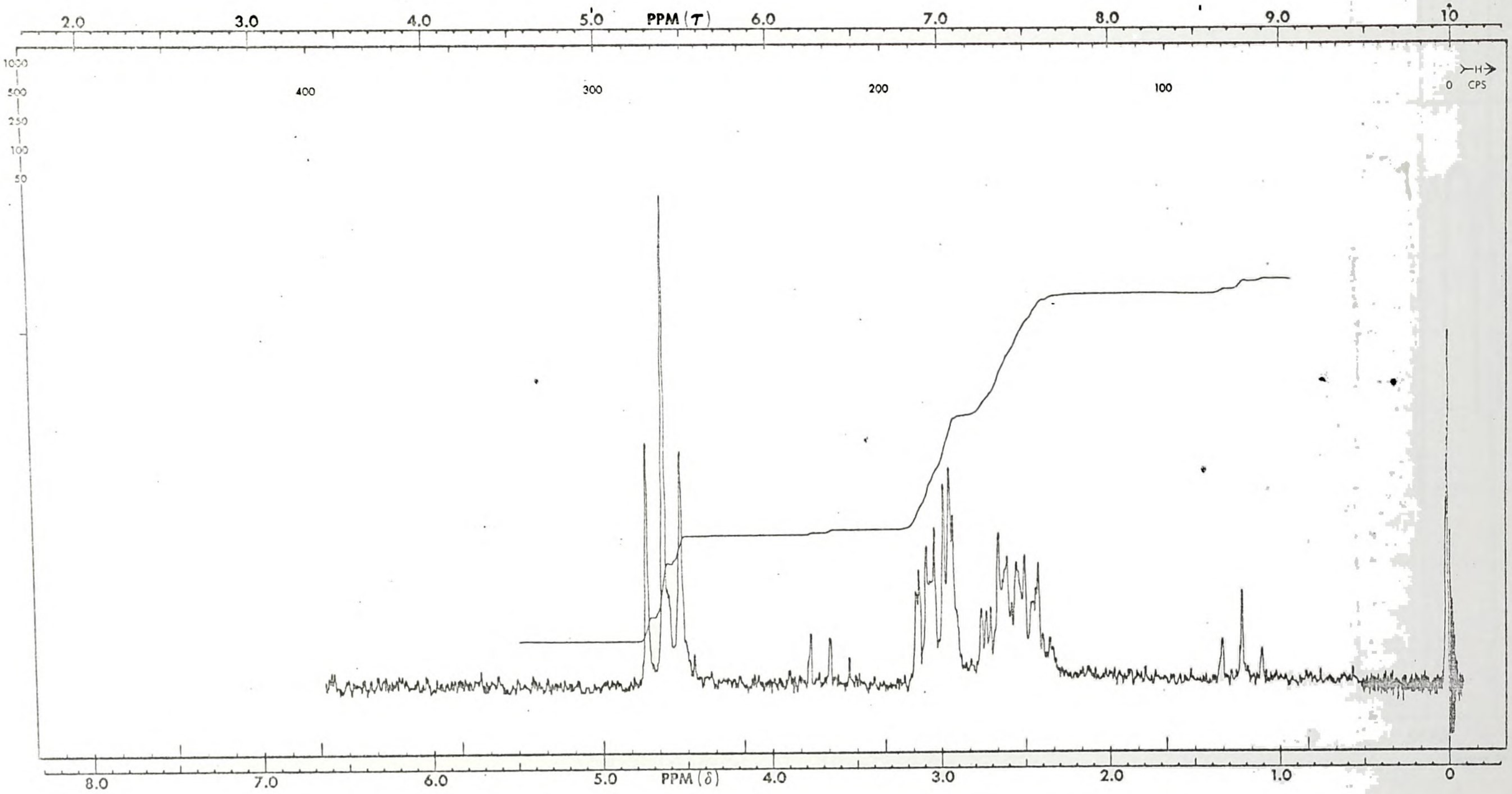


Figure 35. Nuclear magnetic resonance spectrum of 6,6-dichlorotetramethylenetetrazole ($CHCl_3$).

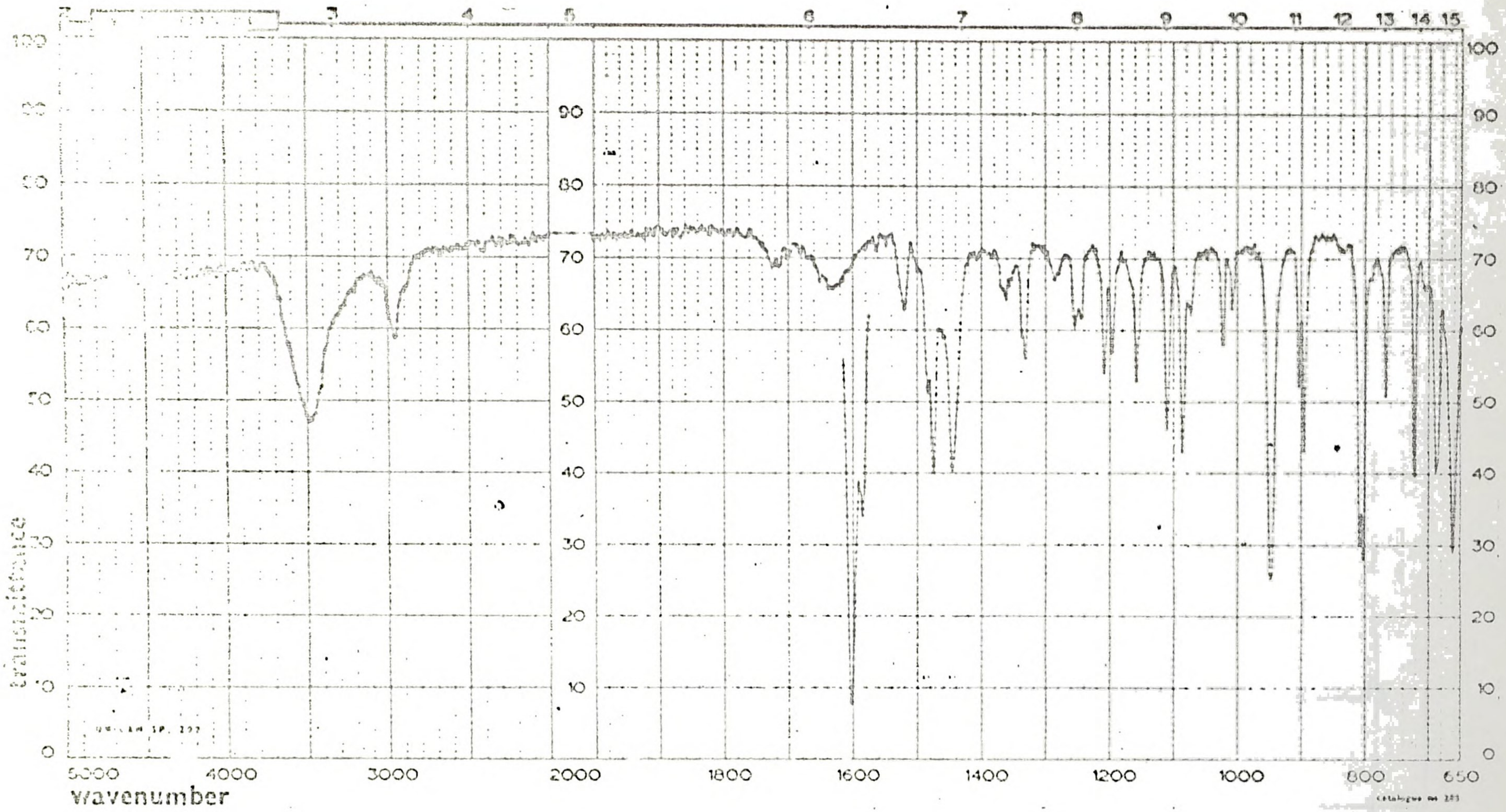


Figure 36. Infrared spectrum of 6,6-dibromotetramethylenetetrazole (KBr).

Figure 37. Nuclear magnetic resonance spectrum of 6,6-dibromotetramethylenetetrazole ($CHCl_3$).

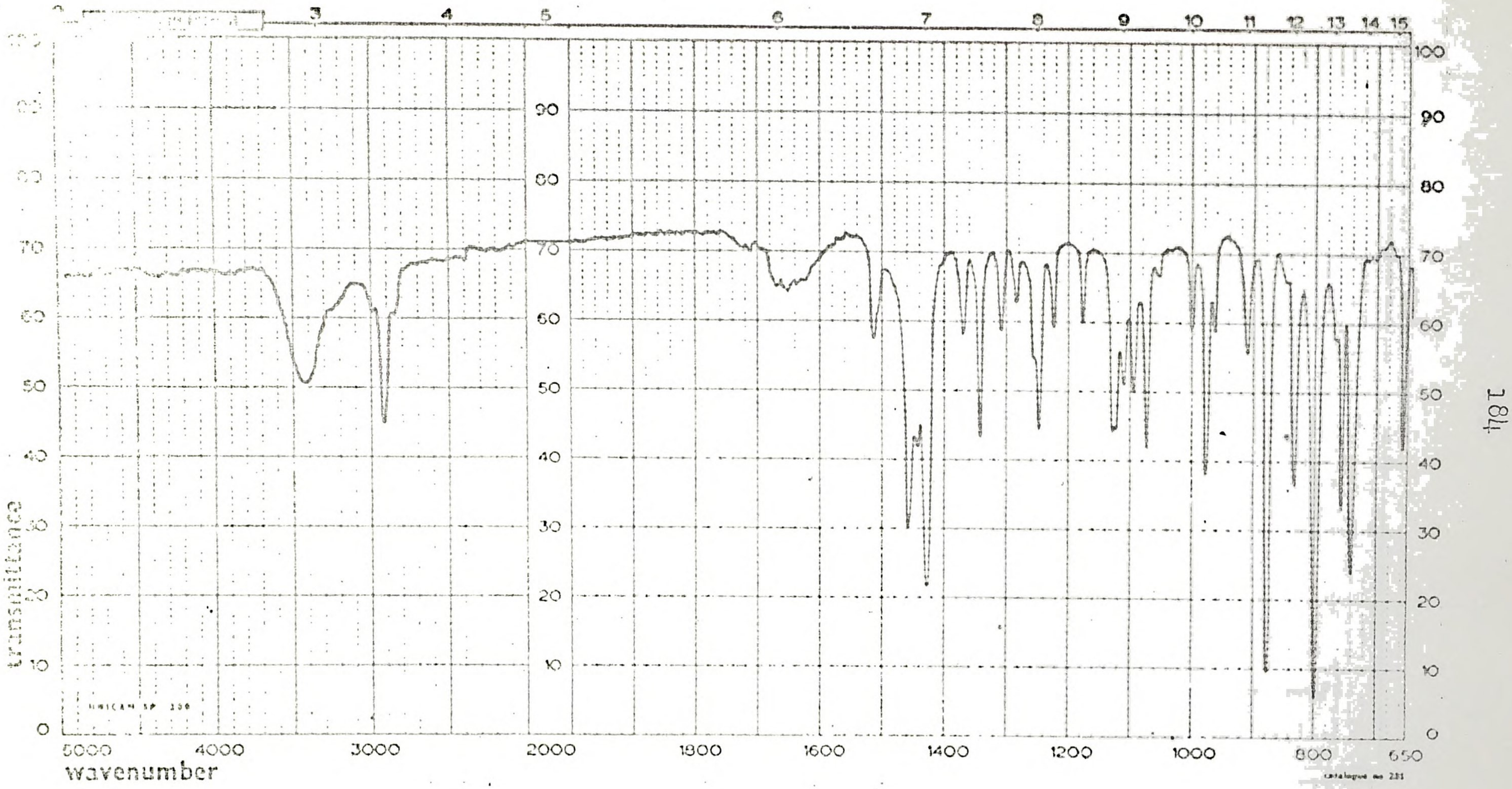


Figure 38. Infrared spectrum of 6,6-dichloropentamethylenetetrazole (KBr).

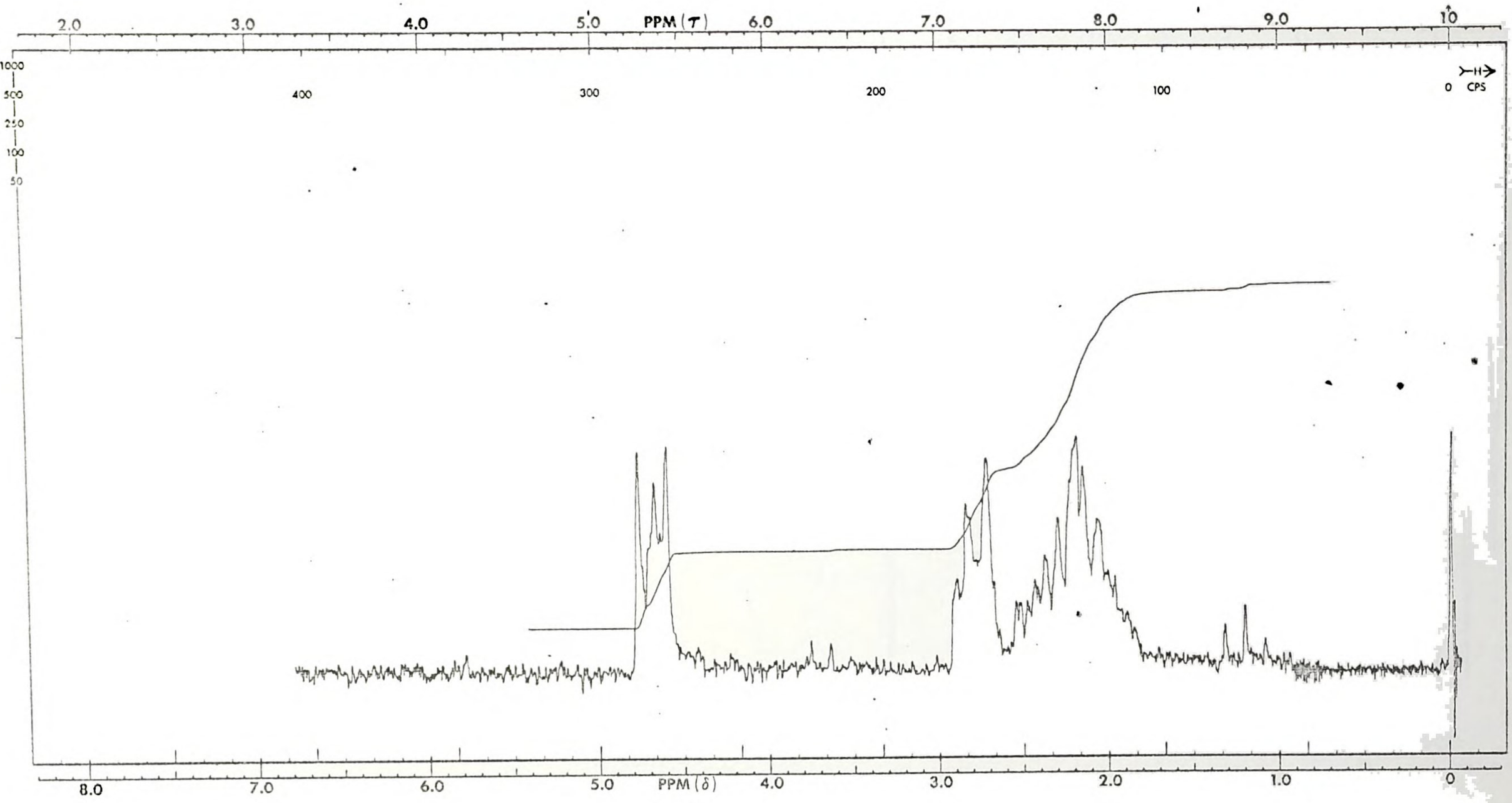


Figure 39. Nuclear magnetic resonance spectrum of 6,6-dichloropentamethylenetetrazole ($CHCl_3$).

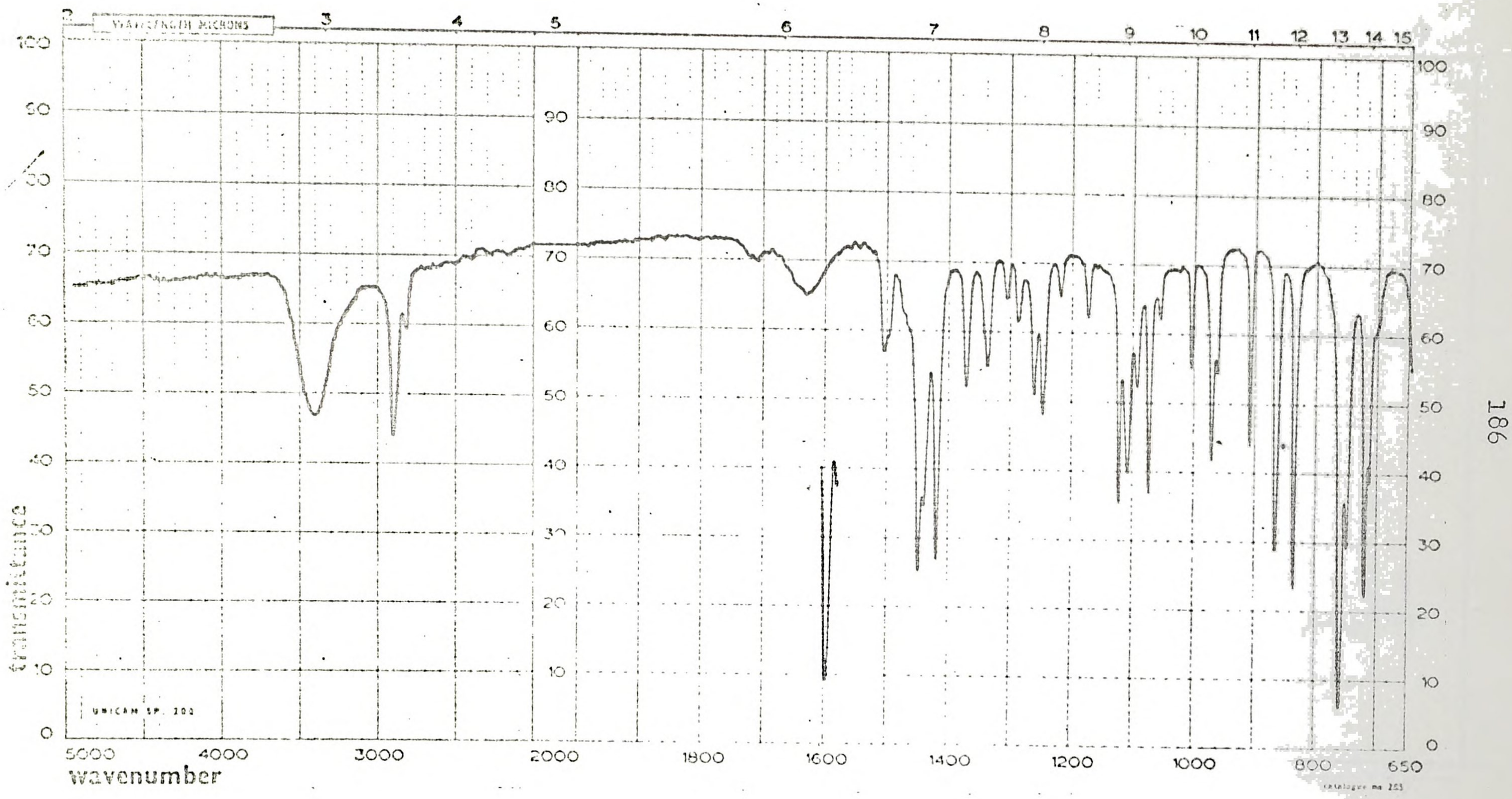


Figure 40. Infrared spectrum of 6,6-dibromopentamethylenetetrazole (KBr).

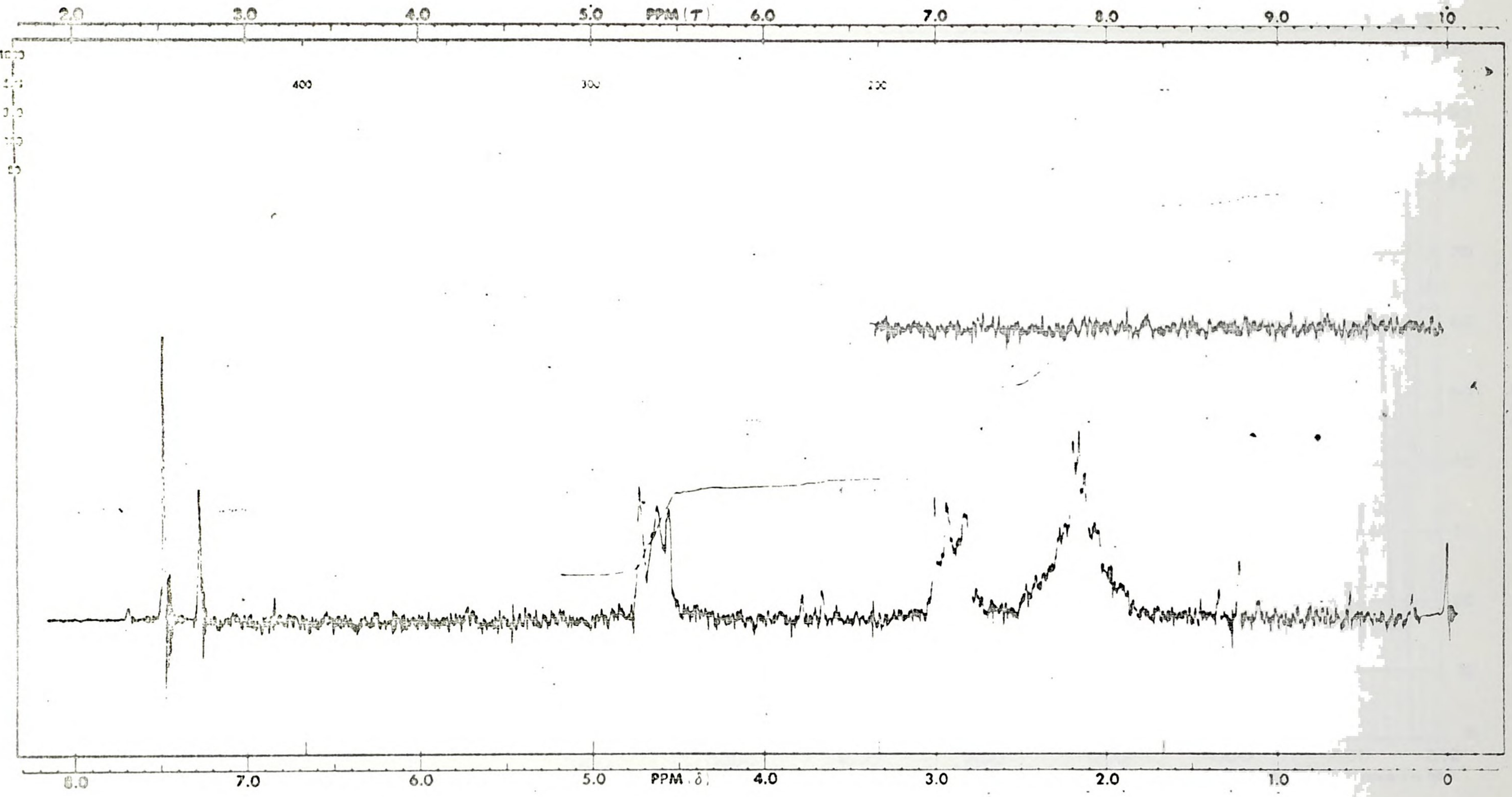


Figure 41. Nuclear magnetic resonance spectrum of 6,6-dibromopentamethylenetetrazole ($CHCl_3$).

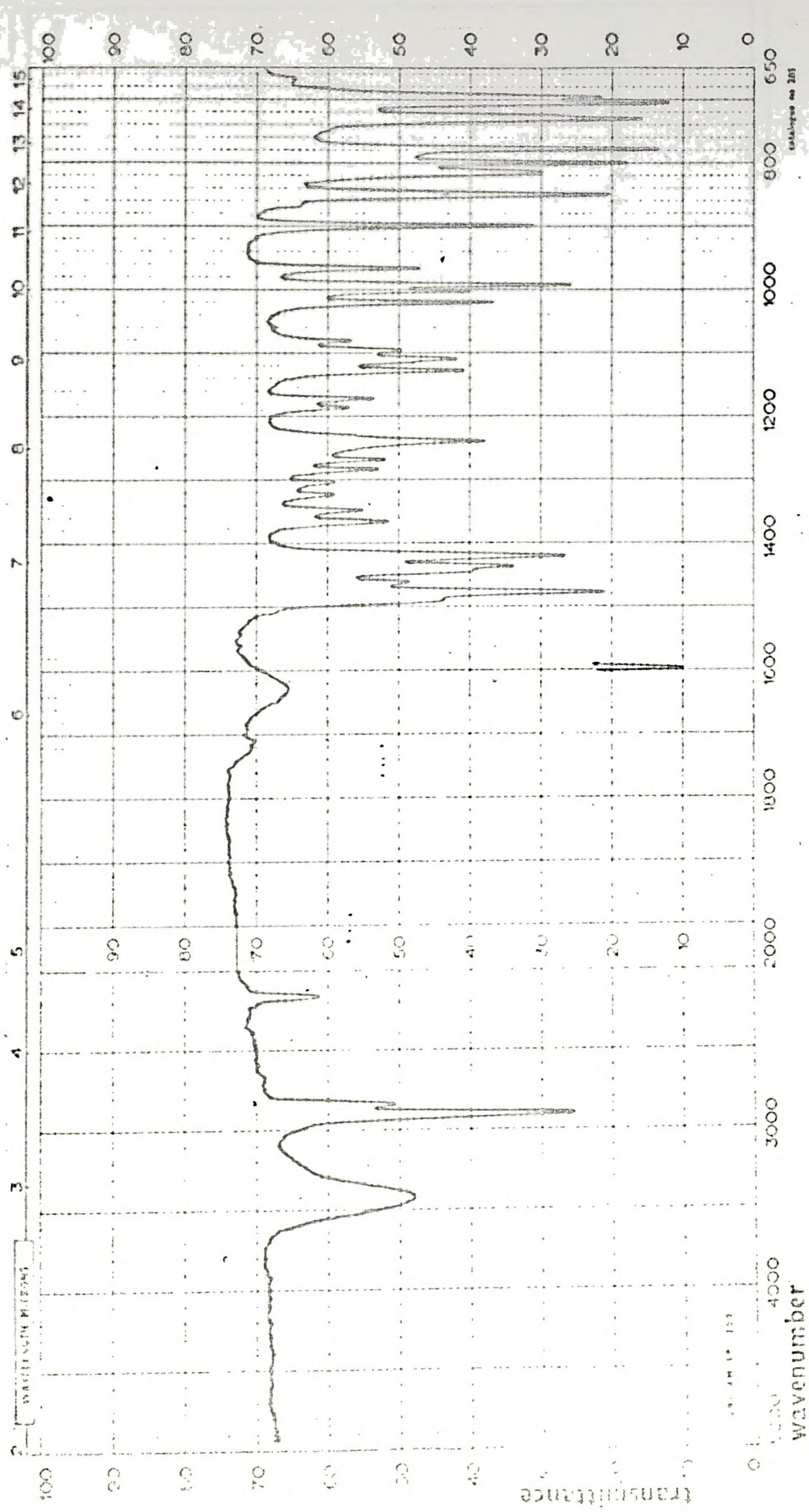


Figure 42. Infrared spectrum of 6,6-dichlorohexamethylenetetrazole (KBr).

10
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0

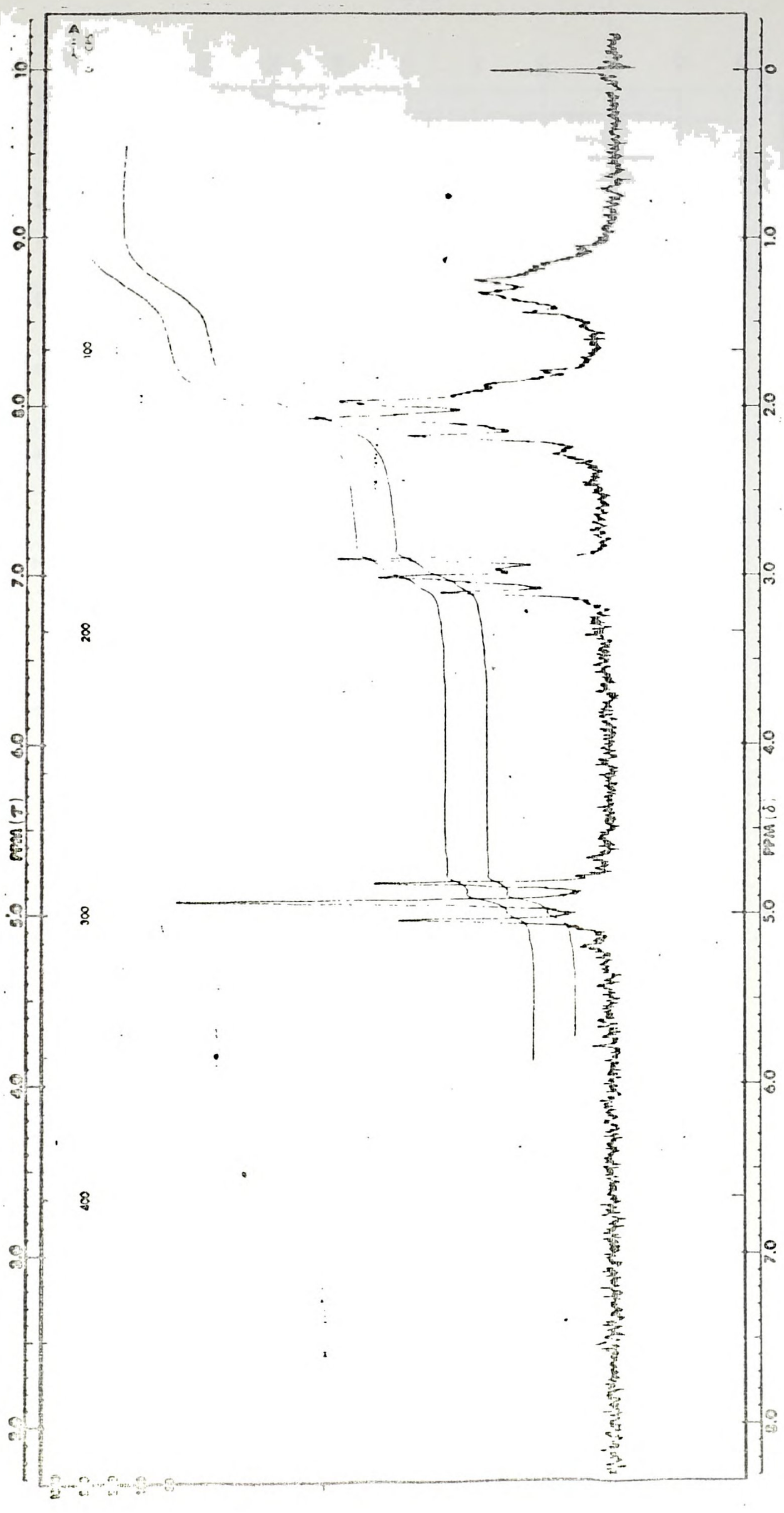


Figure 43. Nuclear magnetic resonance spectrum of 6,6-dichlorohexamethylenetetrazole ($CHCl_3$).

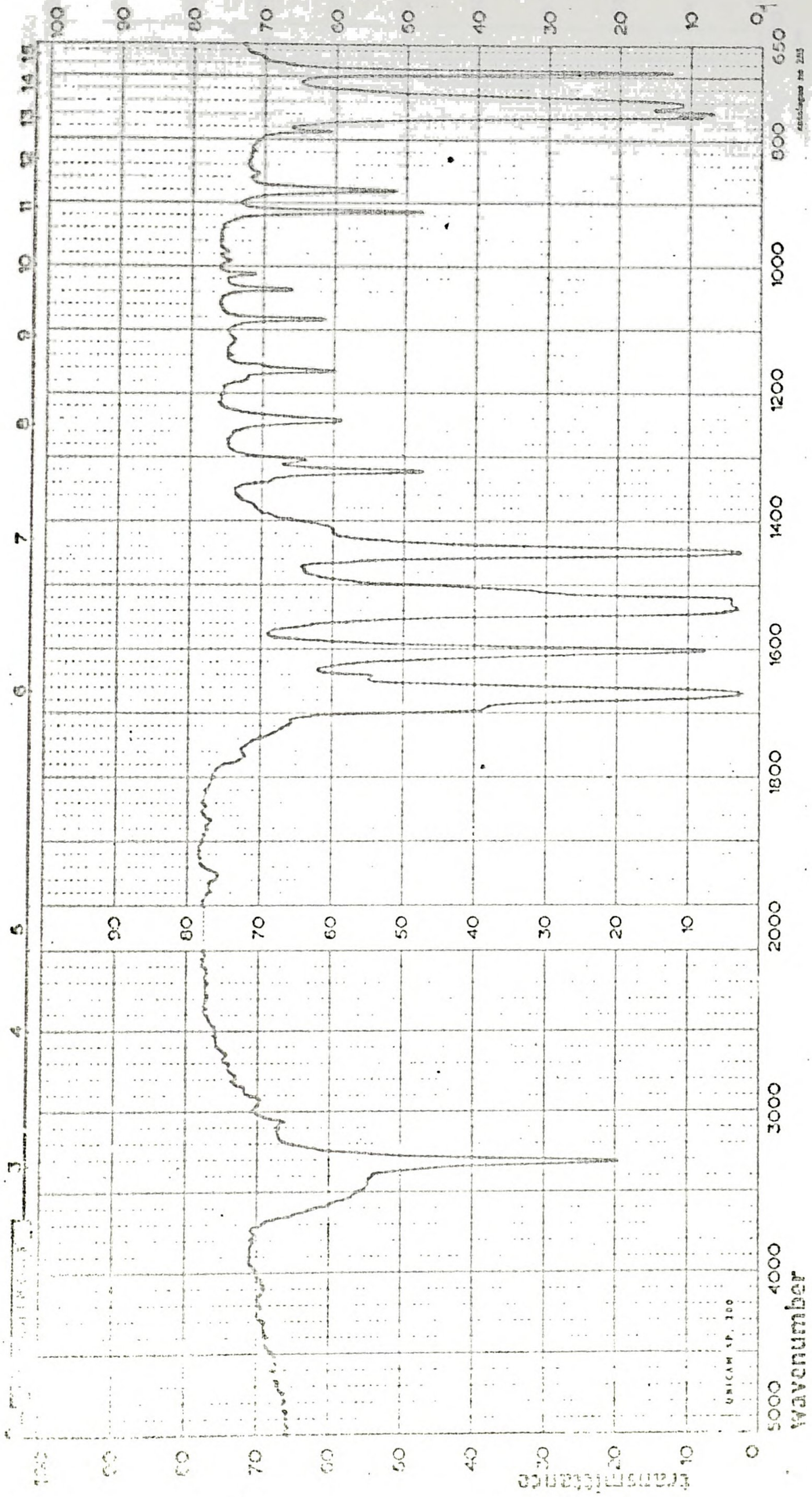


Figure 44. Infrared spectrum of N,N'-diphenyloxamide (KBr).

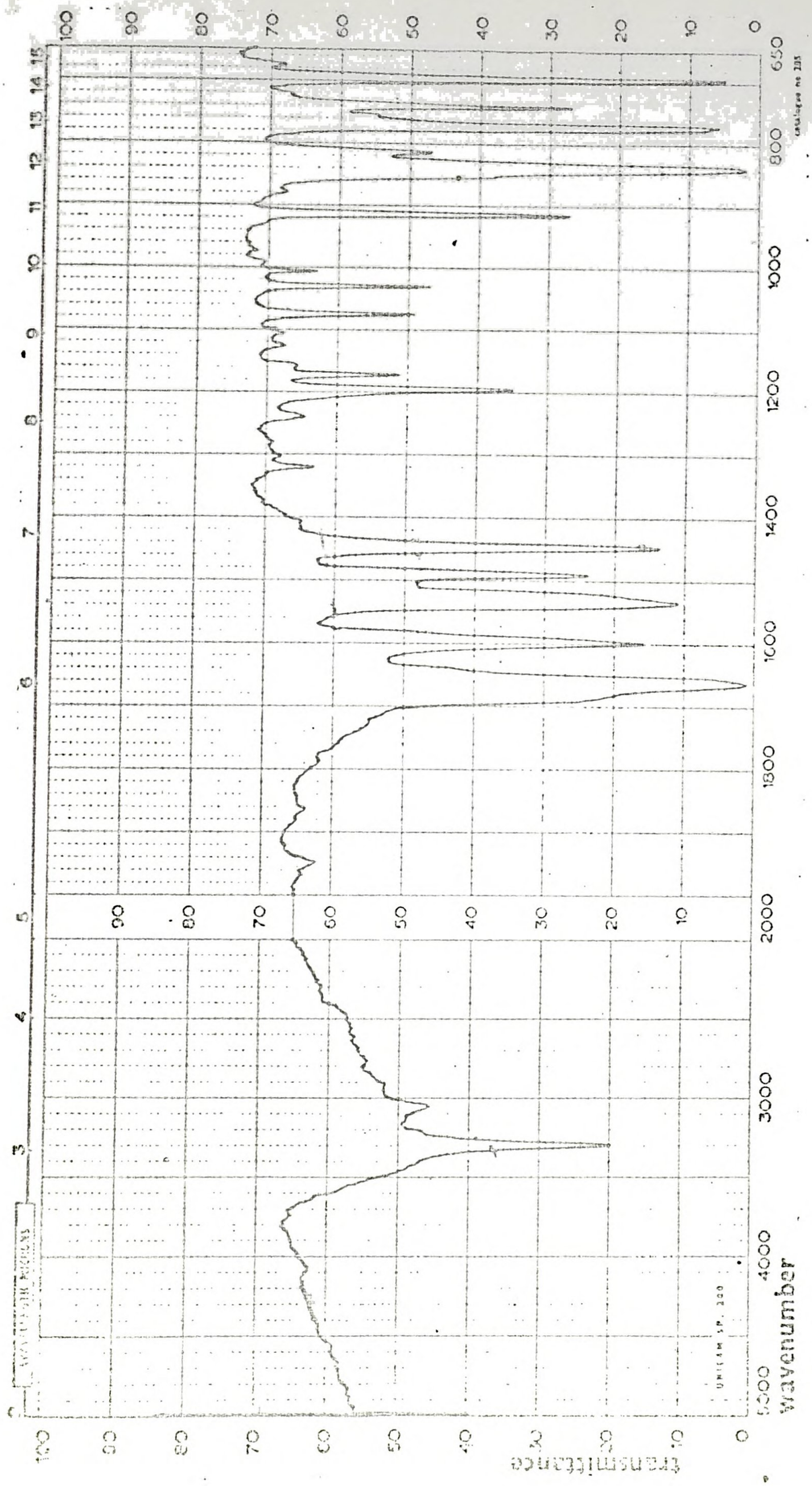


Figure 45. Infrared spectrum of N,N'-diphenyloxalimidyl chloride (KBr).

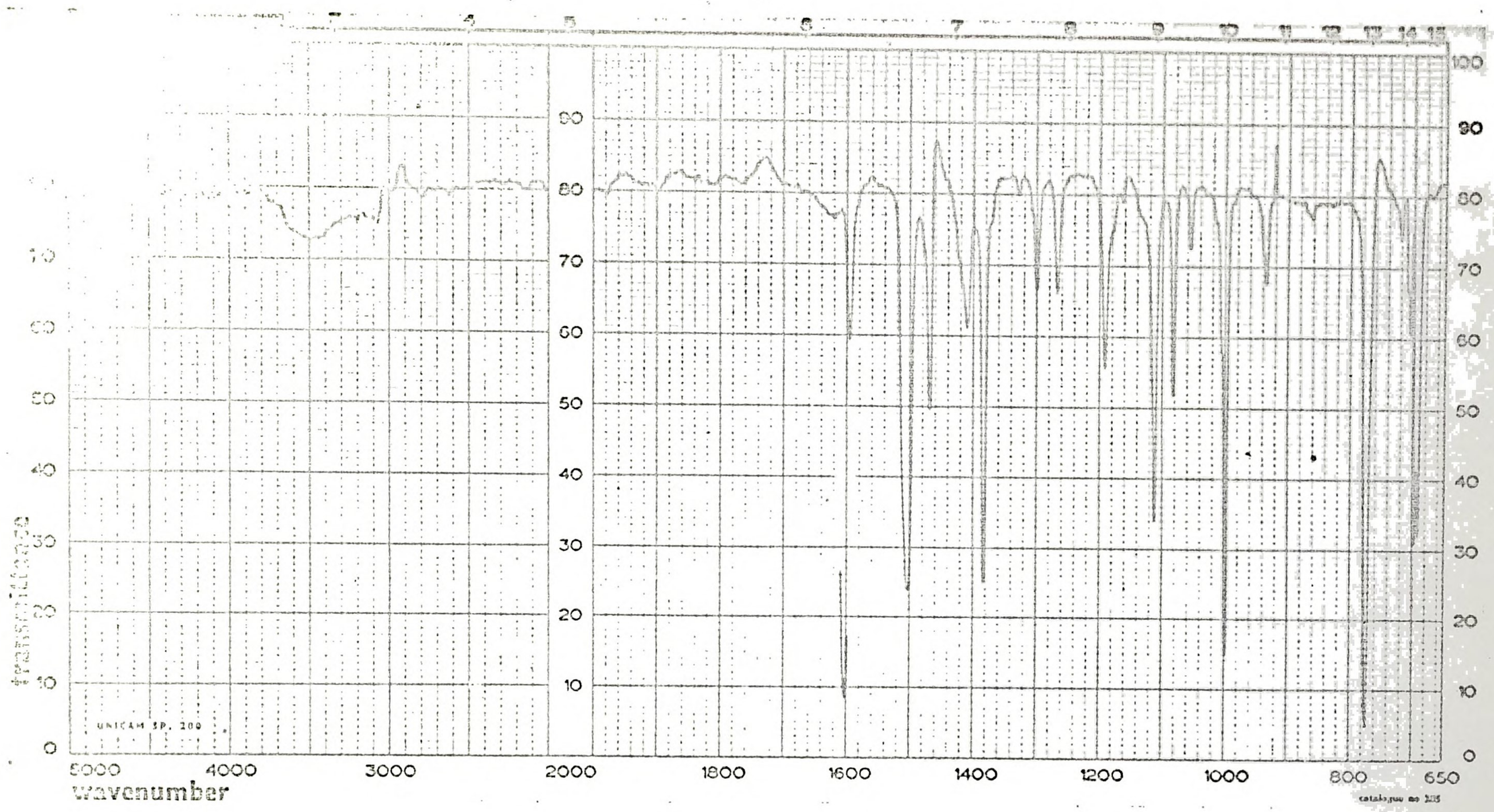


Figure 46. Infrared spectrum of 1,1'-diphenyl-5,5'-bitetrazole (KBr).

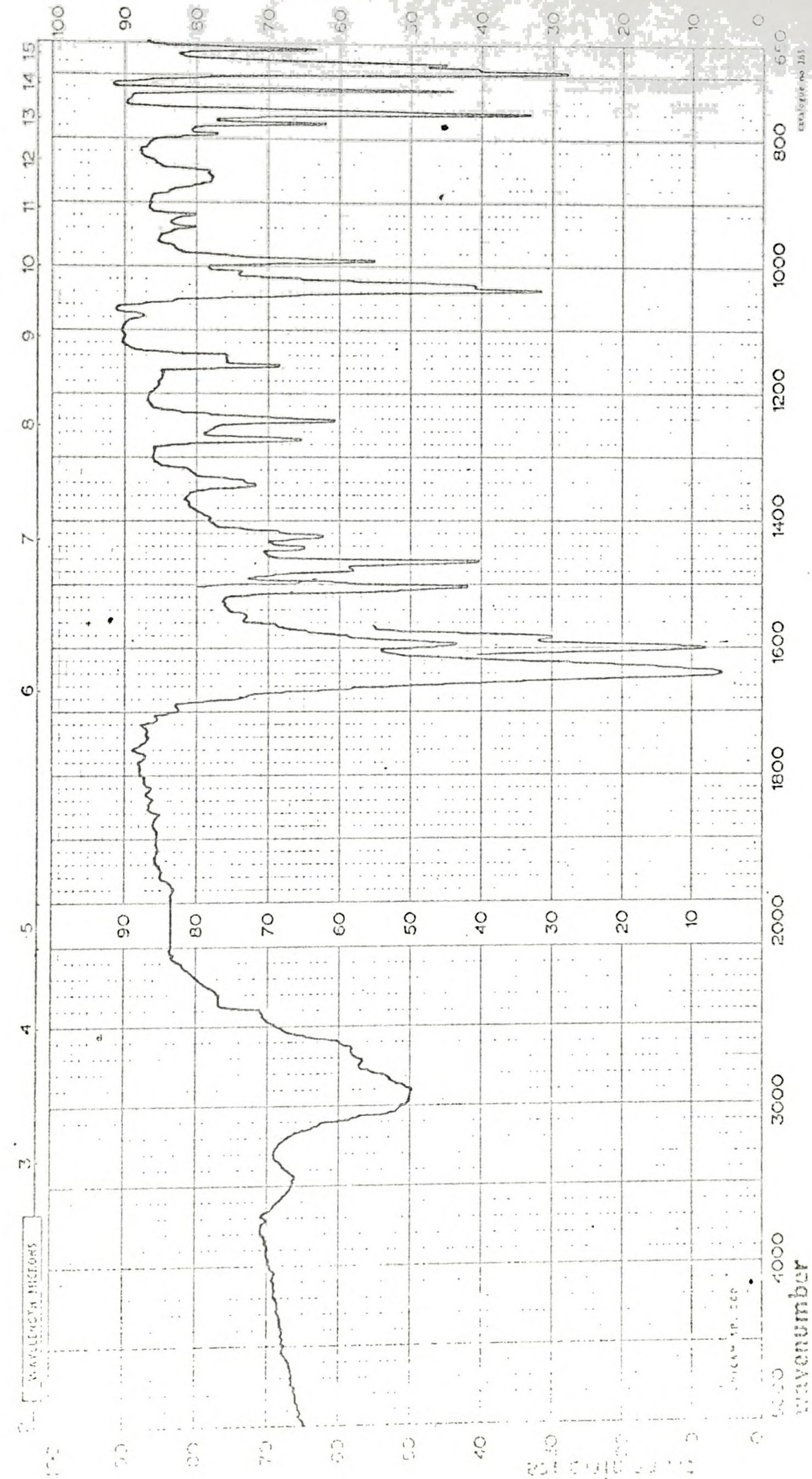
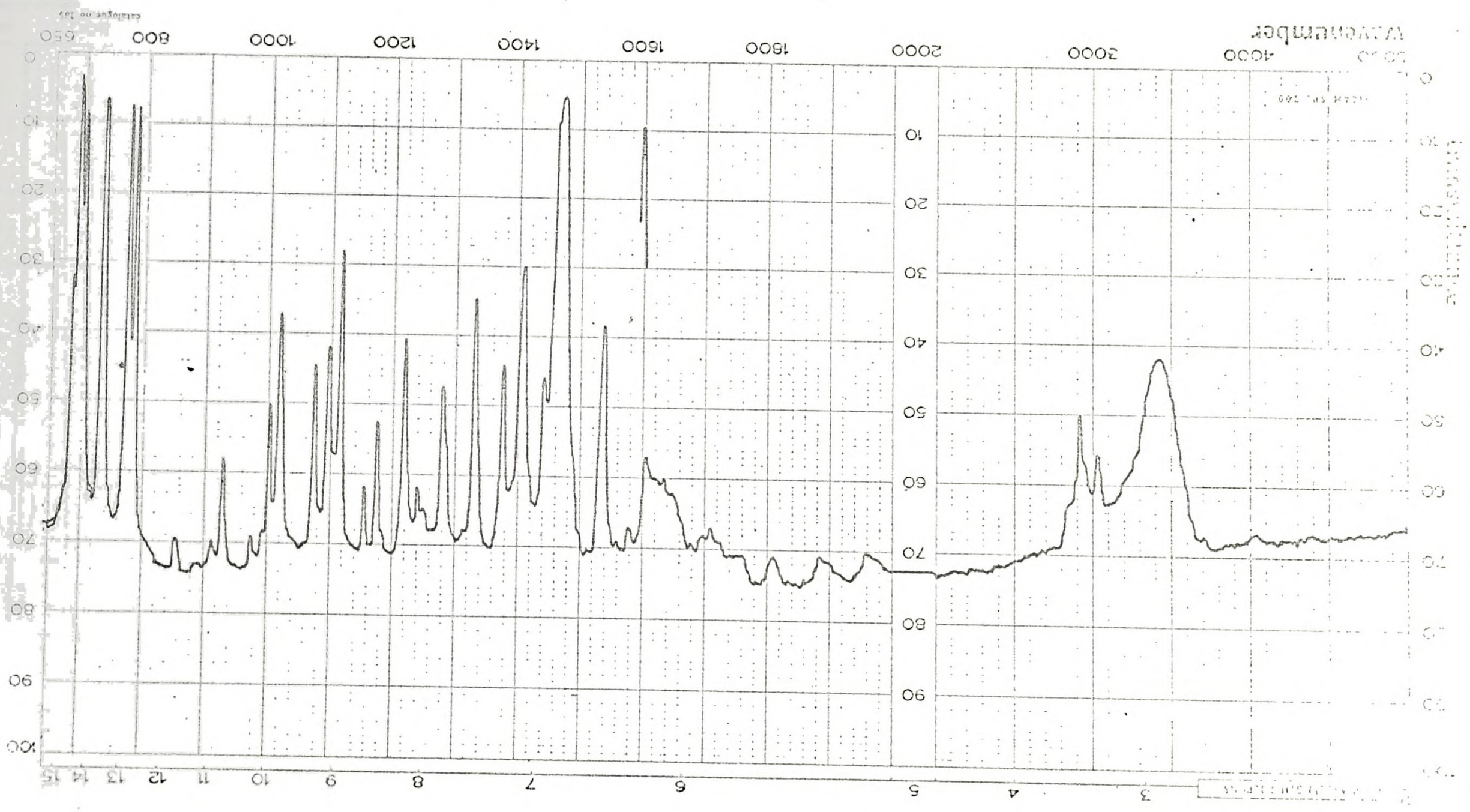


Figure 47. Infrared spectrum of 5,5'-diphenyl-1,1'-bitetrazole (KBr).

Figure 48. Infrared spectrum of 1,4-bis(5-phenyltetrazolyl)-n-butane (KBr).



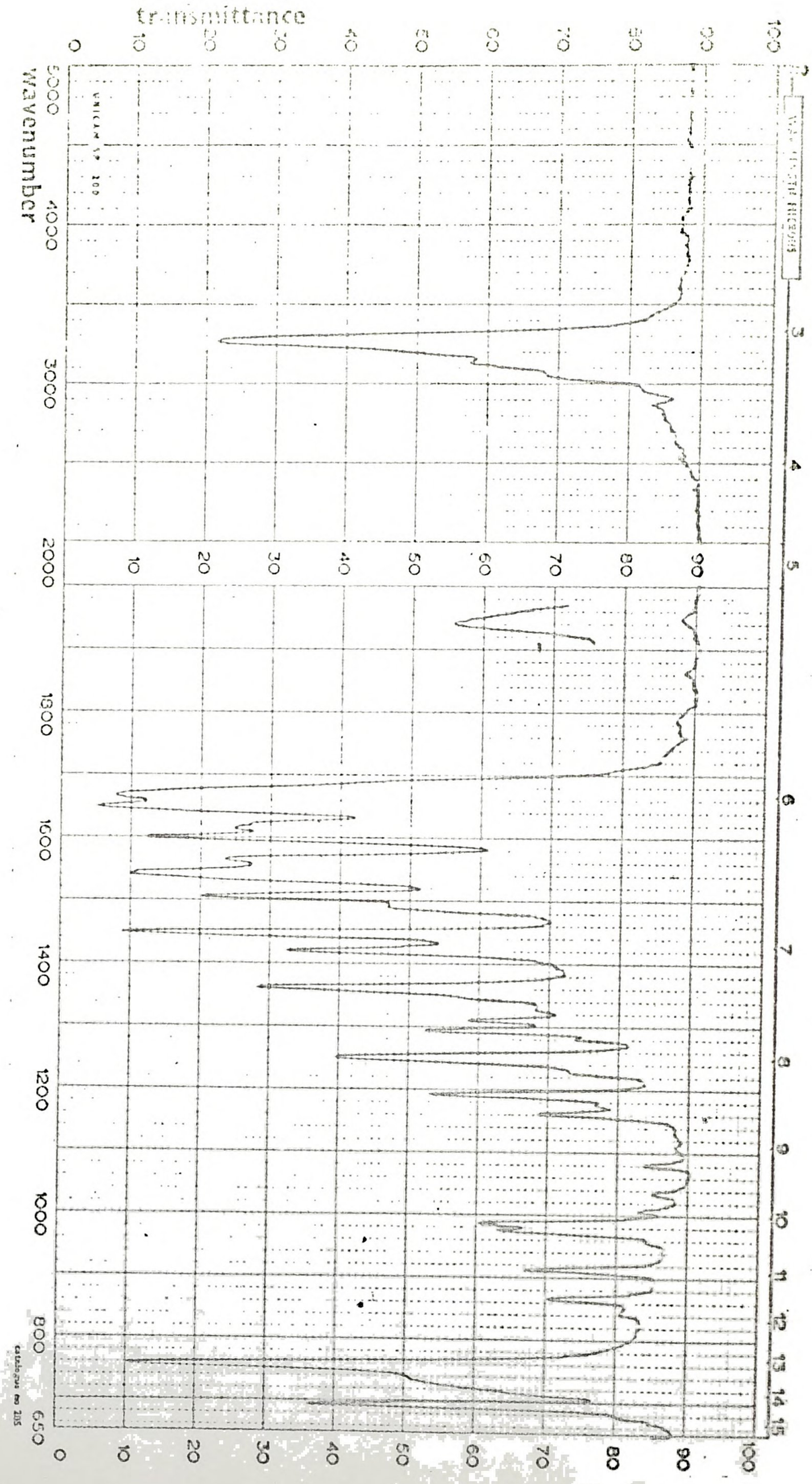


Figure 49. Infrared spectrum of N,N'-diphenylmalonamide (KBr).

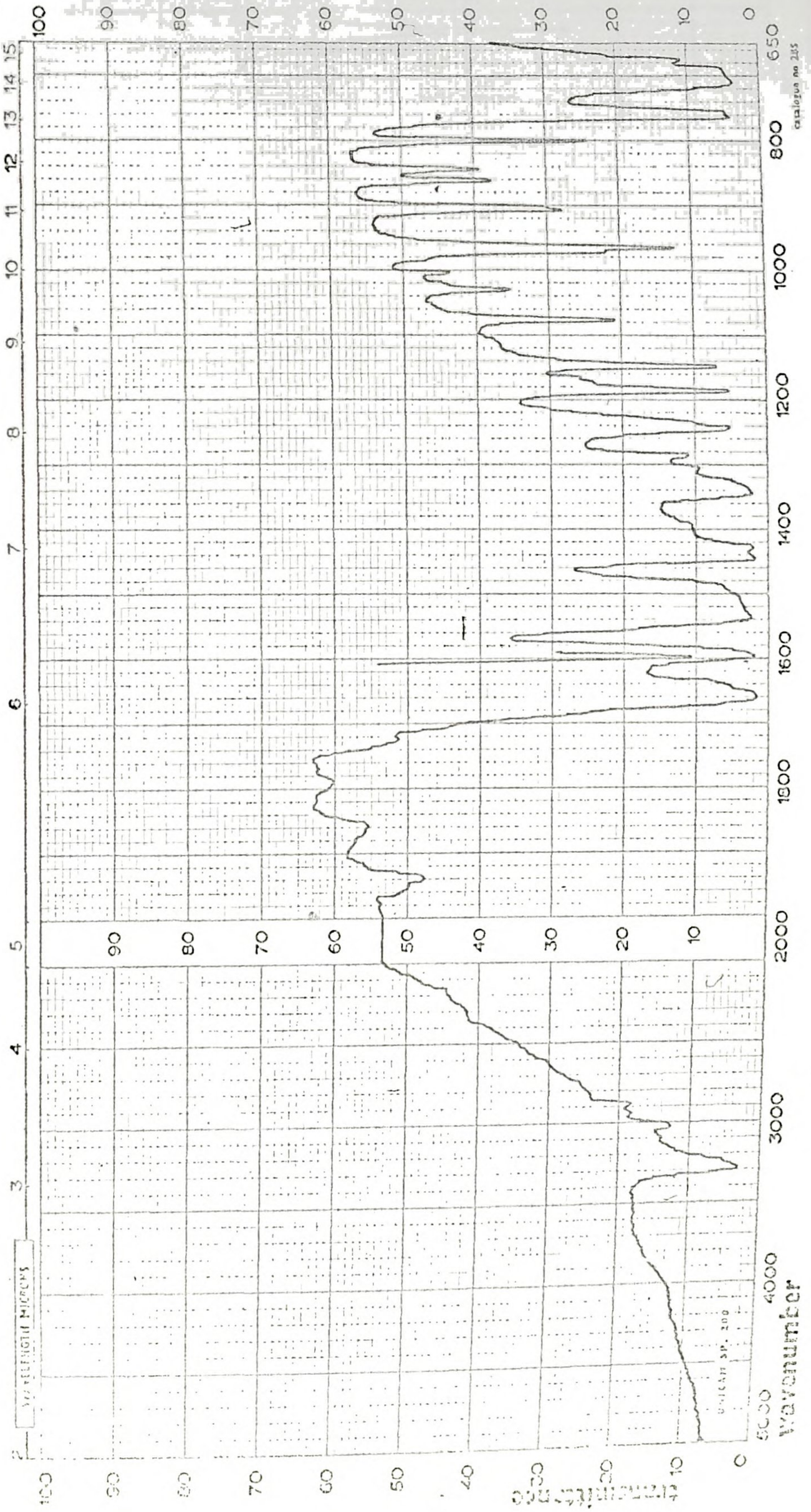


Figure 50. Infrared spectrum of N,N'-diphenylsuccinamide (KBr).

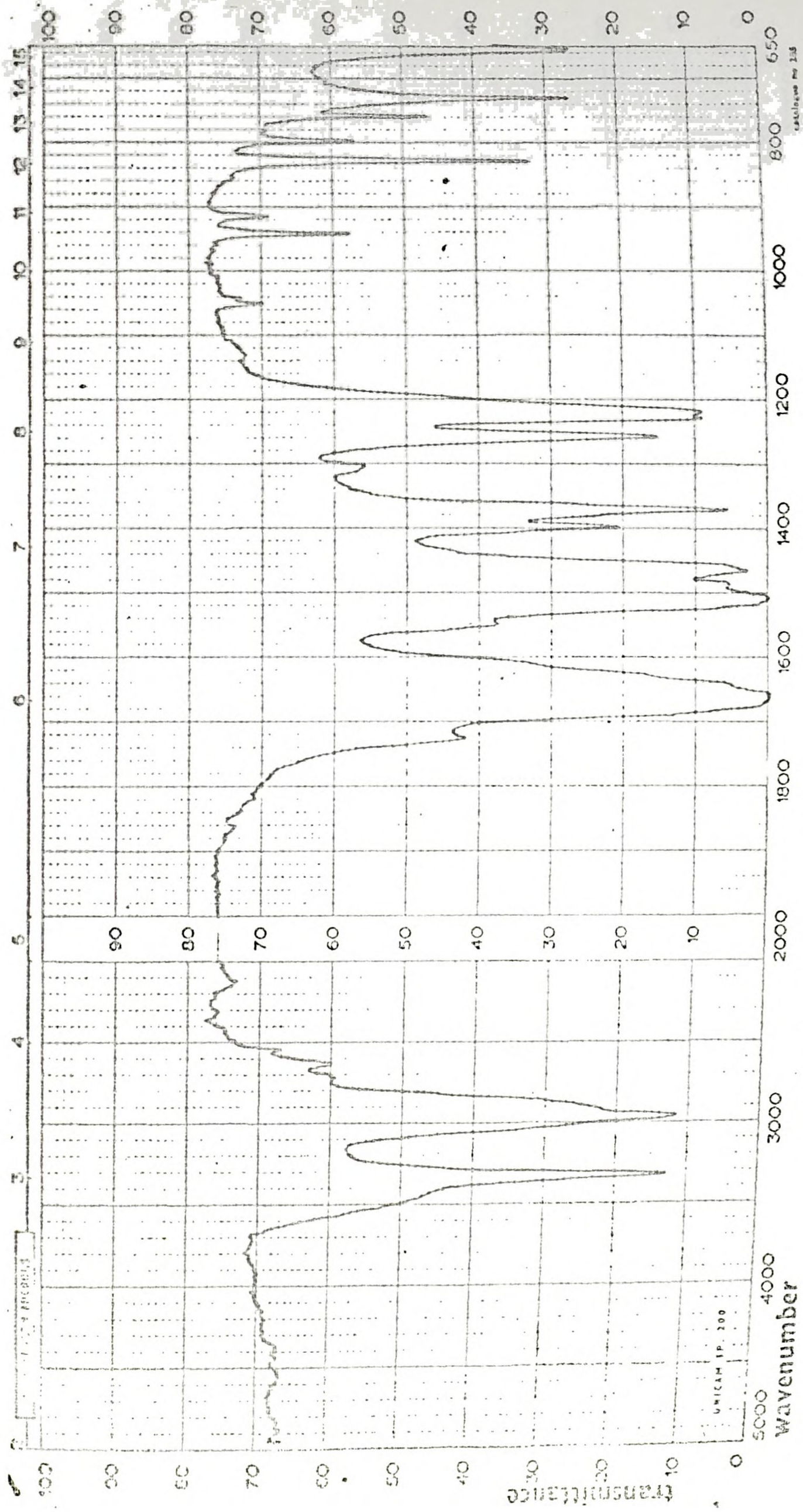


Figure 51. Infrared spectrum of N,N'-tert-butyloxamide (KBr).

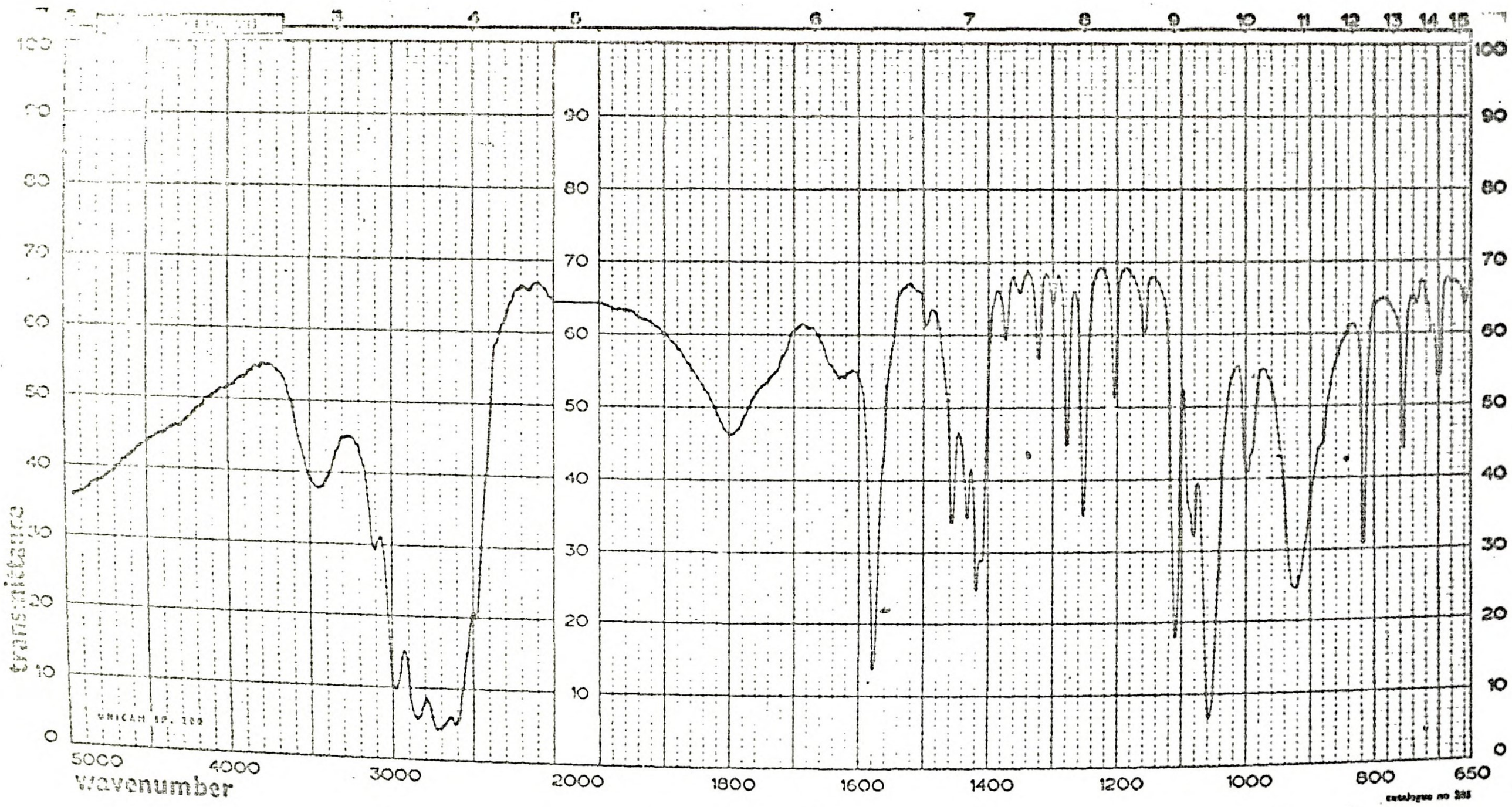


Figure 52. Infrared spectrum of 1,3-bis(5-tetrazolyl)-n-propane (KBr).

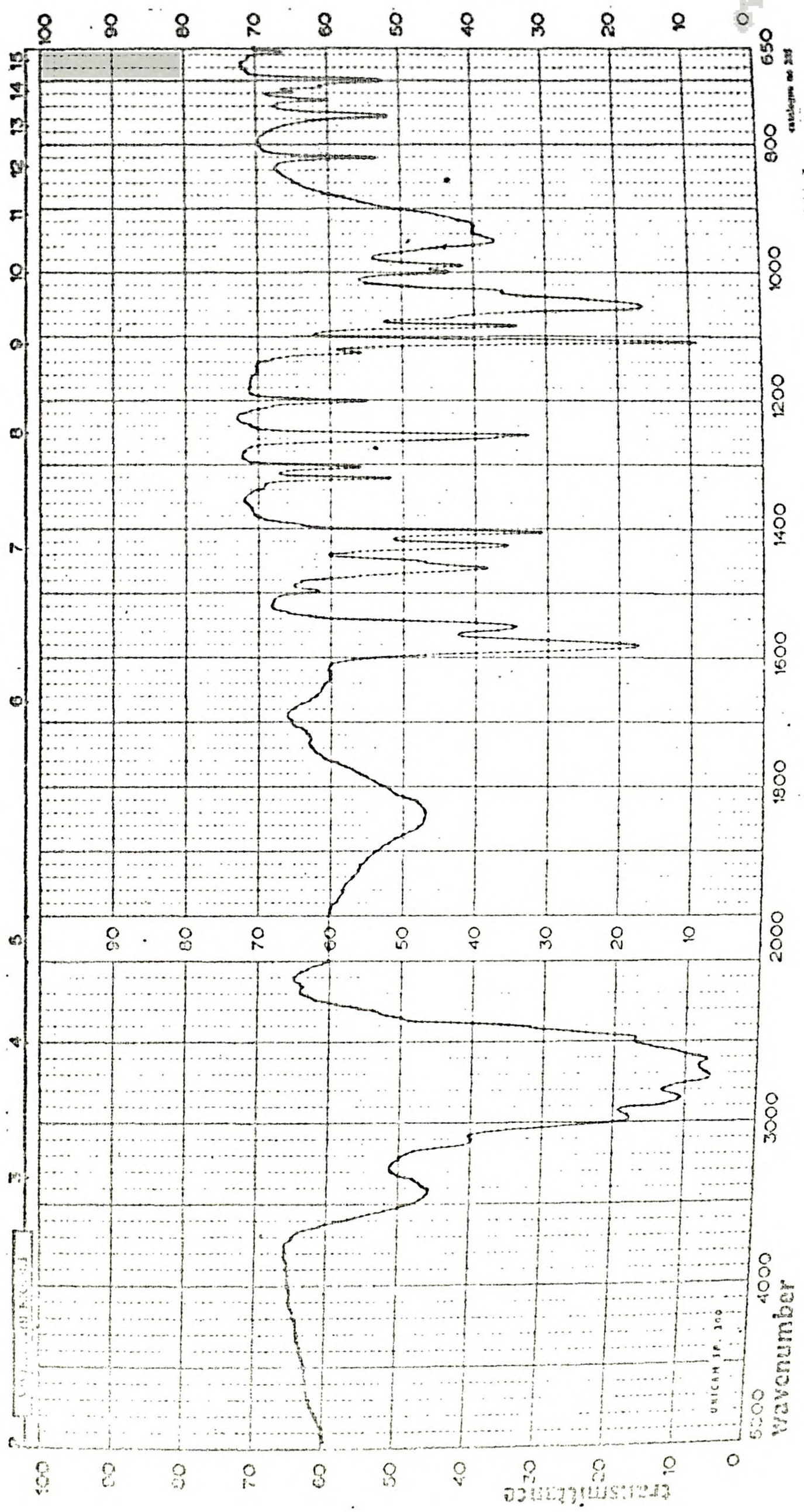


Figure 53. Infrared spectrum of 1,4-bis(5-tetrazolyl)-n-butane (KBr).

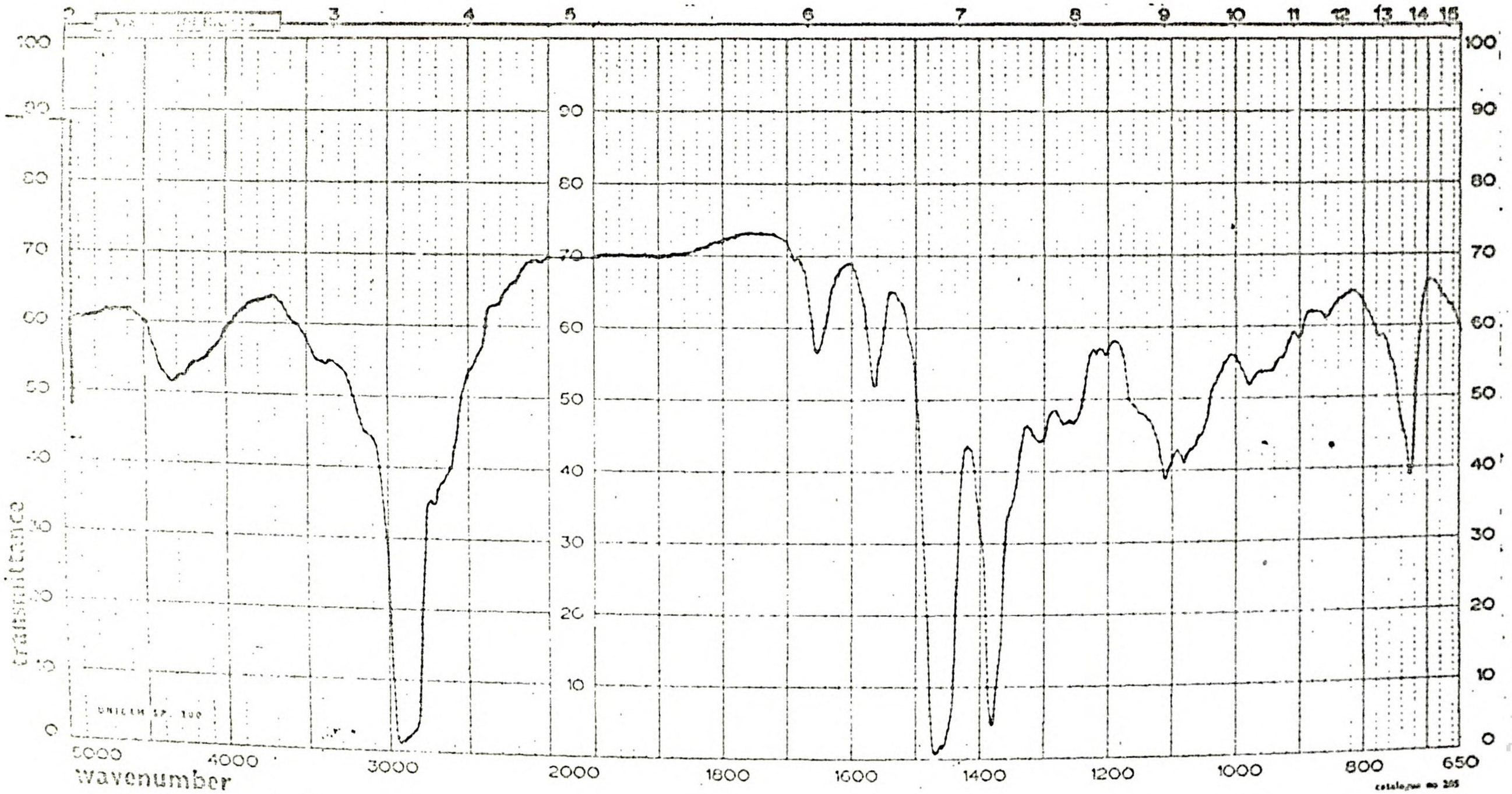


Figure 54. Infrared spectrum of the copper(II) perchlorate complex with 1,4-bis(5-tetrazolyl)-n-butane (Nujol).

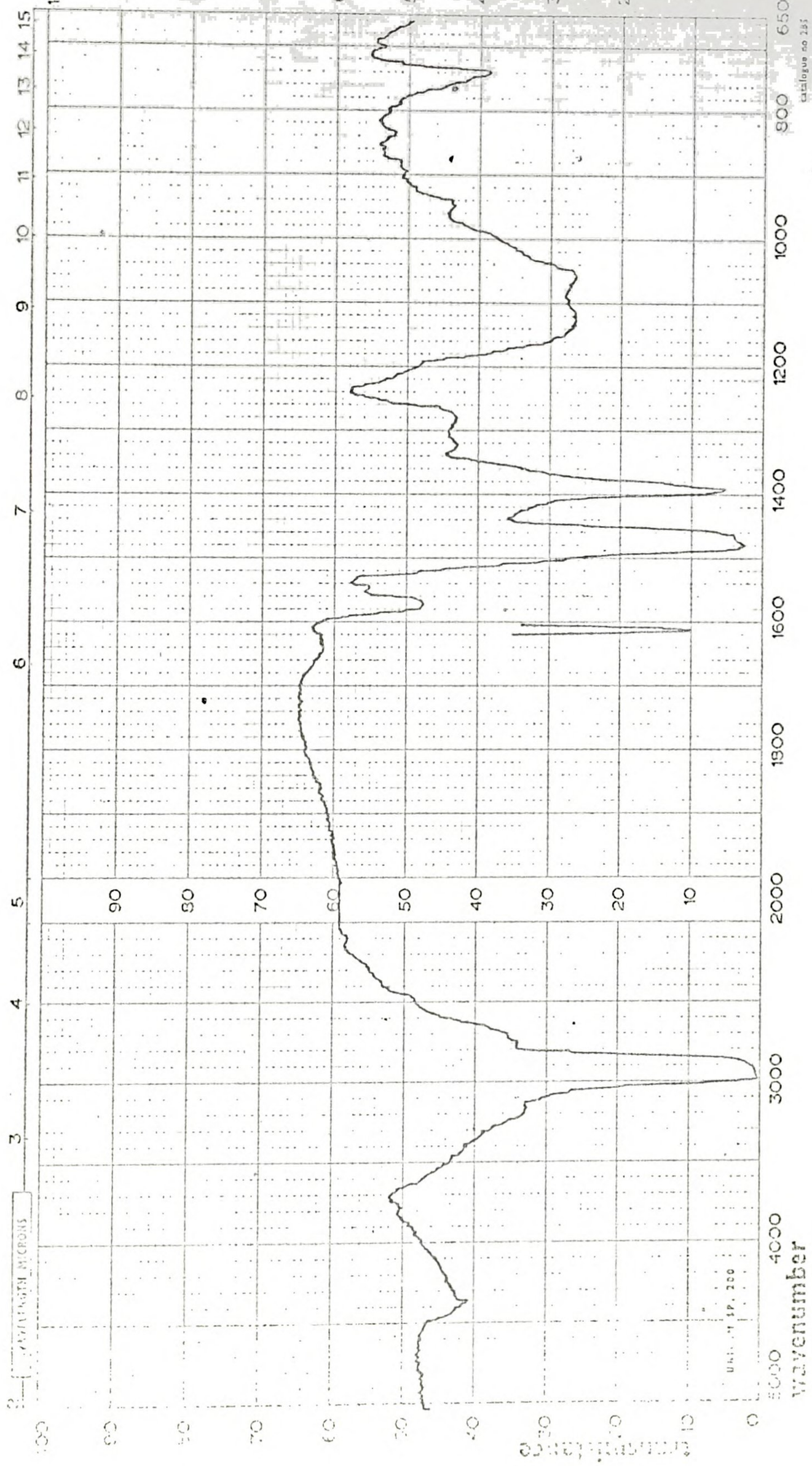


Figure 55. Infrared spectrum of the copper(II) perchlorate complex with 1,3-bis(5-tetrazolyl)-n-propane (Nujol).

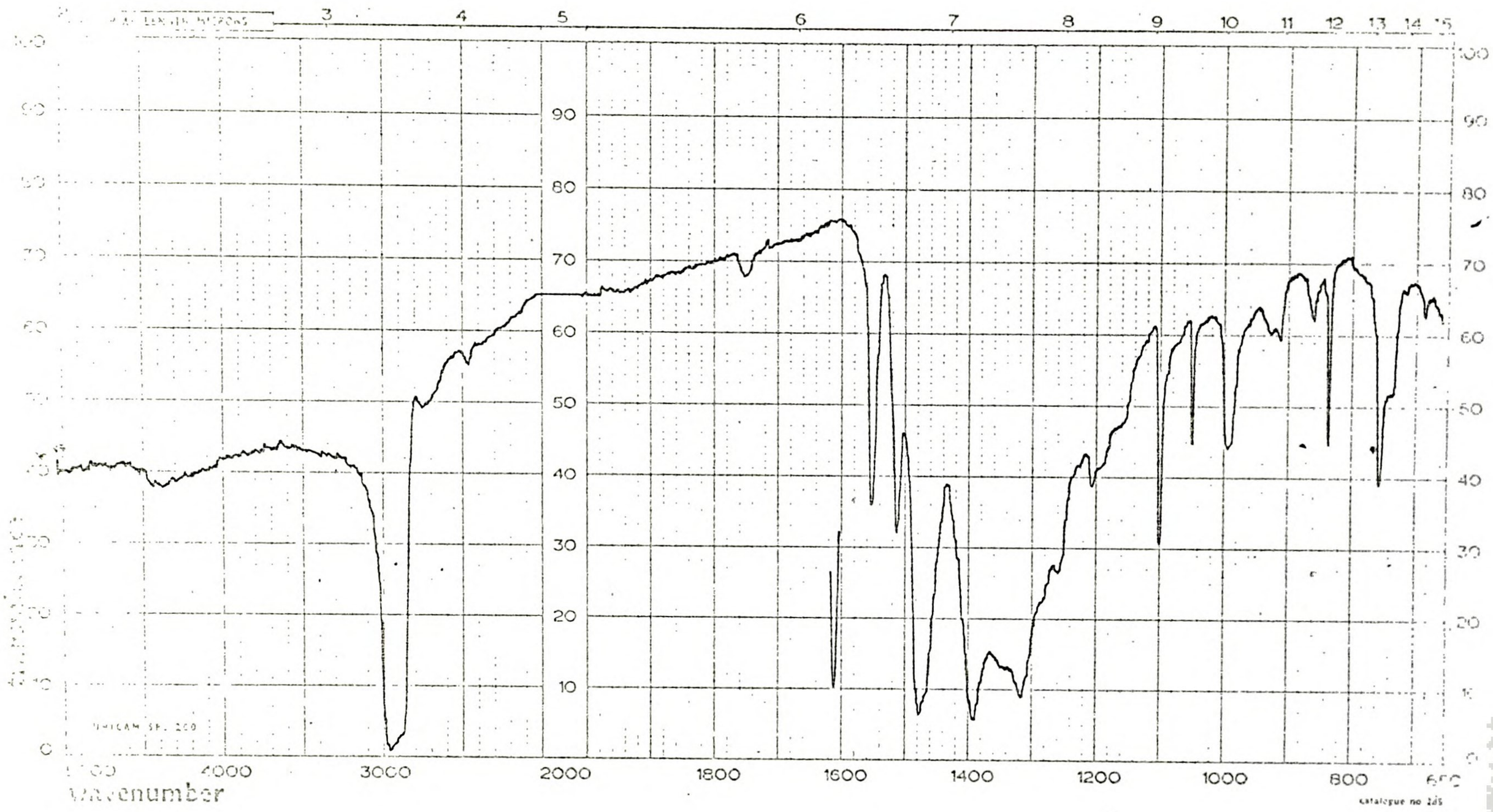


Figure 56. Infrared spectrum of bis(trimethylenetetrazole)silver(I) nitrate (Nujol).

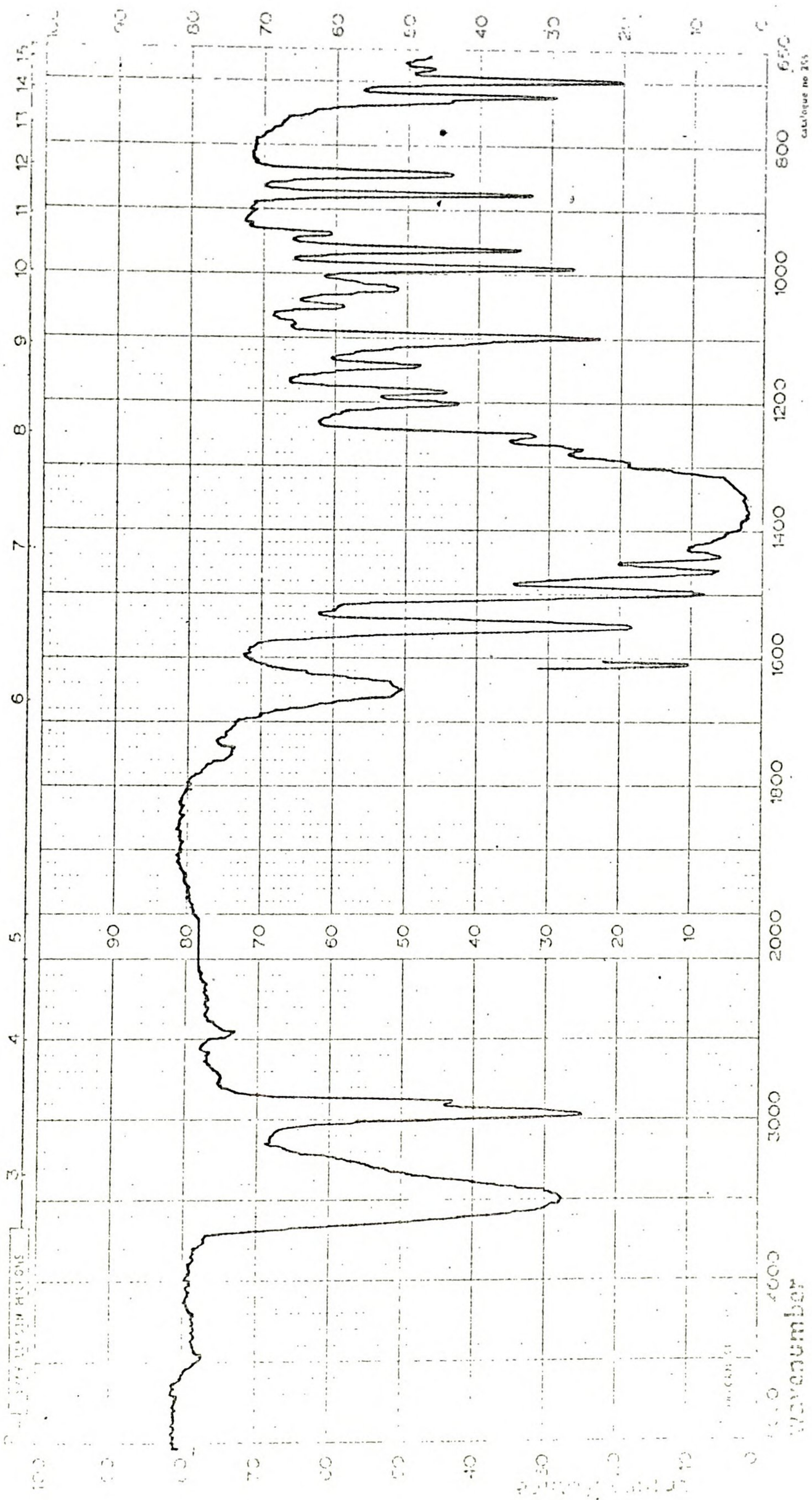


Figure 57. Infrared spectrum of bis(tetramethylenetetrazole)silver(I) nitrate (Nujol).

APPENDIX II

Computer Program of Ketelaar Equation for the Calculation of Formation Constants

The numerical calculations of the formation constants of the respective cyclopolymethylenetetrazole-iodine complexes were performed on a Control Data 3600 digital computer with the program written in FORTRAN. The program listed below was written by William J. McKinney of this laboratory. The author is indebted to him for its use.

The following data are read in for the Ketelaar equation computer program. The first data card is the identification card, ID, and uses columns 1 through 56. The second data card contains in columns 1 through 10 the absorbance of iodine, AI, at the wavelength of interest, the molar concentration of iodine, CI, in columns 11 through 20, and the number of data sets read in, N, in columns 21 and 22. The third through N data cards contain in columns 1 through 10 the absorbance, A, at the wavelength of interest and the molar concentration, CB, of the respective cyclopolymethylenetetrazole in columns 11 through 20. The last data card contains the end of D statement in columns 21 through 28.

```
303 CONST2= 1./(M*(EPSC - EPSX))
    DIFF = ABSF(CONST2 - CONST)
    IF(DIFF.LE. .001*CONST)99,304
304 CONST =CONST2
305 PRINT 11, EPSC, CONST
 11 FORMAT(/10X*MOLAR ABSORPTIVITY = *F8.3, 5X*FORMATION CONSTANT = *F
   110.3)
    FRACT = ((SUMXY - SUMX*SUMY/FN)**2)/(SUMX2 -SUMX**2/FN)
    E = SUMY2 - (SUMY**2/FN) - FRACT
    S2 = E/(FN - 2.0)
    S = SQRTF(S2)
    SA2 = S2/(SUMX2 - (SUMY**2/FN))
    SA = SQRTF(SA2)
    SB2 = S2*SUMX2/(FN*SUMX2 - SUMX**2)
    SB= SQRTF(SB2)
    VAR = (SA/M)**2 + (SB/B)**2
    SKFR= SQRTF (VAR)
    SKF = CONST*SKFR
    PRINT 12, S, SA, SB, SKF
 12 FORMAT(/10X* STD. OF A SINGLE Y = *F14.11,5X*STD. DEV. OF
   1SLOPE = *F14.11,/10X* STD. DEV. OF INTERCEPT = *F14.11,5X*
   2STD. DEV. OF KF = *F10.4)
    PRINT 15
 15 FORMAT(/10X*Y          YCALC          T          DEVIATION*/)
 14 FORMAT(10X, 4F14.8)
    DO 231 I = 1, N
    YCALC(I) = M*X(I) +B
    T(I) = ABSF(Y(I) - YCALC(I))
    DEV(I) = T(I) - 3.0*S
    PRINT 14, Y(I), YCALC(I), T(I), DEV(I)
    IF(DEV(I)) 231, 241, 241
231 CONTINUE
    GO TO 251
241 PRINT 13, Y(I)
 13 FORMAT(1H0,2X,14HREJECTED POINT,5X,E14.8)
    J = I
    DO 261 I = J, N
    CB(I) = CB(I + 1)
    CB3(I) = CB3(I + 1)
261 Y(I) = Y(I + 1)
    N = N -1
    GO TO 111
251 CONTINUE
    DO 888 I = 1,N
    CC(I) = (CONST*CB(I)*CI)/(1+ CONST*CB(I))
    CB2(I) = CB3(I) - CC(I)
888 CB(I) = CB2(I)
    II = 2
    GO TO 111
    END
```

```
      PROGRAM KETTLA?
      TYPE REAL M
      DIMENSION X(50), Y(50), A(50), CR(50), EPST(50), YCALC(50), DEV(50
     1), T(50),  ID(7)          , CC(50), CB2(50), CR3(50)
      CALL080 ERSET(?)
   99 READ 1, ID
    1 FORMAT(7A8)
      PRINT 2, ID
    2 FORMAT (1H1,10X,7A8)
      IF (ID.EQ.8HEND OF R) STOP
C     EPSX = EPSILON SUB X,  CI = IODINE CONC, N = NUMBER OF DATA
      READ 3, AI, CI,
    3 FORMAT(2F10. ?)
      EPSX = AI/CI
      PRINT 4,EPSX,CI,N
    4 FORMAT(/10X*EPSILONX = *F9.3, 5X*IODINE CONC = *F12.10, 5X*N = *I2
     1)
      PRINT 5
    5 FORMAT(/10X*ABSORBANC                CONC BASE*/)
      I=1
  101 READ 6, A(I), CR(I), II
    6 FORMAT(2F10. A8)
      PRINT 7, A(I), CR(I)
    7 FORMAT(12X,F6.4,10X,F12.10)
      CR3(I) = CR(I)
      IF(II.EQ.8HEND OF R) 22, 21
   21 I = I+1 $ GO TO 101
   22 PRINT 8
    8 FORMAT(/10X*Y                    EPSILON T*/)
      DO 201 I=1,N
      EPST(I) = A(I)/CI
      Y(I) = 1./(EPST(I) - EPSX)
  201 PRINT 9,Y(I), EPST(I)
    9 FORMAT(10X,F12.10,10X,F8.2)
      II = 1
  111 SUMX = SUMY = SUMXY = SUMX2 = SUMY2 = 0.0
      PRINT 39
   39 FORMAT(/16X*Y*/)
      DO 999 I = 1, N
      Y(I) = 1./CR(I)
  999 PRINT 49, Y(I)
   49 FORMAT(10X,F15.10)
      DO 301 I = 1, N
      SUMX = SUMY + Y(I)
      SUMY = SUMY + Y(I)
      SUMXY = SUMXY + X(I)*Y(I)
      SUMX2 = SUMX2 + Y(I)**2
  301 SUMY2 = SUMY2 + Y(I)**2
      FN = N
      M = (FN*SUMXY - SUMX*SUMY)/(FN*SUMY2 - SUMY**2)
      B = (SUMY*SUMX2 - SUMXY*SUMX)/(FN*SUMX2 - SUMX**2)
      PRINT 10, M, B
   10 FORMAT(/10X*SLOPE = *F20.10, 5X*INTERCEPT = *F20.10)
      EPSC = (1. + B*EPSX)/B
      IF (IL.EQ.11302,303
  302 CONST = 1./(M*(EPSC - EPSX))  $ GO TO 305
```

APPENDIX III

Determination of Pharmacological Properties of the Various Cyclopolymethylenetetrazoles as Quoted from Communications Received from Professor William E. Stone

Professor William E. Stone, Department of Physiology, University of Wisconsin, Madison, Wisconsin, determined the pharmacological properties of the various cyclopolymethylenetetrazoles. In tests on dogs and white mice, Dr. Stone found that the pharmacological activity of the respective cyclopolymethylenetetrazole increased substantially as methylene groups were added to the cyclopolymethylene chain. The results of the pharmacological testing on the cyclopolymethylenetetrazoles are given in Table III-1.

TABLE III-1.

Tetrazole	MCD* mg/kg
Trimethylenetetrazole	1000
Tetramethylenetetrazole	250
Pentamethylenetetrazole	50
Hexamethylenetetrazole	40
Heptamethylenetetrazole	30
Octamethylenetetrazole	Insoluble
Undecamethylenetetrazole	Insoluble

The 6,6-dihalocyclopolymethylenetetrazoles are not very soluble in water. Therefore, it was necessary to use a mixture of 10% ethanol, 20% propylene glycol, and 70% physiological salt solution as the solvent. After making

more tests, however, it was determined that the above solvent mixture alters the threshold of pentamethylene-tetrazole. The results of the pharmacological testing on the 6,6-dihalocyclopolymethylenetetrazole are given in Table III-2.

TABLE III-2

Tetrazole	MCD* mg/kg
Pentamethylenetetrazole	75
6,6-Dichlorotetramethylenetetrazole	75-85
6,6-Dibromotetramethylenetetrazole	75-85
6,6-Dichloropentamethylenetetrazole	10-13
6,6-Dibromopentamethylenetetrazole	Insoluble
6,6-Dichlorohexamethylenetetrazole	23

The 1,5-cyclopolymethylenetetrazoles with more than seven bridging methylene groups and 6,6-dibromopenta-methylenetetrazole were essentially insoluble in the appropriate solvent and could not be tested accurately.

*MCD = Minimum convulsant dosage (i.e.) the minimum amount of tetrazole necessary to cause the first symptoms of seizure. The dosage is given in milligrams of tetrazole per kilogram of body weight of the animal.

Pharmacological Tests on the Various Cyclopolymethylenetetrazole Compounds

A. Cyclopolymethylenetetrazoles

1. Trimethylenetetrazole

Solution: 175 mg/ml.

Tests of mice:

Mouse	Approx. Dose (i.p.)	
1	500 mg/kg	Brief seizure at 4.5 min. followed by excitement, jumping.
1	Second dose at 20 min.: 500 mg/kg	Severe seizure at 6.5 min. Seizures at 10,25, and 33 min.
2	750 mg/kg	No seizure
3	750 mg/kg	No seizure
4	750 mg/kg	No seizure
4	Second dose at 18 min.: 500 mg/kg	Brief seizure at 6 min.
5	1000 mg/kg	Twitching at 6 min. and thereafter. Mild seizure at 19 min.
6	1000 mg/kg	Twitching at 9.5 min. Mild seizure at 12 min.
7	1000 mg/kg	Twitching, chewing at 4-5 min. Mild seizure at 10 min. Twitching at 14 min.
8	1000 mg/kg	Twitching at 3 min. Seizure at 4 min.

All recovered and showed no after-effects.

Dose required to induce seizures: about 1000 mg/kg.

2. Tetramethylenetetrazole

Solutions: 87.5 mg/ml; 175 mg/ml (in 0.9% NaCl).

Tests on mice:

Mouse	Approx. Dose (i.p.)	Effect
1	200 mg/kg	No seizure
2	200 mg/kg	No seizure Twitching at 8 min., excitement.
3	200 mg/kg	No seizure Slight twitching at 3 min.
4	250 mg/kg	Excitement, jumping after 1 min. Severe seizure at 2.25 min.
5	300 mg/kg	Twitching after 2 min. Seizure at 3.3 min.
6	500 mg/kg	Brief seizures at 50 sec. and 2 min. Twitching at 5-8 min. Severe seizure at 8 min., further twitching after recovery Severe seizure at 16 min., ending in strong tonic contractions. Death after end of tonic phase.

All except #6 recovered and showed no after-effects.

Dose required to induce seizure: about 250 mg/kg.

3. Pentamethylenetetrazole.--Previous studies conducted by Dr. W. E. Stone indicate the dosage of pentamethylenetetrazole required to induce seizure to be about 50 mg/kg.

4. Hexamethylenetetrazole

Solutions: 17.5 mg/ml; 35 mg/ml (in 0.9% NaCl).

Tests on mice:

Mouse	Approx. Dose (i.p.)	Effect
1	34 mg/kg	Twitching at 3 min. Seizure at 3.75 min.
2	41 mg/kg	Seizure at 5 min.
3	44 mg/kg	Excitement; no seizure.
4	50 mg/kg	Twitching at 2.5-3 min. Brief severe seizure at 4 min.
5	60 mg/kg	Mild seizure at 4 min.
6	120 mg/kg	Brief seizure at 40 sec. Death in severe tonic seizure at 2 min.

All except #6 recovered and showed no after-effects.

Dose required to induce seizure: 34-50 mg/kg.

Potency comparable to that of pentamethylenetetrazole.

5. Heptamethylenetetrazole

Solubility in 0.9% NaCl: approx. 10 mg/ml.

Tests on mice:

Mouse	Approx. Dose (i.p.)	Effect
1	25 mg/kg	Twitching at 60 sec. Brief, severe seizure at 80 sec.
2	30 mg/kg	No seizure
3	30 mg/kg	Brief seizure at 80 sec., followed by running movements.

Mouse	Approx. Dose (i.p.)	Effect
4	30 mg/kg	Brief seizure at 45 sec., followed by excitement (jumping).
5	69 mg/kg	Series of brief seizures starting at 25 sec. Death in severe seizure at 110 sec.

All except #5 recovered and showed no after-effects.

Dose required to induce seizures: about 30 mg/kg. (More potent than pentamethylenetetrazole.)

Test on a dog: The animal (weighing 13 kg) was given morphine (5 mg/kg) and transient thiopental anesthesia. A femoral artery and vein were cannulated, and electrodes were placed in drill holes in the exposed calvarium. After thiopental effects had disappeared, control records were taken of cortical electrical activity, arterial blood pressure, and electrocardiogram. An additional dose (5 mg/kg) of morphine was required and heptamethylenetetrazole solution, 5 mg/ml in .09% NaCl solution was given i.v. by infusion pump at 7.64 ml/min (2.94 mg/kg/min).

At 30 sec an alerting pattern appeared.

At 1 min minimal spiking and slight twitching appeared. These increased gradually thereafter.

At 2 min there were large spikes and associated strong muscular contractions. Movement artifacts obscured much of the record. Arterial blood pressure and heart rate were moderately increased.

At 6 min (total dose about 18 mg/kg) this type of activity was continuing and had been intensified. At this point an additional 10 ml (4 mg/kg) was injected quickly; this initiated a severe grand mal seizure, with an associated rise in arterial blood pressure. The seizure lasted 31 sec. Subsequently the brain became isoelectric. Periods of slow wave activity (high amplitude waves) ensued, with no associated movements.

At 14.5 min an additional small dose was given quickly (2 ml, 0.8 mg/kg). A brief, mild seizure occurred.

Comment: The convulsive response was very similar to that induced by pentamethylenetetrazole. The convulsive potency is roughly comparable to that of pentamethylenetetrazole, but the initial excitatory effects appeared at a lower dosage than would be expected with pentamethylenetetrazole.

5. Octamethylenetetrazole.--This compound is quite insoluble in water but slightly soluble in a mixture of 10% ethanol, 20% propylene glycol, and 70% saline solution (with heating).

Solubility in the above solvent mixture: approximately 5.0 mg/ml.

Tested on 4 mice, 25 to 28 g body weight, dose 0.3 ml i.p. (53 to 60 mg/kg). The drug did not induce seizures during one hour of observation, and no toxic effects were evident one or two days after the injection.

Comment: This compound apparently is not a potent convulsant. However, the results may not be strictly comparable to those obtained previously with more soluble compounds because the rate of absorption may be lower when the solution contains propylene glycol and the solvents might affect the convulsive threshold.

7. Undecamethylenetetrazole.--This compound is insoluble in water, but can be dissolved in propylene glycol or ethanol-propylene glycol mixtures. Such solutions were prepared and diluted with 0.9% NaCl until precipitation began. Stated dosages are very rough estimates.

Tests on mice:

Mouse	Est. Dosage (i.p.)	Effects
1	18 mg/kg	none
2	22 mg/kg	none
3	65 mg/kg	none
4	65 mg/kg	none

B. 6,6-Dihalocyclopolymethylenetetrazoles

Since these compounds are not very soluble in water, it was necessary to use a mixture of 10% ethanol-20% propylene glycol-70% physiological salt solution as the solvent. However, after making some of the tests on the new compounds, it was found that the use of this solvent alters the threshold to pentamethylenetetrazole.

The pentamethylenetetrazole threshold in the above solvent mixture was determined as follows. A solution was prepared containing 8 mg of pentamethylenetetrazole per ml of the solvent mixture. With this concentration, the amounts of solvent injected (0.2 to 0.3 ml per mouse) were roughly comparable to those given when testing the new cyclopolymethylenetetrazoles. The results are as follows:

Mouse	Pentamethylene-tetrazole Dose	Effect
1	60 mg/kg	Twitching, no seizure
2	69 mg/kg	Twitching, no seizure
3	70 mg/kg	Severe twitching, no seizure
4	75 mg/kg	Brief seizure at 4.5 min
5	80 mg/kg	Seizure at 1 min 40 sec
6	85 mg/kg	Repeated seizures after 2 min

Thus the dose required to induce a seizure under these conditions is about 75 mg/kg. For pentamethylenetetrazole dissolved in 0.9% NaCl solution, the previously determined convulsant dose of 50 mg/kg was confirmed in one mouse of this group.

In two tests, 0.3 ml of the solvent mixture was injected 10 min prior to a dose of pentamethylenetetrazole in 0.9% NaCl. Severe twitching (resembling petit mal) was induced by 60 mg of pentamethylenetetrazole per kg and a seizure (after 8 min) by 65 mg/kg. These tests were insufficient to determine whether the effect of the solvent is

due to a depressing (anesthetic or anti-convulsive) property or whether it is due to a slower entry of the convulsant into the blood stream, but this question was not pursued further.

1. 6,6-Dichlorotetramethylenetetrazole did not have convulsive or other toxic effects in the doses tested. Four mice were given single doses of 47 to 55 mg/kg, and one was given a total of 69 mg/kg in 2 doses 15 min apart (17 and 52 mg/kg).

In one mouse the test dose of the drug (55 mg/kg) was followed 9 min later by a dose of pentamethylenetetrazole (in 0.9% NaCl), 65 mg/kg. This induced a brief seizure after 7 min. It appears that the 6,6-dichlorotetramethylene-tetrazole did not measurably alter the threshold to penta-methylenetetrazole.

2. 6,6-Dibromotetramethylenetetrazole gave results comparable to the above. The data are as follows:

Mouse	First dose	Second dose	Total injected
1	45 mg/kg	30 mg/kg after 15 min	75 mg/kg
2	57 mg/kg	38 mg/kg after 15 min	95 mg/kg
3	51 mg/kg	-	51 mg/kg
4	52 mg/kg	-	52 mg/kg

No convulsive or other toxic effects were observed.

Three of these mice were subsequently given pentamethylenetetrazole (in 0.9% NaCl)

Mouse	Time after last injection	Pentamethylene-tetrazole dose	Effect
2	24 min	50 mg/kg	No seizure
3	39 min	50 mg/kg	Brief seizure at 5 min
4	64 min	65 mg/kg	Brief seizure at 4.5 min

It appears that the 6,6-dibromotetramethylenetetrazole did not measurably alter the threshold to pentamethylenetetrazole.

3. 6,6-Dichloropentamethylenetetrazole

Solutions: (a) 3.5 mg/ml in 10% ethanol--10% propylene glycol--80% saline solution (0.9% NaCl). This was a saturated solution. (b) 4 mg/ml in 10% ethanol--20% propylene glycol--70% saline solution.

Tests on mice:

Mouse	Approx. Dose (i.p.)	Effect
1	6 mg/kg	No seizure
2	10 mg/kg	No seizure
3	10 mg/kg	Twitching at 4, 6, and 9 min. Seizure at 18 min
4	13 mg/kg	Slight twitching at 8 min Mild seizure at 12 min
5	14 mg/kg	Twitching at 90 sec., then brief seizure Mild seizure at 7 min

6	15 mg/kg	Twitching at 3 min. and thereafter. Mild seizure at 13 min.
7	16 mg/kg	Twitching at 1-2 min. Brief seizure at 3 min.
8	17 mg/kg	Brief seizure at 2 min. Mild seizure at 8 min.
9.	20 mg/kg	Severe seizure at 6 min. Very severe seizures, 38 to 48 min. inclusive. Some coordinated movements between seizures (jumping).

All recovered and showed no after-effects.

Dose required to induce seizures is 10-13 mg/kg. (For pentamethylenetetrazole the comparable dose is 75 mg/kg.

4. 6,6-Dibromopentamethylenetetrazole.--Solubility in the above solvent mixture: approximately 2.8 mg/ml (supersaturated at room temperature; crystallized after several hours).

Tested on 4 mice, 26.5 to 34 g body weight, dose 0.3 ml i.p. (25 to 32 mg/kg). The drug did not induce seizures during one hour of observation, and no toxic effects were evident one or two days after injection.

Comment: This compound apparently is not a potent convulsant. However, the results may not be strictly comparable to those obtained previously with more soluble compounds because the rate of absorption may be lower when the solution contains propylene glycol and the solvents might affect the convulsive threshold.

c

a

5. 6,6-Dichlorohexamethylenetetrazole is a potent convulsant, inducing seizures at 23 mg/kg. The data are a as follows:

Mouse	Dose	Effect
1	21 mg/kg	No seizure
2	22 mg/kg	Twitching, no seizure
3	23 mg/kg	Seizure at 38 sec
4	24 mg/kg	Seizure at 90 sec
5	25 mg/kg	Seizure at 65 sec
6	46 mg/kg	Seizure at 30 sec, severe seizure at 90 sec with death in extensor tonus

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