A STUDY OF 1, 1, 3, 3-TETRAMETHYLGUANIDINE AS A NONAQUEOUS SOLVENT

Thesis for the Degree of Ph. D.
MICHIGAN STATE UNIVERSITY
Melvin Lee Anderson
1965

This is to certify that the

thesis entitled

A STUDY OF 1, 1, 3, 3-TETRAMETHYLGUANIDINE
AS A NONAQUEOUS SOLVENT

presented by

Melvin Lee Anderson

has been accepted towards fulfillment
of the requirements for

Ph. D. degree in Chemistry

Robert N. Hammer
Major professor

Date April 20, 1965

O-169

[redacted]

ABSTRACT

A STUDY OF 1, 1, 3, 3-TETRAMETHYLGUANIDINE AS A NONAQUEOUS SOLVENT

by Melvin Lee Anderson

Although 1, 1, 3, 3-tetramethylguanidine has been known for a long time, it has only recently been studied as a nonaqueous solvent. In order to evaluate its solvent properties, a number of general areas were investigated: physical properties, salt solubilities, coordinating characteristics, general reactivity, and acid-base character.

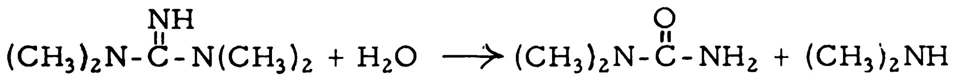
The high heat of vaporization of tetramethylguanidine and its transformation to a glass when cooled indicate considerable association in the liquid. Its infrared spectrum gives evidence for hydrogen bonding at the imine nitrogen. The proton magnetic resonance spectrum is consistent with the conventional molecular structure.

Tetramethylguanidine was found to have such a low dielectric constant (11.5) that ionic solutes are probably only partially dissociated in solution. Solubilities of a number of sodium and potassium salts were measured and were found to have the same relative order with respect to one another as solubilities of inorganic salts in liquid ammonia, but tetramethylguanidine is a somewhat poorer solvent. Tetramethylguanidine is completely miscible with most common organic solvents.

Transition metal salts form highly colored solutions in tetramethylguanidine but the colored complexes are difficult to isolate. The solvent functions as a monodentate ligand, apparently by coordination through the imine nitrogen. Cobalt(II) complexes in tetramethylguanidine seem to be tetrahedral, and the concentration or identity of the anion has little

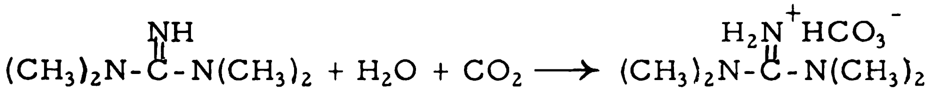
effect on the visible absorption spectrum of the complex. In general, Beer's law is not obeyed by cobalt(II) salts in tetramethylguanidine. The following complex species are postulated in these systems: $Co(TMG)_4^{++}$, $Co(TMG)_4^{++};X$, and $Co(TMG)_4^{++};2X^-$, where the latter two are ion-pairs.

Tetramethylguanidine hydrolyzes slowly at room temperature to form 1, 1 -dimethylurea and dimethylamine:



$$(CH_3)_2N-\overset{\overset{\displaystyle NH}{\|}}{C}-N(CH_3)_2 + H_2O \longrightarrow (CH_3)_2N-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2 + (CH_3)_2NH$$

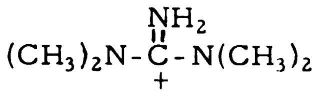
Moist solvent reacts rapidly with carbon dioxide to precipitate tetramethylguanidinium bicarbonate:



$$(CH_3)_2N-\overset{\overset{\displaystyle NH}{\|}}{C}-N(CH_3)_2 + H_2O + CO_2 \longrightarrow (CH_3)_2N-\overset{\overset{\displaystyle H_2\overset{+}{N}HCO_3^-}{\|}}{C}-N(CH_3)_2$$

Tetramethylguanidine does not react with metallic sodium or potassium, but lithium decomposes it. The liquid is oxidized by permanganate, dichromate, periodate, or silver(I). Mercury(I) salts undergo disproportionation.

Tetramethylguanidine titrates as a strong base in either aqueous or nonaqueous medium. The chloride, bromide, bicarbonate, and acetate salts were isolated and their melting points determined. Only monoprotonation occurs (at the imine nitrogen), followed by charge localization on the carbon atom:



$$(CH_3)_2N-\underset{+}{\overset{\overset{\displaystyle NH_2}{\|}}{C}}-N(CH_3)_2$$

Eight visual indicators for acid-base titrations were studied in tetramethylguanidine as a solvent. Their color changes correspond to conductometric end points if the indicator is a weaker acid than the acid being titrated. Good conductance curves were obtained for p-toluenesulfonic, benzoic, and salicylic acids as well as for phenol, ammonium bromide, and tetramethylguanidinium bromide. Titration with tetra-n-butylammonium hydroxide gave two conductance breaks for o-nitrophenol and 1, 3-dinitrobenzene, whereas 1, 3, 5-trinitrobenzene exhibits three distinct end points. These phenomena can be interpreted as addition of one, two, and three hydroxyl ions to the respective nitroaromatic ring. The fact that maleic and citric acids show two and three conductance breaks, respectively, in their titrations, indicates that differential titration of mixed acids in tetramethylguanidine is possible. No acidic properties were found for urea, acetamide, benzene, or nitrobenzene.

A STUDY OF 1, 1, 3, 3-TETRAMETHYLGUANIDINE AS A NONAQUEOUS SOLVENT

By

Melvin Lee Anderson

A THESIS

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

DOCTOR OF PHILOSOPHY

Department of Chemistry

1965

ACKNOWLEDGMENTS

The author wishes to express his appreciation to Drs. Robert N. Hammer and Alexander I. Popov under whose guidance this investigation was accomplished.

To the Dow Chemical Company, Midland, Michigan, the author extends his gratitude for a leave of absence, for a one-year fellowship and a summer research grant, and for the toxicological investigation of 1, 1, 3, 3-tetramethylguanidine.

Thanks go to the American Cyanamid Company, Wayne, New Jersey, for their gift of several gallons of tetramethylguanidine.

A heartfelt expression of gratitude is extended to the author's wife, Fern, for many years of patience and understanding throughout the pursuit of the Ph. D. degree and for typing the preliminary drafts of this dissertation.

* * * * * * * * * * * * * * *

TABLE OF CONTENTS

LIST OF TABLES

LIST OF TABLES - Continued

LIST OF FIGURES

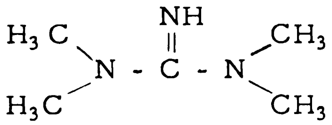
LIST OF FIGURES - Continued

LIST OF FIGURES - Continued

LIST OF APPENDICES

INTRODUCTION

Since the solvent properties of 1, 1, 3, 3-tetramethylguanidine,



are essentially unknown and because the compound has become available from the American Cyanamid Company (1), this investigation was undertaken to determine the utility of tetramethylguanidine as a nonaqueous ionizing solvent.

Five general areas of study were investigated to a limited extent: physical properties of tetramethylguanidine, solubilities in the solvent, inorganic reactions of tetramethylguanidine, acid-base equilibria, and coordination characteristics of tetramethylguanidine toward transition-metal ions.

Tetramethylguanidine contains two tertiary amine nitrogens and one imine group, each with a lone pair of electrons. Therefore it should be a strong donor ligand in the formation of metal ion complexes (2). Because of the closeness of the nitrogen atoms, however, chelation seems unlikely. Thus, if tetramethylguanidine were bidentate, the resulting complex would contain an improbable four-membered ring. On the other hand, tetramethylguanidine may act as a bridging group in a polynuclear complex (2).

Tetramethylguanidine has a conveniently wide liquid range extending from well below room temperature to a boiling point of 159-160° C. (1).

The exceptionally strong basic nature of tetramethylguanidine (pKa in water at $25^{\circ} = 13.6$) (1) should make it very useful as a solvent for the study of weak acids. Hydrogen-containing compounds which are only weakly acidic or even basic in water should have their acidic character sufficiently enhanced for titration in tetramethylguanidine (3). Tetramethylguanidine is a strong proton acceptor which levels acids to the acidity of the solvent cation, $TMGH^{+}$ (4):

$$TMG + HA \longrightarrow TMGH^{+} + A^{-} . \qquad (\underline{1})$$

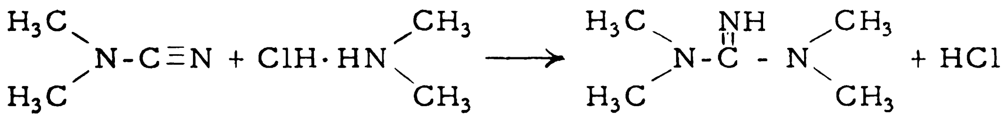
This reaction, however, does not imply complete dissociation of the resulting electrolyte. The degree of dissociation depends upon the dielectric constant of the solvent, the nature of the anion A^{-}, etc. (3).

As a basis for further work, it was also desirable to determine some solubilities of alkali metal salts in tetramethylguanidine and to characterize certain reactions of the solvent.

HISTORY

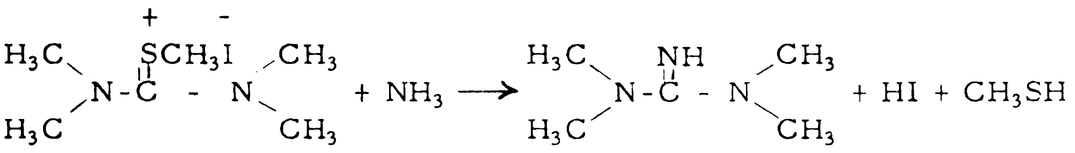
Preparation of 1, 1, 3, 3-Tetramethylguanidine and Related Compounds

The earliest known reference to 1, 1, 3, 3-tetramethylguanidine is the work reported by Berg (5) in 1893 in which he found that tetramethylguanidine is formed by the action of dimethylcyanamide on dimethylamine hydrochloride:



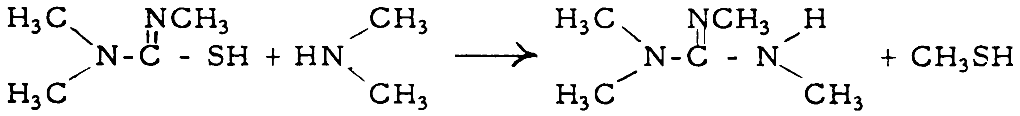
(2)

In a fairly complete study of the preparation and properties of a number of the methylated guanidines, Schenck (6) in 1912 prepared 1, 1, 3, 3-tetramethylguanidine by heating ammonia and pentamethylthiuronium iodide in ethanol solution:



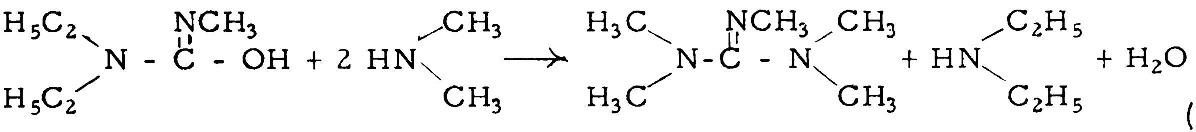
(3)

The isomeric compound 1, 1, 2, 3-tetramethylguanidine was prepared by Schenck from dimethylamine and trimethylpseudothiourea:

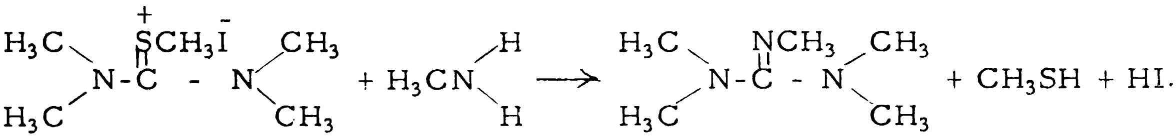


(4)

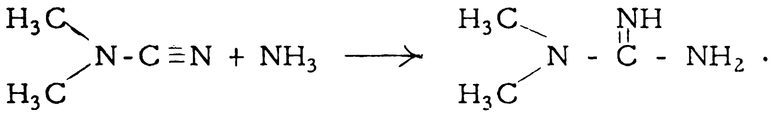
Schenck also prepared the completely methylated compound pentamethylguanidine by heating methyliminodiethylcarboxylic acid and dimethylamine:


(5)

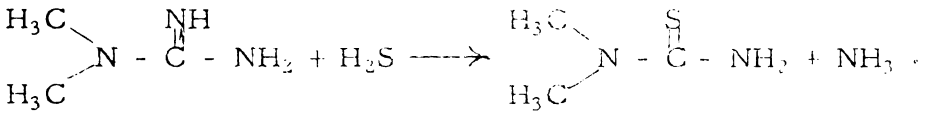
as well as by the action of methylamine on pentamethylthiuronium iodide:


(6)

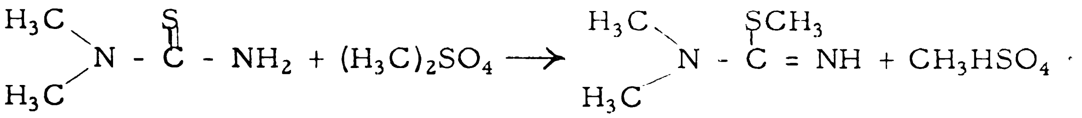
In 1924 Schenck and von Graevenitz (7) reported another preparation of 1, 1, 3, 3-tetramethylguanidine. 1, 1-Dimethylguanidine was first prepared by treating dimethylcyanamide with alcoholic ammonia:


(7)

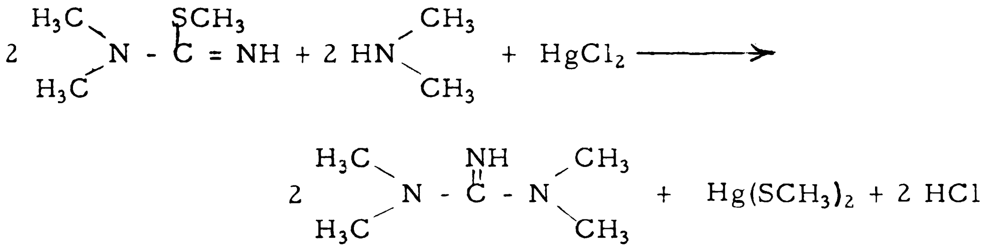
The solution was then saturated with hydrogen sulfide to give 1, 1-dimethylthiourea:


(8)

Methylation with dimethyl sulfate gave 1, 1, 2-trimethylpseudothiourea,


(9)

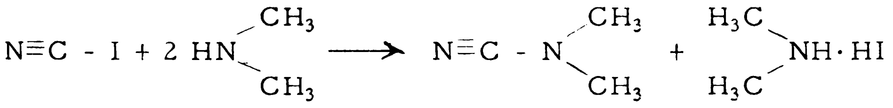
This product was treated with alcoholic dimethylamine and mercuric chloride to give the desired symmetrical guanidine derivative which was isolated as the chloroaurate.



$$2\,(\mathrm{H_3C})_2\mathrm{N}-\mathrm{C}(\mathrm{SCH_3})=\mathrm{NH} + 2\,\mathrm{HN}(\mathrm{CH_3})_2 + \mathrm{HgCl_2} \longrightarrow 2\,(\mathrm{H_3C})_2\mathrm{N}-\mathrm{C}(=\mathrm{NH})-\mathrm{N}(\mathrm{CH_3})_2 + \mathrm{Hg(SCH_3)_2} + 2\,\mathrm{HCl}$$

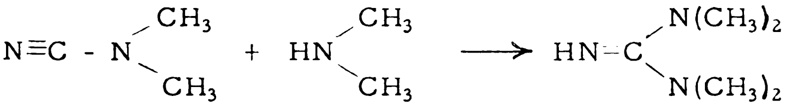
(10)

Schenck and von Graevenitz (7) also obtained 1, 1, 3, 3-tetramethylguanidine by treatment of cyanogen iodide with dimethylamine:



$$\mathrm{N{\equiv}C-I} + 2\,\mathrm{HN}(\mathrm{CH_3})_2 \longrightarrow \mathrm{N{\equiv}C-N}(\mathrm{CH_3})_2 + (\mathrm{H_3C})_2\mathrm{NH{\cdot}HI}$$

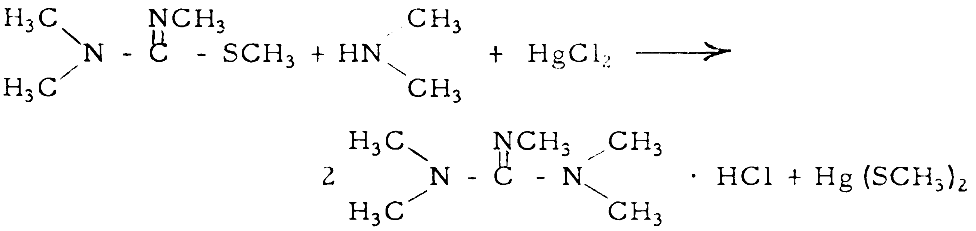
(11)



$$\mathrm{N{\equiv}C-N}(\mathrm{CH_3})_2 + \mathrm{HN}(\mathrm{CH_3})_2 \longrightarrow \mathrm{HN{=}C}(\mathrm{N(CH_3)_2})_2$$

(12)

At about the same time a number of papers were published by Lecher and co-workers (8a, b, c) on the preparation and characterization of completely alkylated guanidines such as pentamethylguanidine and hexamethylguanidinium iodide. As an example, the former was prepared by treating dimethylamine with 1, 1, 2, 3-tetramethylpseudothiourea and removing methyl mercaptan from the reaction with mercuric chloride:

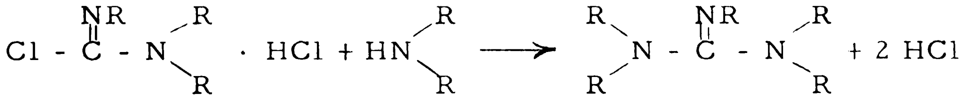


$$(\mathrm{H_3C})_2\mathrm{N}-\mathrm{C}(=\mathrm{NCH_3})-\mathrm{SCH_3} + \mathrm{HN}(\mathrm{CH_3})_2 + \mathrm{HgCl_2} \longrightarrow 2\,(\mathrm{H_3C})_2\mathrm{N}-\mathrm{C}(=\mathrm{NCH_3})-\mathrm{N}(\mathrm{CH_3})_2\cdot\mathrm{HCl} + \mathrm{Hg\,(SCH_3)_2}$$

(13)

The free base was then obtained by heating the hydrochloride salt and driving off hydrochloric acid.

Only a few scattered and incidental preparative methods for alkyl-substituted guanidines can be found in the literature after 1925. In 1959 a patent was issued to Cain (9) on the preparation of 1, 1, 2, 3-tetraethylguanidine and its salts, but the method is generally the same as that of Lecher et al. (8). A genuinely new method for the preparation of pentaalkylguanidines was reported by H. Z. Lecher and co-workers in a 1958 patent (10). In this case, the hydrochloride of a C-chloro-N, N, N-trialkylformamidine reacts with a dialkylamine in nitrobenzene solution:

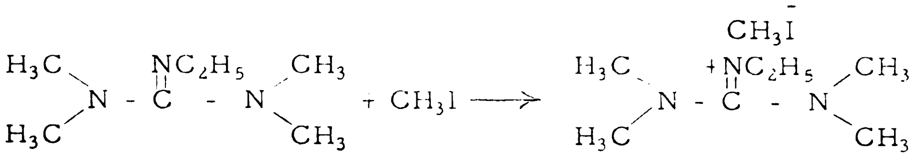


$$\mathrm{Cl-\overset{\overset{\displaystyle NR}{\|}}{C}-N\!\!\begin{array}{l}\diagup R\\ \diagdown R\end{array}\cdot HCl + HN\!\!\begin{array}{l}\diagup R\\ \diagdown R\end{array} \longrightarrow \begin{array}{r}R\diagdown\\ R\diagup\end{array}\!\!N-\overset{\overset{\displaystyle NR}{\|}}{C}-N\!\!\begin{array}{l}\diagup R\\ \diagdown R\end{array} + 2\,HCl} \qquad (\underline{14})$$

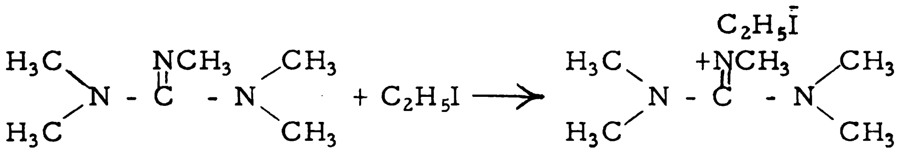
The method can be used to prepare either iso- or hetero-pentaalkylguanidines such as pentamethylguanidine or 1, 1, 2-trimethyl-3, 3-diethylguanidine.

Properties of 1, 1, 3, 3-Tetramethylguanidine and Related Compounds

Until the work of Lecher and Graf (8b), it was generally assumed that in a guanidinium salt such as the hydrochloride, the proton is bound by one of the amine, or $-NH_2$, groups. These authors showed, however, that the reaction of methyl iodide with 1, 1, 3, 3-tetramethyl-2-ethylguanidine as well as of ethyl iodide with pentamethylguanidine yields identical reaction products:



$$\mathrm{\begin{array}{r}H_3C\diagdown\\ H_3C\diagup\end{array}\!\!N-\overset{\overset{\displaystyle NC_2H_5}{\|}}{C}-N\!\!\begin{array}{l}\diagup CH_3\\ \diagdown CH_3\end{array} + CH_3I \longrightarrow \begin{array}{r}H_3C\diagdown\\ H_3C\diagup\end{array}\!\!N-\overset{\overset{\overset{\displaystyle CH_3\bar{I}}{\displaystyle +NC_2H_5}}{\|}}{C}-N\!\!\begin{array}{l}\diagup CH_3\\ \diagdown CH_3\end{array}} \qquad (15)$$



(16)

As shown in equations 15 and 16, this could only be explained on the assumption that salt formation involved the imine, or =NH, group.

Lecher and Graf (8b) also pointed out that guanidinium hydroxide and its alkyl derivatives are bases of about the same strength as the alkalies. These hydroxides were not isolated but by using acid-base indicators, it was shown that aqueous solutions of the various guanidinium iodides do not hydrolyze but behave as salts of strong bases and strong acids.

In 1951 Angyal and Warburton (11) did a fairly complete study of the basic strength of guanidine and several of the methylated guanidines. Most of the salts of the methyl-substituted guanidines were prepared by the methods of Schenck (6, 7) and Lecher (8), and the respective pKa values were measured by potentiometric titration in aqueous solution. The results of this work are shown in Table I where it is seen that all of the guanidines have pKa's of the same order of magnitude. The value found (11) for free guanidine was 13.6 at 25°, in good agreement with an older value of 13.6_5 (12) and a newer one of 13.54 (13). Recently a value of 14.06 has been reported (14) for the pKa of tetramethylguanidine (isomer not reported) in aqueous solution.

Angyal and Warburton (11) state that the absolute error of their results (Table I) may be as much as 0.2 pKa unit, but since all values were obtained under identical conditions, they believe that differences in relative values are significant. This conclusion seems open to question.

Melting points of a number of salts of the methyl-substituted guanidines have been reported by Schenck (6), Angyal and Warburton (11), and Kitawaki (15). These are given in Table II.

Table I. Basic Strengths of Guanidines

Guanidines	pKa	Reference
Guanidine	13.6	11
Guanidine	13.6_5	12
Guanidine	13.54	13
1-Methylguanidine	13.4	11
1, 1-Dimethylguanidine	13.4	11
1, 3-Dimethylguanidine	13.6	11
1, 1, 3-Trimethylguanidine	13.6	11
1, 2, 3-Trimethylguanidine	13.9	11
1, 1, 2, 3-Tetramethylguanidine	13.9	11
1, 1, 3, 3-Tetramethylguanidine	13.6	11
Tetramethylguanidine (isomer not reported)	14.06	14
Pentamethylguanidine	13.8	11

Table II. Melting Points of Guanidinium Salts, °C

Guanidine	Sulfate	Picrate	Iodide	Nitrate	Chloroaurate	Chloride
1-Methyl-	240					
1, 1-Dimethyl-	295-7	224-5				
1, 3-Dimethyl-	298-300d.	178-9	103.5-5	102-4		153-4
1, 1, 3-Trimethyl-		151-1.5	202.5-4			
1, 2, 3-Trimethyl-	>300	214-5	>300			
1, 1, 2, 3-Tetramethyl-		130-1	131.-1.5		115-7	
1, 1, 3, 3-Tetramethyl-		159-60	120-0.5		142-4	
Pentamethyl-		163-5	136-8		250-2	

Essentially the only available values of physical constants for 1, 1, 3, 3-tetramethylguanidine come from Market Development Department reports (1, 16) of the American Cyanamid Company. These data are given in Table III along with an additional boiling point measurement from the literature (17a).

Recently Williams and co-workers (17a, b) used 1, 1, 3, 3-tetramethylguanidine as a solvent for the titration of weak acids. They found that phenol and several substituted phenols could be titrated potentiometrically with tetramethyl- or tetrabutylammonium hydroxides using a glass electrode and a modified calomel electrode. Good equivalence point inflections were obtained in all titration curves. Other electrode systems as well as indicators for the titration of weak acids in tetramethylguanidine also were investigated. A glass electrode coupled with a silver-silver bromide reference electrode was most satisfactory. The indicators alizarin yellow and azo violet gave results in agreement with potentiometric end-point values.

Infrared Spectra of Guanidines

It was not until approximately fifteen years ago that the infrared spectra of some of the guanidines were reported in the literature. The extensive work by Randall et al. (18) includes the infrared spectra for guanidinium acetate, carbonate, and thiocyanate; methylguanidinium chloride and sulfate; and triphenyl- and symmetrical diphenylguanidine.

Few frequency assignments have been made for guanidines. Fabian et al. (19), in their review, report wavelengths for the C=N stretching absorption in the range of 5.92-6.17 μ. The Sadtler compilation (20) contains the infrared spectrum from 2-15 μ of liquid 1, 1, 3, 3-tetramethylguanidine (Figure 1, curve a). Curve b in Figure 1 is the infrared spectrum of a five percent solution of tetramethylguanidine in cyclohexane obtained by Drago (21).

Table III. Physical Properties of 1, 1, 3, 3-Tetramethylguanidine

Property	Value	Reference
Boiling point, °C	159-60	1
Boiling point, °C (738 mm)	159-61	17a
pKa, 25°	13.6	1
pH (1% solution)	12.7	1
Solubility	Soluble in water and common organic solvents	1
Vapor pressure, mm		
at 160°	760	16
at 100°	100	16
at 65°	20	16
at 25°	0.2	16

Protonation of Guanidines

Angyal and Warburton (11) in 1951 stated that "guanidines are theoretically not expected and have never been found to be diacid bases." However, two years later, Williams and Hardy (22) found 1.28 protons per guanidine molecule in 99.9 percent sulfuric acid solution. This is the only evidence in the literature for anything greater than monoprotonation of guanidines.

Most of the research within the past few years has dealt with the position of protonation rather than the amount. From positions of the infrared absorption bands of guanidine salts and some methyl-substituted guanidine salts, Goto and co-workers (23) concluded that the positive charge resides mainly on the central carbon atom rather than being distributed over the entire guanidinium group.

From molecular orbital calculations, Paoloni (24) concluded that the guanidinium ion should be considered as a tertiary positive carbon or triaminocarbonium ion, $(NH_2)_3C^+$, analogous to the quaternary nitrogen ion.

Kotera et al. (25) attempted to determine the location of proton addition in guanidine by analyzing the proton magnetic resonance spectrum of crystalline guanidinium iodide. They concluded that protonation occurs predominantly on the imine (=NH) nitrogen but that amine ($-NH_2$) addition could not be ruled out.

Guanidines as Ligands in Metallic Complexes

There is a dearth of information in the literature on the use of guanidine as a complexing agent for metallic ions. The related compounds, urea and thiourea and their derivatives, on the other hand, have been extensively investigated as ligands. The metal complexes of the alkyl-substituted ureas have been studied to a limited extent.

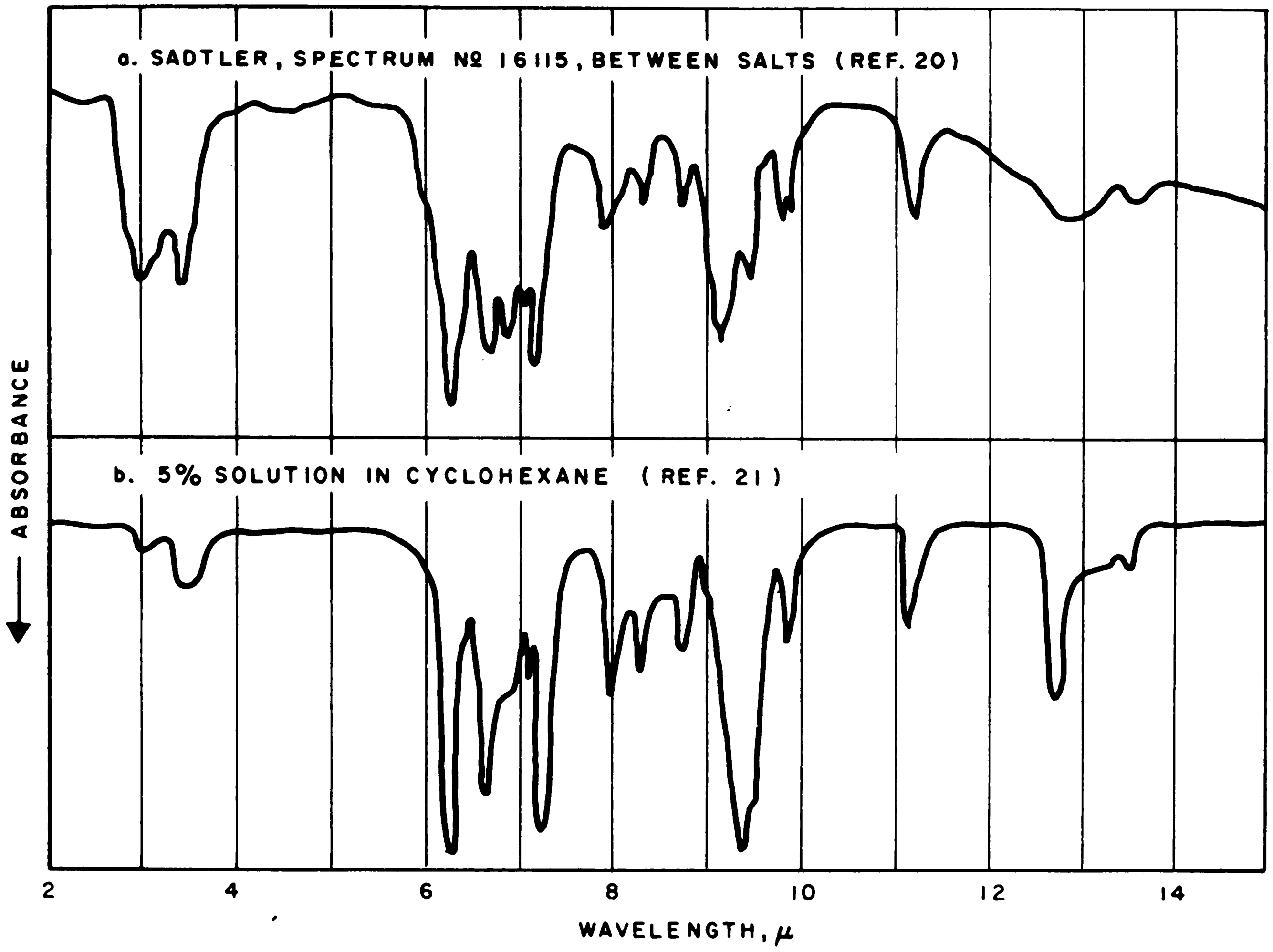


Figure 1. Infrared Spectra of 1, 1, 3, 3-Tetramethylguanidine.

Considerable work on complex compounds of biguanides and guanylureas, especially in India, has been thoroughly covered in a recent review (26).

The only major references in the literature to guanidine as a ligand are those of Gentile and Talley (27) and of Wirth and Davidson (13). By spectrophotometric studies in absolute ethanol, the former authors found that the uranyl ion (UO_2^{++}) forms only a 1:1 complex with guanidine. It is of interest to note that urea and thiourea form only the corresponding 1:2 complexes under similar conditions. Wirth and Davidson found that mercury(II) forms complexes of the type Hg-$(\text{guanidine})_2^{++}$ and Hg(guanidine)OH^+. In a biochemical study, Akihama and Toyoshima (28) prepared a guanidine complex of zinc presumed to be $[\text{Zn(guanidine)}_2\text{Cl}_2]\cdot 4H_2O$.

Some research is currently under way on the preparation and characterization of metal complexes of 1, 1, 3, 3-tetramethylguanidine. Longhi and Drago (29) have obtained the infrared spectra of the complexes $[\text{M(TMG)}_4](\text{ClO}_4)_2$, where M = cobalt(II), copper(II), and zinc(II). The spectra of the complexes are similar to each other but differ from that for free tetramethylguanidine (20, 21) in showing broader absorption bands, some wavelength shifts, etc. Drago's method of preparation involved the precipitation of the complex from solution by the addition of a solvent in which the complex was sparingly soluble.

It has been observed by Kennedy (30) in this laboratory that a blue-violet solid precipitates from solutions of copper(II) salts in tetramethylguanidine exposed to air. This precipitate is possibly a carbonate or bicarbonate salt of a tetramethylguanidine copper complex. Kennedy also found that solutions of copper(II) acetate monohydrate in tetramethylguanidine do not obey Beer's law in the range 0.002 to 0.01 $\underline{M}$.

Also in this laboratory Bloor (31) attempted to apply Job's method of continuous variations (32) to visible absorption spectra to characterize tetramethylguanidine complexes of some first-row transition metals. However, the method was generally unsuccessful because of low solubilities of these complexes in available solvents. Bloor was able to prepare a complex, presumed from elemental analysis to be $[Co(TMG)_3H_2O](NO_3)_2 \cdot H_2O$, by addition of tetramethylguanidine to a solution of cobalt(II) nitrate in tetrahydrofuran. Conductance measurements in nitromethane supported the conclusion that both nitrate ions are outside the coordination sphere.

Bloor studied the visible spectra of cobalt(II) salts in tetramethylguanidine and concluded that this compound is a very strong coordinating ligand. Neither changes in the anion used nor in the anion concentration had sufficient effect on spectra to suggest much displacement of tetramethylguanidine from the coordination sphere. In addition, deviations from Beer's law and the existence of identical spectra in tetramethylguanidine for the two complex cobalt salts $[Co(H_2O)_6]Cl_2$ and $[(CH_3)_4N]_2CoCl_4$ support this conclusion.

EXPERIMENTAL SECTION

Purification of 1, 1, 3, 3-Tetramethylguanidine

Stock tetramethylguanidine obtained from the American Cyanamid Company was a pale yellow liquid with an amine-like odor. It had a boiling point of 153.5-154.5° at 743 mm as measured by the micro capillary tube method (33). However, during heating to this temperature, some gas evolution occurred upwards from about 75°, probably due to the presence of some lower-boiling impurities.

During an initial attempt to distill stock tetramethylguanidine at atmospheric pressure, a very low yield of distillate was obtained and the undistilled residue turned black and nearly completely solidified. Therefore all future distillations were done at reduced pressure. It may be, however, that with close temperature control tetramethylguanidine could be distilled at atmospheric pressure since other workers have apparently not had to resort to a vacuum method (17). On the other hand, distillation at reduced pressure is believed to be advantageous since a subsequent experiment showed that boiling tetramethylguanidine rapidly darkened and decomposed when oxygen was bubbled through the liquid. Surprisingly, in a similar experiment using an atmosphere of dry nitrogen, decomposition of the tetramethylguanidine also occurred, but at a much slower rate than with oxygen.

The following distillation method was used to purify tetramethylguanidine with the apparatus shown in Figure 2. Barium oxide, boiling chips, and stock tetramethylguanidine were placed in a one-liter round-bottom flask A. To the flask was connected a $\frac{1}{2}$ x 12-inch electrically heated fractionating column B packed with 1/8-inch Pyrex glass helices.

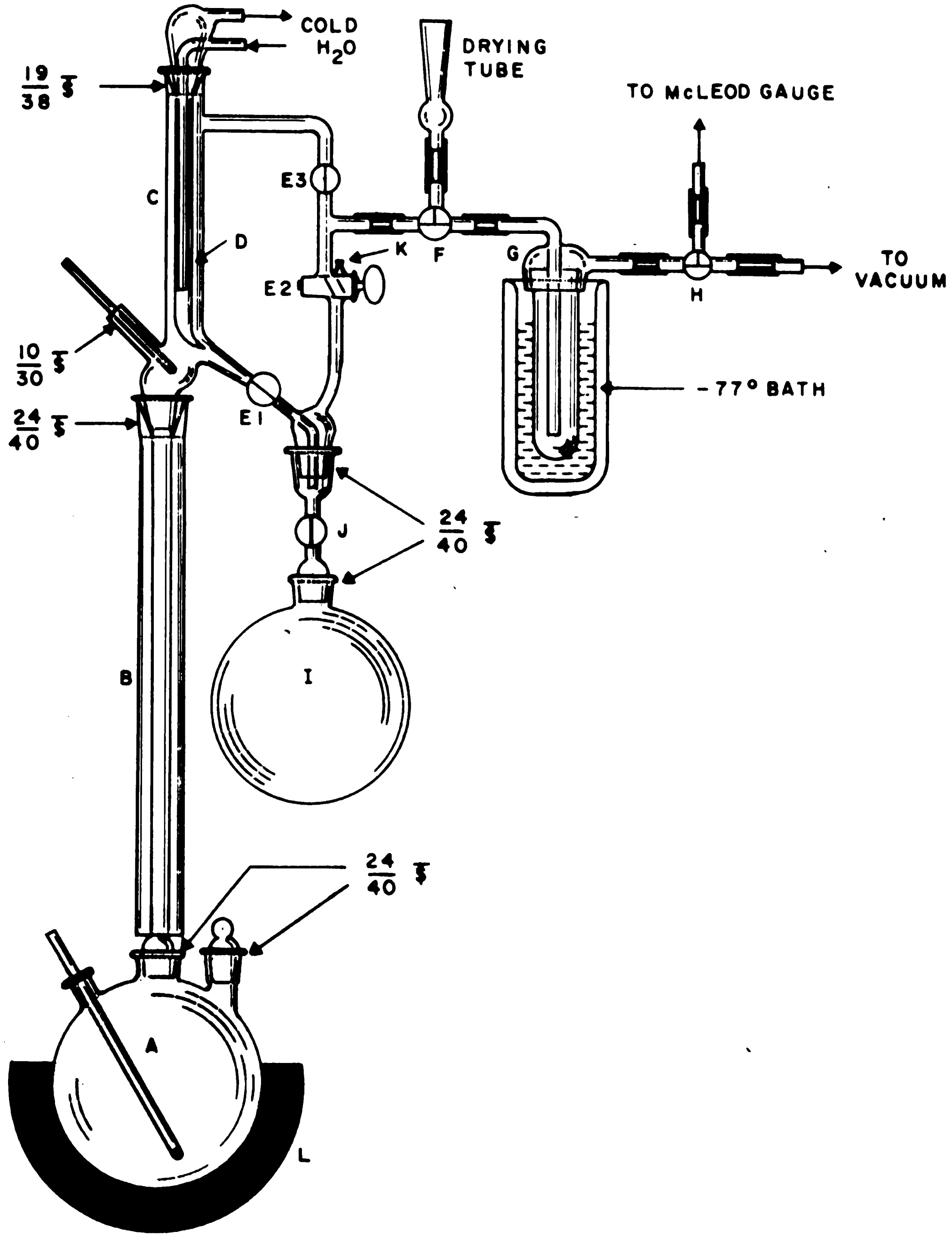


Figure 2. Apparatus for Distillation of 1, 1, 3, 3-Tetramethylguanidine.

A distillation head C attached to the top of the column served both to condense the tetramethylguanidine with a cold-water finger D and to allow a vacuum to be applied to any part of the system through proper manipulation of one or more of the stopcocks El, E2, or E3. Between the head and the vacuum pump were connected a three-way stopcock F with an attached Ascarite-Drierite-filled drying tube, a cold trap G inserted into a Dewar flask containing a Dry Ice-Methyl Cellosolve slush bath (-77°C.), and a second three-way stopcock H connected to a McLeod guage. When it was necessary to remove and empty the cold trap, stopcock H was closed to the system and stopcock F was opened to the atmosphere. The one-liter receiving flask I was connected to the distillation head through a separate 2 mm-bore glass stopcock J. At the completion of a distillation, the receiving flask could be removed without exposure of the contained distillate to the atmosphere simply by closing stopcocks J and El and opening stopcock E2 to allow air to enter the constricted tube K. In a typical distillation, the initial application of vacuum on the stock tetramethylguanidine at room temperature causes appreciable boiling and collection of most of the gaseous product as a viscous liquid in the cold trap. After 1.5-2 hours, stopcock El is opened and distillate is collected. This is done for several hours or overnight with the material still at room temperature. The receiving flask I is then replaced with a similar flask and the undistilled tetramethylguanidine is heated to about 35° with an oil bath L for about one hour. Distillate (pure tetramethylguanidine; calculated: C, 52.14; H, 11.38; N, 36.48%; found: C, 52.17; H, 11.24; N, 36.31%) is then collected at 36-38° under about 0.01 mm Hg until nearly all has distilled. Distilled tetramethylguanidine in flask I is transferred to a nitrogen-atmosphere dry box for storage and subsequent use.

Techniques for Handling 1, 1, 3, 3-Tetramethylguanidine

Barium oxide was used as a drying agent for stock tetramethylguanidine during storage and, as mentioned above, during distillation. Since it reacts with water and carbon dioxide to give insoluble $Ba(OH)_2$ and $BaCO_3$, respectively, BaO is commonly used (34) with basic solvents. The storage bottle for distilled solvent was fitted with a squeeze-bulb pump so that given volumes of solvent could be withdrawn as needed. In most cases, after removal from storage, a given sample of tetramethylguanidine was protected from contact with air until completion of the particular experiment. For instance, in solubility determinations, addition of both solvent and solute to the equilibration flasks was done inside the dry box, certain reactions in tetramenthylguanidine were done in a moisture- and CO_2-free atmosphere, etc. When it was inconvenient to maintain complete isolation of the tetramethylguanidine from the atmosphere, dry nitrogen was bubbled through the solvent, as in the conductance titrations. Physical constants of tetramethylguanidine were measured on freshly distilled material after pre-checking the purity by a boiling point (159-160°) measurement.

A persistent problem associated with tetramethylguanidine was that of frozen stopcocks and stoppers when using glass apparatus. This apparently is due to the highly alkaline nature (11) of tetramethylguanidine. No stopcock lubricant seems completely suitable, although the clear silicone greases produced by Dow Corning Corporation were the most resistant to tetramethylguanidine.

When working with tetramethylguanidine, safety glasses with side shields should be worn since severe eye damage or blindness can result from direct contact of the eye with the liquid solvent (1, 16). Tetramethylguanidine vapor tends to irritate the eyes. Unless it is promptly rinsed off with large amounts of water, tetramethylguanidine causes skin burns similar to those of concentrated sulfuric acid. The conclusions from an independent toxicological investigation of tetramethylguanidine are given in Appendix I.

Instrumental Methods

A. Physical Constants

The density of tetramethylguanidine as a function of temperature was obtained with a 50 ml pycnometer (Sargent S-9285) with attached thermometer and capillary side tube with vented ground glass cap. The thermometer had a range from 12 to 38°C calibrated in intervals of 0.2°. Three series of weighings were made over the 10 to 35° temperature range at about 2° intervals. The empty pycnometer, the pycnometer filled with water, and the pycnometer filled with tetramethylguanidine were weighed. By filling the pycnometer with liquid cooled to less than 10° it was possible to warm the apparatus slowly, wipe off excess liquid which had expanded out the capillary side tube, and make weighings to correspond to temperatures at which the capillary was filled exactly to the tip. In the case of tetramethylguanidine, the pycnometer was filled under nitrogen with solvent cooled to 10°. The subsequent weighings were made in normal laboratory atmosphere. Each series of weighings were plotted versus temperature and from the three sets of data the density of tetramethylguanidine was calculated at even-numbered temperatures from 12 to 32°. For the calculations, the density of water was taken from tables (35).

Refractive index measurements on tetramethylguanidine were made with an Abbé-Bausch and Lomb refractometer. Water-jacketed prisms connected to a variable-temperature bath made possible the determination of n_D for tetramethylguanidine from 17 to 33°. The solvent under nitrogen in sealed flasks was pre-equilibrated at each given temperature, a small sample was removed and introduced between the prisms of the refractometer, and readings were taken until they became constant. Constant values were obtained in less than one minute in all cases. The refractive index remained constant for several minutes, indicating neglible effect of atmospheric moisture or carbon dioxide during the period of measurement.

The dielectric constant of tetramethylguanidine was measured in this laboratory in collaboration with R. L. Titus using the apparatus illustrated in Figure 3a. The equipment consisted of a condenser and coil in a resonant circuit. The cell containing the condenser was originally built to determine dielectric constants of liquid eluate from a chromatographic column, but it was adapted for batch samples of liquid. Figure 3b is a drawing of the test cell. The shiny copper discs, 28 mm in diameter, which formed the plates of the condenser were spaced sufficiently close together to give the cell a capacitance of about six micromicrofarads in air. This value together with the inductance of the coil of about 0.5 microhenry determined the resonant frequency of the circuit. The condenser-coil circuit was energized using a radio frequency generator modulated with a 400 c.p.s. signal which was amplified and measured with a voltmeter. To make a measurement with a given liquid in the cell, the radio frequency signal was gradually increased until a maximum voltage was obtained. A number of solvents of known (36) dielectric constants were measured to give a standard curve of frequency vs. ϵ and from this curve the frequency determined for tetramethylguanidine gave directly its dielectric constant. Standard reagent grade solvents were used without further purification.

The specific conductance of tetramethylguanidine was determined by measuring conductances of freshly distilled solvent under nitrogen at 24.8 and 25.2° and the two values were averaged. The Wheatstone

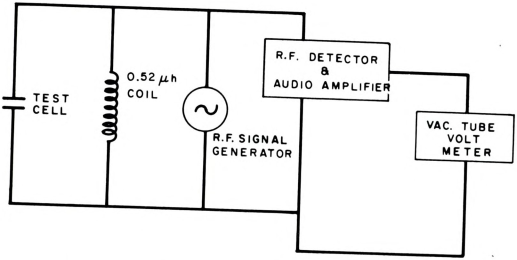


Figure 3a. Dielectric Constant Apparatus: Schematic Diagram.

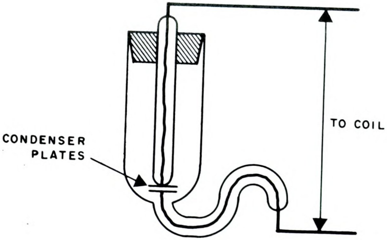


Figure 3b. Dielectric Constant Apparatus: Test Cell.

bridge and cell (conductance cell number I) were the same as those used for conductance titrations and will be described below.*

The viscosity of tetramethylguanidine was determined using an Ostwald viscometer with freshly distilled solvent at 24.8 and 25.2°, and the two values were averaged. The viscometer was filled under a dry nitrogen atmosphere and measurements were made with Drierite-Ascarite tubes fitted to the open ends of the apparatus.

B. Solubilities

Solubilities of a number of sodium and potassium salts in tetramethylguanidine were determined by standard methods (37). The method involved flame photometric analysis for the alkali metal in the residue obtained by evaporation of excess solvent from a weighed portion of saturated solution.

Salts used for quantitative and some semiquantitative solubility measurements were stock materials purified and dried by the methods listed in Table IV. Excess samples of salt and 7-10 ml portions of tetramethylguanidine were added in the dry box to a series of twelve ten-milliliter Kjeldahl flasks. The flasks were then sealed with corks covered with aluminum foil followed by tightly fitting rubber septum caps. Each salt was run in triplicate, i.e., each series of twelve Kjeldahl flasks allowed solubility measurements on four sets of alkali metal salts. After removal of the sealed flasks from the dry box, one flask of each set was cooled to 0°, one was warmed to 50°, and the remaining four flasks were left at room temperature. All flasks were then immersed to within one inch of their tops in a constant-temperature water bath (25.04 ± 0.04° C) and equilibrated by shaking for 72 hours. The bath thermometer was compared with a National Bureau of Standards

---

*See p. 31.

Table IV. Purification of Alkali Metal Salts

Purification Method	Salts
Recrystallized from H_2O	NaCl, NaBr, $NaClO_3$, $NaHSO_4$, KNO_3, $KClO_3$, $KBrO_3$
Recrystallized from H_2O-Ethanol	$NaIO_3$, $NaC_2H_3O_2$, KCl, KBr, KI, $KClO_4$, $KC_2H_3O_2$
Recrystallized from Ethanol	NaNCS
Recrystallized from H_2O-Acetone	$NaNO_3$, KNCS
Dried at 110° at 1 atm, and 100° under vacuum	NaI, $NaClO_4$, Na_2SO_4, KIO_3, K_2SO_4, LiCl, LiBr, $LiNO_3$, Li_2SO_4, Li_2CO_3, $Li_2C_2O_4$

calibrated thermometer. In separate experiments with sodium chloride and sodium bromide it was determined that equilibrium was usually reached in a matter of a few hours or after overnight shaking. Attempts were made to eliminate any effect of crystal size on dissolution by adding the salt in the form of varying crystal sizes. Mixing of the solvent and solute was assisted by placing two glass beads in each flask.

A drawing of the shaker used in the solubility studies is shown in Figure 4. The shaker was operated by means of an eccentric weight attached to the 300 r.p.m. shaft of a Waco stirring motor with the motor speed regulated by a variable transformer. The motor was clamped near one end of a 24-inch horizontal aluminum rod. On the opposite end of the rod, hanging down inside the water bath, was a rectangular framework carrying twelve rubber-lined spring clamps to hold the Kjeldahl equilibration flasks. Between the motor and framework, the horizontal rod was clamped to a tall aluminum-rod ring stand bolted to the bench top. The ring stand was modified using a loose fitting rod and rubber washers in the connection of the rod to the base. This allowed lateral movement of the entire assembly during shaking. The degree and type of shaking of the samples were controlled by suitable horizontal or vertical adjustments of the position of the motor, the speed of the motor, the angle of the rack of flasks from the vertical, and the closeness of fit of the flasks in the spring clamps. The clamp holders and motor were kept firmly in place by forcing the thumb screws of the clamp holders against suitable flat-surfaced portions of the rods.

After shaking, the flask contents were allowed to settle for 24 hours with the flasks remaining partially immersed in the water bath. Aliquots of the saturated solutions were removed from each flask using 1, 2, or 5 ml graduated pipets which were fitted with glass wool plugs in their tips to filter out any unsettled solids. The saturated solutions

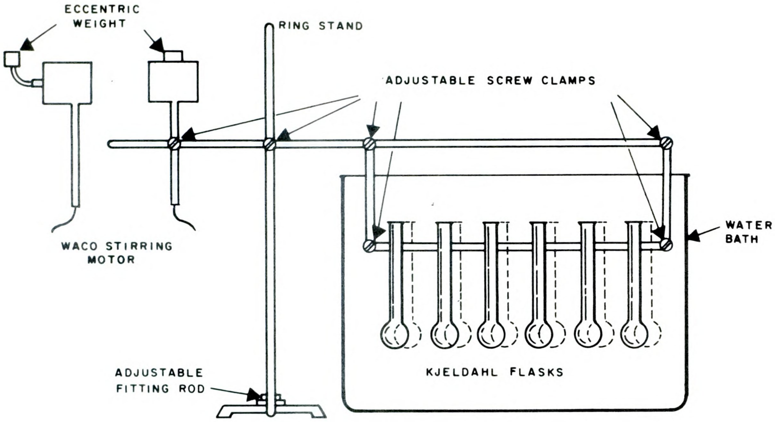


Figure 4. Apparatus for Solubility Equilibrations.

were run into calibrated pycnometers (usually 5 ml), weighed, and their densities calculated. Excess tetramethylguanidine solution was removed from the outside of the pycnometers by rinsing them with water and acetone. They were allowed to dry in air. During weighing, the pycnometers were handled only with Kimwipes.

From the pycnometers, saturated solution was transferred to weighed weighing bottles (12 ml capacity, 29/12 ₮ stopper) and the mass of the solution was determined by difference. Solvent was then evaporated from the saturated solutions at room temperature under vacuum in a desiccator for three to five days. Residue mass was then obtained. For some of the more soluble solutes, elevated temperatures (about 50°) were necessary to remove solvent completely, and occasionally complete removal could not be effected except by heating the sample above the decomposition temperature of the solute. In every case residues were analyzed for both solute and solvent to detect solvate formation. Undissolved solute remaining after equilibration was also examined for tetramethylguanidine of solvation.

The strongly basic nature of tetramethylguanidine made possible its determination by titration in aqueous solution with standard acid using a glass-calomel electrode system and a Beckman Model G pH meter. In separate experiments with known amounts of tetramethylguanidine it was found that titration to pH 5 gave results within ± 1% of theoretical. A typical titration curve for tetramethylguanidine will be shown and discussed below.*

The amount of solute in a given residue of alkali metal salt was usually determined by flame photometry, especially in cases of very small amounts (< 1 mg). A Beckman Model B spectrophotometer was used in the measurements, generally following the procedure of

---

*See pp. 69-70.

Willard, Merritt, and Dean (38). To minimize any anion effect on the flame, separate standard curves were constructed for each salt from measurements on standard aqueous solutions. A typical standard curve is shown in Figure 5.

After each residue was titrated for tetramethylguanidine, the solution was diluted with water to a convenient volume (usually 25 ml) in a volumetric flask. Samples of these solutions were then aspirated in the flame photometer several times and an average flame intensity calculated. The actual flame intensity due to the alkali metal content was obtained by subtraction of the flame background and the average intensity of a blank. The blank solutions contained tetramethylguanidine (titrated to pH 5) in roughly similar concentrations to the samples. The amount of alkali metal in the sample was obtained directly from the standard curve, and salt solubilities were then calculated in grams of solute per hundred grams of solvent. A typical tabulation of data and calculation of solubility (for $NaHSO_4$) is given in Appendix II.

A second method of solute analysis in the residue from samples of saturated solution was by titration of the anion in question. For instance, sodium bromide was determined by titration with standard silver nitrate solution.

The third method of solute analysis was simply that of determining the weight of the residue after evaporation of excess solvent. Any weight due to residual tetramethylguanidine was subtracted from the total weight of the residue after titration for the solvent. This method was used only in cases where flame photometry was unsuitable and where the precision of the results of at least two of the triplicate samples was five percent or less. The solubilities of $KBrO_3$ and $KClO_3$ were obtained by the weight-residue method.

Semiquantitative solubilities of a large number of inorganic compounds were also obtained by the weight-residue method. In addition,

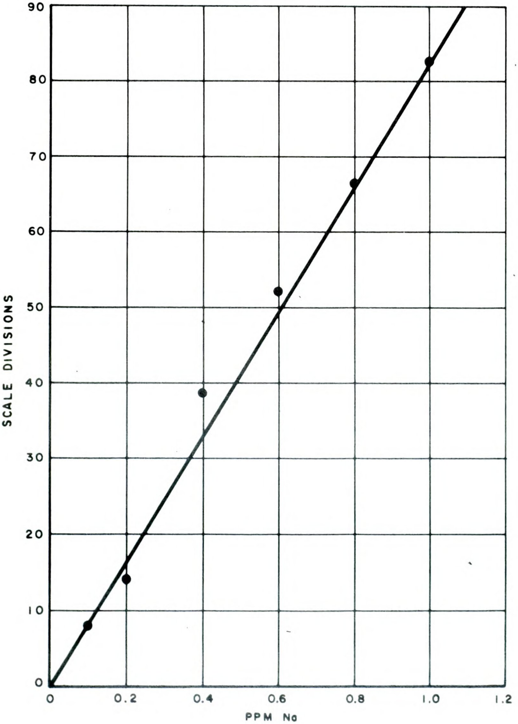


Figure 5. Standard Flame Photometric Curve for Sodium Hydrogen Sulfate Solutions.

solubility ranges or minimums were obtained in conjunction with experiments in which tetramethylguanidine was used as a solvent.

C. Spectra

Ultraviolet, visible, and near infrared spectra of tetramethyl- dine solutions were obtained with a Beckman Model DK-2 recording rophotometer. Glass-stoppered 1 cm silica cells were used in measurements to minimize exposure to air.

Infrared spectra from 2-15 μ were measured with a Perkin-Elmer l 21 spectrometer using cells with either sodium chloride or sium bromide windows. Proton magnetic resonance spectra were ıed with a Varian Model A-60 spectrometer.

D. Titrations

All potentiometric titrations in aqueous solution for acids or bases done with a Beckman Model G pH meter using a glass--calomel ode system. A glass--silver, silver chloride electrode system sed in argentometric titrations for halide ion. Tetramethylguanidine etermined by nonaqueous titrations in glacial acetic acid and in ıitrile using glass--silver, silver chloride electrodes and perchloric ı acetic acid as the titrant. Dry nitrogen was bubbled into these ıeous solutions during titration, and the titrant was protected from ch a tube of Drierite on top of the buret.

Conductometric titrations in tetramethylguanidine as a solvent were sing a Serfass Model RC M15 Conductivity Bridge. Solutions ontained in a 48 x 87 mm beaker closed with a rubber stopper h which passed the tip of a 10 ml buret, a nitrogen inlet, and a en outlet. Sample and titrant solutions were protected from the phere with drying tubes containing Ascarite and Drierite. During on, solutions were mixed with a small magnetic stirrer. No ature control was used.

For the series of titrations reported in this thesis, two conductance ells with slightly different cell constants were used. The electrodes cell number I were those of a commercial dip cell fitted into the rubber opper and sufficiently immersed in the sample solution to cover the ectrode surfaces. The two electrodes were of shiny platinum, each x 13.5 mm, and positioned 2 mm apart. The measured constant for is cell using 0.0100 M KCl solution was 0.1168 cm^{-1}. A drawing of e cell is shown in Figure 6a.

Cell number II had a constant of 0.05143 cm^{-1}. It was constructed th electrodes fastened to the inside wall of the cell as shown in gure 6b. The electrodes were 15 x 20 mm shiny platinum separated 3.5 mm.

Conductance titrations were done by a standard procedure. For ample, in the titration of weak acids with a base in tetramethylguanidine ution, sufficient solid acid to give about a 0.01 M solution was weighed and dissolved in tetramethylguanidine in a 100 ml volumetric flask. ese operations were done in a dry box. Fifty or sixty milliliters solution was pipetted into the conductance cell which was immediately ppered, dry nitrogen was bubbled through the solution, and stirring un. The titration was then carried out.

The titrant (base) used in these conductance titrations was a hanol solution of tetra-n-butylammonium hydroxide (Eastman). This erial was obtained as a 25 percent solution of the base in methanol was diluted further with dry methanol to give titrant solutions rang- from 0.2-0.8 M. The concentration of base was such that only it three milliliters was required for sixty milliliters of acid solution. conductance of pure methanol in tetramethylguanidine was determined a standard conductance curve was drawn (Figure 7). Methanol con- ance values were then subtracted from measured conductances in itrations.

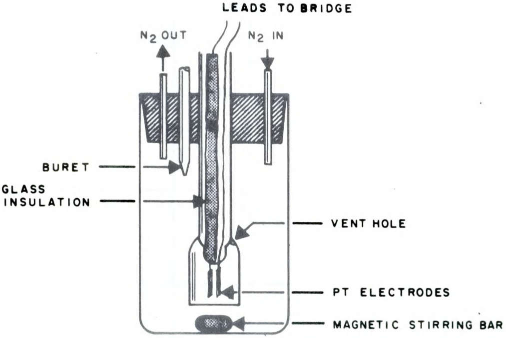


Figure 6a. Conductometric Titration Cell Number I.

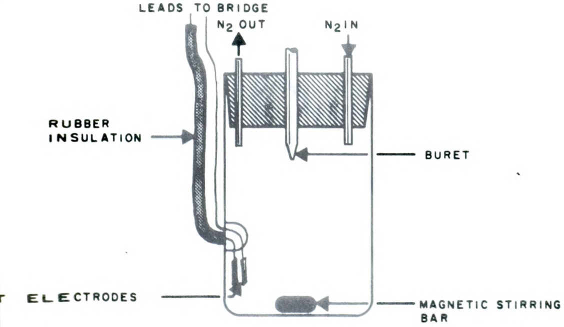


Figure 6b. Conductometric Titration Cell Number II.

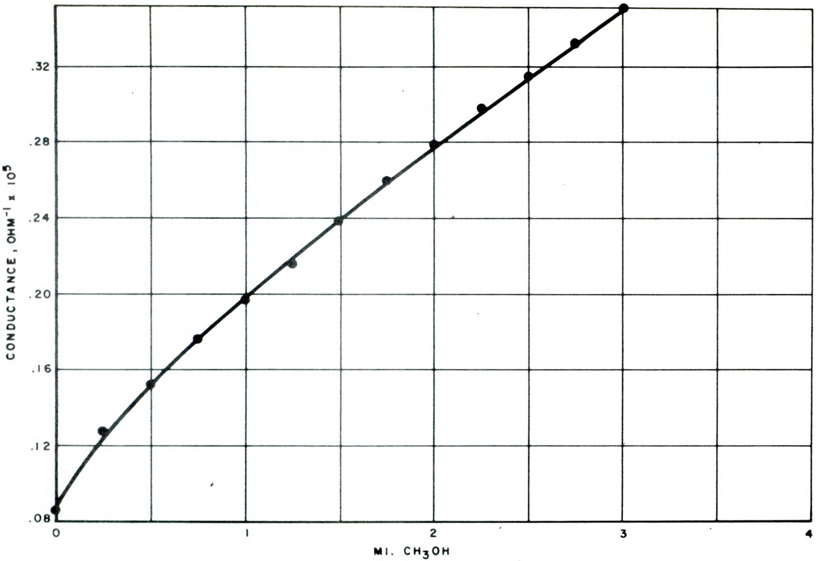


Figure 7. Conductance of Methanol in 1, 1, 3, 3-Tetramethylguanidine.

When indicators were used in titrations, they were generally added as oven-dried (110°) solids. Initial indicator concentrations were approximately 10^{-4} $\underline{M}$ except in a few cases where a somewhat higher concentration was necessary to develop sufficient color intensity.

Derivatives of 1, 1, 3, 3-Tetramethylguanidine

Tetramethylguanidinium salts were prepared as precipitates by addition of acid to an excess of tetramethylguanidine, followed by filtration. The precipitate was washed with pure solvent. Occluded solvent was then removed under vacuum at room temperature. The chloride and bromide salts were prepared in this manner from anhydrous hydrogen halides, while the acetate was obtained by addition of glacial acetic acid to tetramethylguanidine. No precipitate formed when seventy percent aqueous perchloric acid was added to tetramethylguanidine; neither did precipitation occur when the mixture stood in air. Tetramethylguanidinium bicarbonate was prepared by addition of solid or gaseous carbon dioxide to a 1:1 TMG:H_2O mixture. All the tetramethylguanidinium salts were found to be hygroscopic and were stored over $Mg(ClO_4)_2$ or P_2O_5 in a vacuum desiccator.

Colored solid transition metal compounds, presumed to be complexes, of tetramethylguanidine with the acetates of cobalt(II), nickel(II), and chromium(III) were prepared and analyzed. The method involved preparation of an essentially saturated solution of the hydrated metal acetate and vacuum evaporation of excess tetramethylguanidine at temperatures below the point of decomposition. After the resultant filmy solid was ground in a dry atmosphere, it was dried further under vacuum at the temperature previously used. The cobalt and nickel products were heated to 115-20° while only a 65-70° temperature was used for the chromium compound. Higher temperatures decomposed or melted the substances.

rocedures similar to these were tried using hydrated copper(II) in attempts to prepare a solid copper-tetramethylguanidine . An intensely blue solution was obtained which could be ted to a dark blue tacky material which showed little change olonged heating under vacuum at 65-70°, but which decomposed ated at 80°. Thus, no analysis of the copper-tetramethyl- ie reaction product was made.

als

. Purification

he purification method developed for liter quantities of tetra- uanidine has been described above (p. 16 ff.). In addition, hods used for the purification of the alkali metal salts used in ntitative solubility measurements have been previously described V). The inorganic salts used for the semiquantitative solu- udies and other miscellaneous applications were simply dried to t weight. Acid-base indicators used in some conductance ns were dried at 110°.

ransition metal salt hydrates were generally stock material used further purification. Anhydrous $CoCl_2$ and $Co(C_2H_3O_2)_2$ were d by vacuum dehydration of the hydrates at temperatures (130° °, respectively) below their hydrolysis or decomposition points o$(ClO_4)_2 \cdot 6H_2O$ was purified by recrystallization from water and in air. The acids used in the conductometric titrations were aterials purified, if necessary, by sublimation or distillation eir melting or boiling points agreed closely with literature values. enesulfonic acid was used as the stock monohydrate since it was t to dehydrate completely (40). Subsequently, experiments showed ter of hydration from the monohydrate had no effect on the results cid-base titrations.

rganic solvents such as methanol or acetonitrile used in this
ere purified by distillation from 4A Linde molecular sieves or
rying agents (41). These distillations were customarily done
small (<u>ca</u>. 1 cm x 20 cm) columns packed with Pyrex glass
.

. Elemental Analyses

ommercial analysis of stock and distilled tetramethylguanidine
ne of its derivatives was done by Alfred Bernhardt Micro-
al Laboratory, Mülheim (Ruhr), West Germany. Analysis of
f the tetramethylguanidine derivatives was also done by Spang
nalytical Laboratory, Ann Arbor, Michigan. The elemental
s of transition metal complexes of tetramethylguanidine was
out by Schwarzkopf Microanalytical Laboratory, Woodside,
rk.

RESULTS AND DISCUSSION

Physical Constants of 1, 1, 3, 3-Tetramethylguanidine

Several physical constants of pure, distilled 1, 1, 3, 3-tetramethylguanidine were determined. A list of measured as well as some calculated constants is given in Table V.

A. Heat of Vaporization

The heat of vaporization of tetramethylguanidine was calculated from the vapor pressure data of Table III published by the American Cyanamid Company (16). In order for all the data to describe a linear relationship between log p and 1/T, the assumption was made that the vapor pressure of tetramethylguanidine at 25° is 2.0 mm rather than 0.2 mm as reported (typographical error?). This assumption is supported by measurements made in this laboratory. The Trouton constant was determined from the calculated value of ΔH_v and the measured boiling point. The relatively high value for the heat of vaporization indicates considerable association in the liquid state. The value of 11.2 kcal mole^{-1} for the heat of vaporization of tetramethylguanidine is quite close to that of other nitrogen-containing solvents. For instance, the heat of vaporization of ethylenediamine is 11.2 kcal mole^{-1} (42), while that of dimethylformamide is nearly the same (11.37 kcal mole^{-1}) (43). The high Trouton constant of 25.9, on the order of that for water at 26.1 and methanol at 24.9 (44), is an additional indication of a reasonably high degree of self-association in liquid tetramethylguanidine.

Table V. Physical Constants for 1, 1, 3, 3-Tetramethylguanidine

Measured		
Boiling point (745 mm)		159.5° C
Density, d^{25}		0.9136 g ml^{-1}
Dielectric Constant, ϵ^{25}		11.5
Refractive Index, n_D^{25}		1.4658
Specific Conductance (25°)		9.9×10^{-7} ohm^{-1}
Viscosity (25°)		1.40 cp
Infrared Absorption:	ν (N-H)	3311 cm^{-1}
	ν (C=N)	1594 cm^{-1}
Proton Magnetic Resonance:	CH_3	2.62 ppm
	NH	5.17 ppm
Calculated		
Heat of Vaporization, ΔH_V		11.2 kcal $mole^{-1}$
Trouton Constant		25.9 cal $mole^{-1}$ deg^{-1}
Molar Refraction, Mr_D^{25}		34.91 cm^3 $mole^{-1}$

B. Freezing Point

It was not possible to measure the freezing point of tetramethylguanidine. All attempts to cool samples of tetramethylguanidine to very low temperatures resulted only in "glass" formation. At -75 to -70° C, tetramethylguanidine flows as a viscous liquid which becomes glassy at temperatures below about -80°. No crystallization occurs down to -190° C. Apparently there are intermolecular forces in liquid tetramethylguanidine that are too strong to permit rearrangement into the ordered crystalline state.

C. Molar Refraction

The molar refraction of tetramethylguanidine was calculated by the Lorenz-Lorentz equation using the measured value of the refractive index, n_D^{25}. The value for Mr_D^{25} of 34.91 cm^3 $mole^{-1}$ is smaller by about 1.6 units than the molar refraction estimated from tables of atomic and bond refractions (45). This fact may indicate some contraction of the tetramethylguanidine molecule by intramolecular hydrogen bonding since the molar refraction represents the actual volume of the molecules in one mole of substance.

D. Boiling Point

The high boiling point of 1, 1, 3, 3-tetramethylguanidine together with its glass temperature of about -80° give this substance an extremely wide liquid range. Thus, solutions in tetramethylguanidine could perhaps reasonably be studied over a two-hundred degree temperature range. A few other compounds containing C-H and N-H bonds with similar wide liquid ranges are known. As indicated in Table VI, tetramethylguanidine appears to lie intermediate between N-methylaniline and diisobutylamine in a number of fundamental physical properties. This may indicate that the true melting point of tetramethylguanidine is somewhere between -57 and -70° C.

Table VI. Comparison of Properties of 1, 1, 3, 3-Tetramethylguanidine with Related Compounds

	N-Methylaniline	Tetramethylguanidine	Diisobutylamine
Formula	$C_6H_5N(H)CH_3$	$(CH_3)_2NC(:NH)N(CH_3)_2$	$[(CH_3)_2CHCH_2]_2NH$
Molecular Weight	107.2	115.2	129.2
Refractive Index	1.5702	1.4658	1.4093
Density, gm l^{-1}	0.986	0.914	0.745
Melting point, °C	-57	∼-80 (glass)	-70; f.p. -77
Boiling point, °C	195.7	159.5	139.5

The boiling points of the free base forms of only two of the eleven theoretically possible methyl-substituted guanidines have been reported. These are 1, 1, 3, 3-tetramethylguanidine, b. 159.5 (this work, 1, 16, 17) and pentamethylguanidine, b. 155-160 (8a), both liquids at ordinary temperatures. Nevertheless, it is felt that at least four methyl groups are required per guanidine moiety in order that the compound be a liquid at room temperature. This would be similar to the corresponding family of methyl-substituted ureas where tetramethylurea is the only member which is liquid at room temperature (46, 47). Luettringhaus and Dirksen (47) point out that the normally strong association of amides due to hydrogen bridges involving the hydrogen on the amide nitrogen is precluded in tetramethylurea. The material thus can act only as a hydrogen-bond acceptor. The same argument can indeed be used for pentamethylguanidine, a liquid at room temperature (8a), and also for 1, 1, 3, 3-tetramethylguanidine if the hydrogen on the imide nitrogen in the latter shows a lesser tendency to form hydrogen bridges than a corresponding amide hydrogen. It would be interesting to know some of the common physical properties of all the other methylated guanidines. Even though most of them have been prepared as salts (6, 8a), apparently it is difficult to isolate the free bases (11).

E. Density

The density of 1, 1, 3, 3-tetramethylguanidine appears normal for a C, H, N- compound of its molecular weight (see Table VI). The plot of specific gravity of tetramethylguanidine vs. temperature from 12 to 32^{o} C is given in Figure 8a. The refractive index of tetramethylguanidine over the range from 17 to 33^{o} is shown in curve b of the same figure. The nearly linear relationships found for these properties is an indication of ideal behavior over the given temperature ranges which were studied.

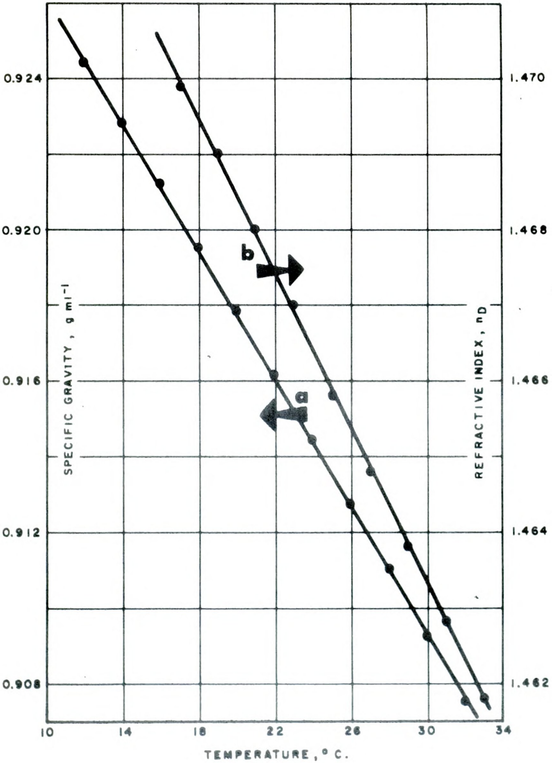


Figure 8. Effect of Temperature on the Specific Gravity and the Refractive Index of 1, 1, 3, 3-Tetramethylguanidine.

F. Dielectric Constant

The standard curve used for the determination of the dielectric constant of 1, 1, 3, 3-tetramethylguanidine is shown in Figure 9. As indicated in the Experimental Section and shown in the figure, a number of reagent grade solvents of known dielectric constants were measured to construct the standard curve of measured frequency vs. dielectric constant. The frequency of 20.2 x 10^6 c.p.s. for tetramethylguanidine corresponds to a dielectric constant of 11.5. It is felt that the error involved in this figure, all factors considered, is ± 5%. This would mean a resultant ϵ for tetramethylguanidine of 11.5 ± 0.6. Many of the more familiar basic nonaqueous solvents have similar dielectric constants. For instance, that of ethylenediamine at 20° is 14.2 while that of pyridine at 25° is 12.3 (48). By analogy, therefore, it is hoped that tetramethylguanidine may prove equally as useful a nonaqueous solvent as ethylenediamine or pyridine. The solvent properties of the latter two, of course, depend not only upon their dielectric constants but also on their strong electron-pair donating ability. The fact that tetramethylguanidine possesses a lone pair of electrons on each of its three nitrogen atoms also should make it a good donor solvent.

G. Specific Conductance

The measured specific conductance for 1, 1, 3, 3-tetramethylguanidine of 9.9 x 10^{-7} ohm^{-1} is a tentative upper limit. This value might be lowered by extremely careful purification. The observed specific conductance is about an order of magnitude greater than that for ethylenediamine and larger by a factor of 10^3 than the lowest value obtained for pyridine (48). However, since there is some indication (elemental analysis, sharpness of boiling point) that relatively pure tetramethylguanidine was used in this work, then the "high" specific

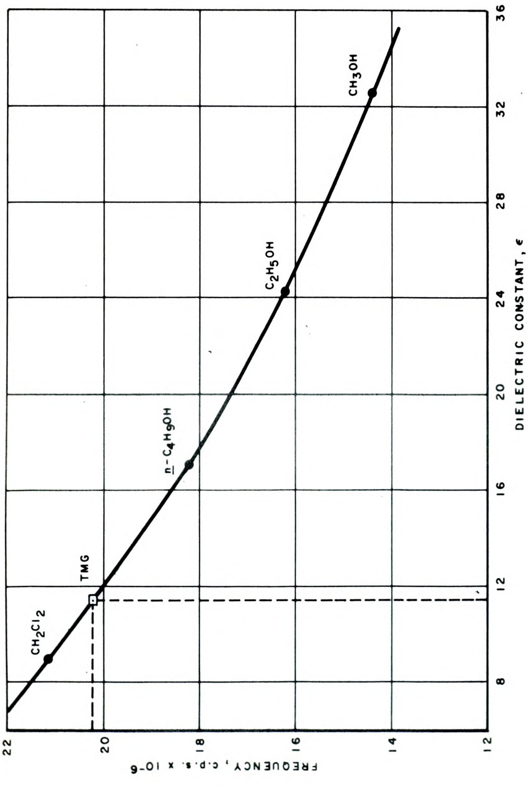


Figure 9. Standard Curve: Dielectric Constant Measurement.

conductance would have to be accounted for by a high degree of self-ionization. The determination of the self-ionization constant for tetramethylguanidine, i.e., the constant for the reaction

$$2[(H_3C)_2N]_2C{:}NH \rightleftharpoons [(H_3C)_2N]_2CNH_2^{\,+} + [(H_3C)_2N]_2CN^- \qquad (\underline{17})$$

was felt to be beyond the scope of this initial broad study of the solvent. The above cation, $[(H_3C)_2N]_2CNH_2^{\,+}$ or ($TMGH^+$) is well-known from the various tetramethylguanidinium ion salts which have been prepared in this and other studies (6, 11). However, the solvo-anion from tetramethylguanidine, $[(H_3C)_2N]_2CN^-$, is unknown and at this time can only be postulated.

H. Viscosity

The measured viscosity of tetramethylguanidine of 1.40 centipoises at 25° lies between that of pyridine (0.945 cp at 20°) and ethylenediamine (1.725 cp at 25°) (49). Thus the viscosity of tetramethylguanidine should cause no serious handling or processing problems. In addition, the mobility of ionic species and the conductance of electrolytes in tetramethylguanidine should be sufficiently large for convenient measurement. As the solvent is cooled below room temperature, the increasing viscosity may become a disadvantage. Very likely a complex network of hydrogen bonds develops in the solvent as the glass temperature (-80°) is approached (50). Perhaps a study of viscosity of tetramethylguanidine *vs.* temperature would shed some light on its liquid structure.

I. Infrared Absorption

The infrared absorption bands assigned to the stretching vibrations of the N-H and C=N bonds of 1, 1, 3, 3-tetramethylguanidine are given in Table V as 3311 and 1594 cm^{-1}, respectively. These assignments are based on the spectrum of the neat liquid recorded in this laboratory and shown in Figure 10. The path length in the liquid cell used in the

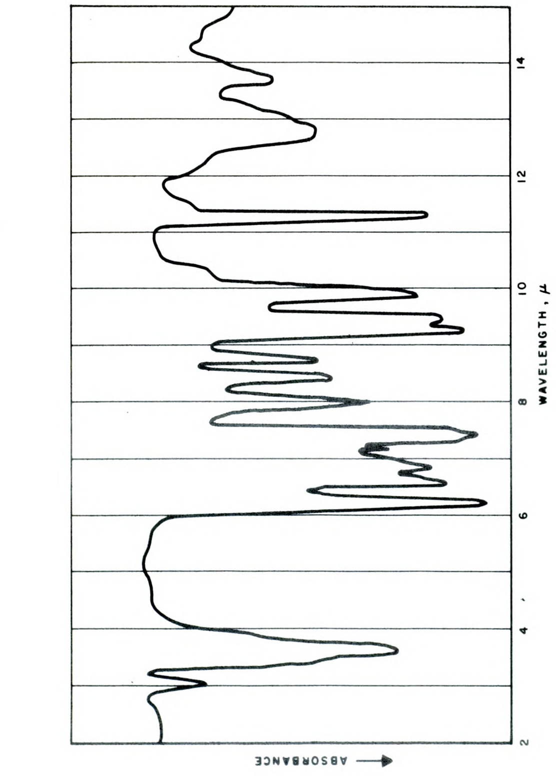


Figure 10. **Infrared Spectrum of Liquid 1, 1, 3, 3-Tetramethylguanidine.**

measurement was 0.015 mm. The N-H absorption band of tetramethylguanidine lies within, but at the low frequency end of, the 3300-3400 cm^{-1} range generally associated with the N-H bond in compounds containing the C=N-H group (51). The C=N bond in tetramethylguanidine, however, absorbs some 45 cm^{-1} below the low end of the 1640-1690 cm^{-1} range generally found in guanidines (18, 19, 51, 52). Since considerable evidence has already been discussed for some degree of self-association in liquid tetramethylguanidine, and since it is well-known that hydrogen bonding causes shifts to lower frequencies (53), the 45 cm^{-1} shift in tetramethylguanidine probably can be attributed to hydrogen bonding. This explanation seems much more likely than the postulation of some single bond character in the C=N bond.

Whether hydrogen bonding also occurs at the amine nitrogens in tetramethylguanidine probably cannot be determined from infrared spectra. If this type of hydrogen bonding were present in liquid tetramethylguanidine, one might expect frequency shifts in the absorbances of the C-N single bonds compared to that for such related compounds as tertiary amines. However, insufficient band assignments for these compounds have been made in the 1030-1230 cm^{-1} range (53) to allow observance of any shifts due to hydrogen bonding.

Recently a band at 1609 cm^{-1} was reported for the C=N absorption in the spectrum of a dilute solution of tetramethylguanidine in cyclohexane (see Figure 1b). The difference between this observation and the value of 1594 cm^{-1} found in the present work may be due to the effect of solvent or to experimental error in the two independent measurements.

A comparison of the infrared spectrum of tetramethylguanidine obtained in this work (Figure 10) with that previously published by Sadtler (Figure 1a) shows some major differences in curve shape in the N-H and C-H stretching frequency region. This portion of the two

spectra is shown in greater detail in Figure 11. Although infrared spectroscopy is not a good tool for detection of small amounts of impurities, there nevertheless appears to be some evidence for the presence of water in the tetramethylguanidine sample used to obtain the spectrum published by Sadtler (20). Referring to Figure 11, it appears that the sharp but weak N-H band at 3311 cm^{-1} in the spectrum of purified tetramethylguanidine (this work) is completely masked in the Sadtler spectrum by a large broad band typical of that found for water from about 3200-3450 cm^{-1} (54). Supporting evidence for the postulation of moisture in the tetramethylguanidine used for the Sadtler spectrum was found in this work by obtaining a nearly identical spectrum to that of Sadtler using a 1:1 solution of water in tetramethylguanidine.

J. Proton Magnetic Resonance

The proton magnetic resonance spectrum of purified 1, 1, 3, 3-tetramethylguanidine is shown in Figure 12. It contains a large singlet band at 2.62 ppm from the methyl protons and a much smaller singlet line at 5.17 ppm from the =NH proton. These chemical shifts were obtained using tetramethylsilane (TMS) as the internal standard (zero ppm). Integration gave a relative NH-to-CH_3 proton ratio of 0.95:12 compared to the true ratio for the compound of 1:12.

Solubilities in 1, 1, 3, 3-Tetramethylguanidine

A. Quantitative Solubilities

Measured solubilities of a number of sodium and potassium salts in tetramethylguanidine are listed in Table VII. The order of solubilities is generally the same as found for the more familiar nonaqueous solvents. For instance, sodium salts are more soluble than the corresponding potassium salts and the order of solubility of the halide salts of the same

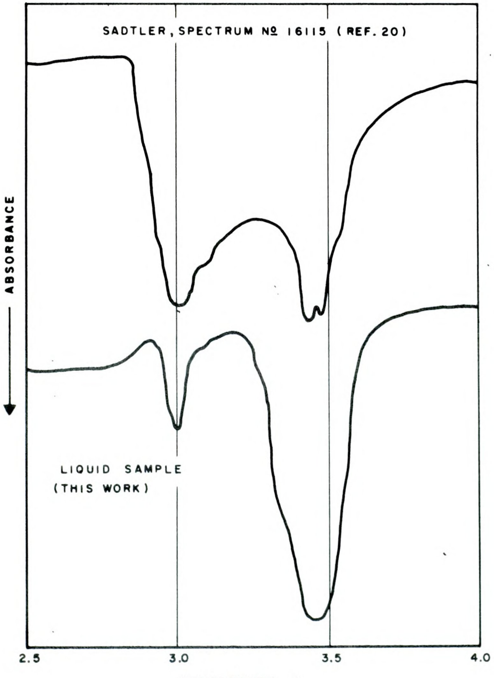


Figure 11. Comparison of Infrared Spectra of 1, 1, 3, 3-Tetramethylguanidine.

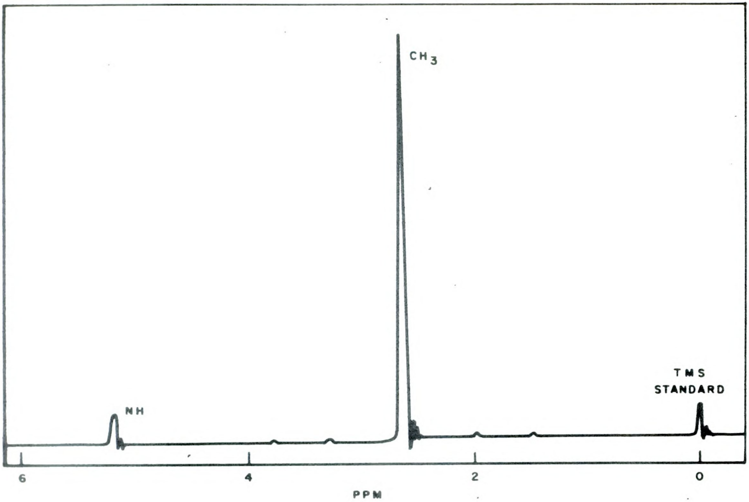


Figure 12. Proton Magnetic Resonance Spectrum of 1, 1, 3, 3-Tetramethylguanidine.

Table VII. Quantitative Solubilities in 1, 1, 3, 3-Tetramethylguanidine (g/100 g TMG) at 25°

	Na^+	K^+
ClO_4^-	52.	...
NCS^-	31.	...
I^-	21.	...
ClO_3^-	4.0	0.14
NO_3^-	1.4	...
BrO_3^-	...	0.062
Br^-	0.68	0.058
IO_3^-	0.0058	...
Cl^-	0.0041	0.0035
$C_2H_3O_2^-$	0.0031	...
HSO_4^-	0.0015	...
SO_4^{--}	0.00054	...

cation is $I^- > Br^- > Cl^-$. As expected, salts of the large anions such as ClO_4^-, NCS^-, and I^- possess high solubility while more ionic salts (HSO_4^-, Cl^-, etc.) are quite insoluble. Perhaps surprisingly, of the sodium salts the chlorate and nitrate show reasonably good solubilities while the acetate is low.

Some idea of how tetramethylguanidine compares as a solvent with other nonaqueous solvents and with water appears in order. Table VIII lists the solubilities of a few common sodium salts in water, ammonia, and ethylenediamine (en) (55) and compares these values with the corresponding solubilities found in tetramethylguanidine in this work. In general, solubilities in tetramethylguanidine parallel those in liquid ammonia and in ethylenediamine, but tetramethylguanidine is a somewhat poorer solvent. It may be therefore that tetramethylguanidine does not solvate the cation or the anion of the solute as readily as does ammonia or ethylenediamine. It might also be expected that the entropy of solution in tetramethylguanidine would be quite large due to disruption of the hydrogen-bonded liquid structure. The greater dissolving power of ammonia over tetramethylguanidine is likely due to the smaller size of the former. In the case of ethylenediamine, its chelating ability could confer a stronger solvating tendency upon it than is possible for tetramethylguanidine.

Under the conditions of analysis used in the quantitative solubility measurements, stable tetramethylguanidine solvates of only two of the salts in Table VII, sodium acetate and potassium bromide, were isolated. In other words, vacuum desiccation at room temperature used to remove excess solvent from a sample of saturated solution also may have decomposed any solvate species. In the case of sodium acetate and potassium bromide, residue analysis corresponded approximately to $NaC_2H_3O_2 \cdot 1.5$ TMG and $KBr \cdot 3.5$ TMG. However, the precision of analysis for tetramethylguanidine in these residues was not good enough

Table VIII. Comparison of Solubilities (g/100 g) in Various Solvents at 25°

	H_2O	NH_3	en	TMG
$NaClO_4$	209.6	...	30.1	52.
NaNCS	142.6	205.5	93.5	31.
NaI	183.7	161.9	34.6	21.
$NaNO_3$	91.5	97.6	33.5	1.4
NaCl	35.98	3.02	0.33	0.0041

to determine the above formulas with certainty. In addition, it seems unreasonable that these two salts would form solvates with tetramethylguanidine while all the others listed in Table VII do not. If this were the case, sodium acetate and potassium bromide should possess enhanced solubilities in tetramethylguanidine, but they do not appear to be out of their expected order in the table.

A definite tetramethylguanidine solvate stable at room temperature and above appears to be formed, however, by lithium chloride. Although only semiquantitative solubility measurements on this salt ($S = \sim 10$ g LiCl/100 g TMG) were made, the residue analysis corresponded quite well to the formula of a hemisolvate, LiCl·0.5 TMG. In addition, no weight loss nor change in analysis occurred on heating this residue to 60° under vacuum.

B. Semiquantitative Solubilities

Semiquantitative solubilities of a large number of compounds were obtained generally by single equilibrations followed by the weight-residue method of analysis or indirectly from attempts to prepare stock solutions as concentrated as possible. Table IX categorizes these compounds from the very soluble to the relatively insoluble with their approximate solubility ranges in terms of grams of solute per 100 grams solvent. As mentioned below in the section on reactions, the solubilities of a number of the compounds is no doubt enhanced by reaction with the solvent. For instance, ammonium salts undergo solvolysis, transition metal salts form complexes with tetramethylguanidine, $K_2Cr_2O_7$ is slowly reduced at room temperature, presumably to some Cr(III) species (a green solution was formed), etc.

When a group of related compounds, e.g., salts of the same cation or same anion, are listed in Table IX, they are given in order of decreasing solubility. In other words, NH_4NCS is more soluble than NH_4ClO_4, etc., and LiNCS is more soluble than $LiNO_3$, etc. However,

Table IX. Semiquantitative Solubilities in 1, 1, 3, 3-Tetramethylguanidine

Very Soluble ($\sim > 10$ g/100 g TMG):

NH_4NCS, NH_4ClO_4, NH_4NO_3, NH_4I, LiNCS, $LiNO_3$, $LiClO_4$, LiI, LiBr, LiCl, KNCS, $Mg(ClO_4)_2$, $Ca(NO_3)_2$, $Pb(NO_3)_2$, $Co(C_2H_3O_2)_2 \cdot 4H_2O$, $Cu(C_2H_3O_2)_2 \cdot H_2O$, $Cr(C_2H_3O_2)_3 \cdot H_2O$

Moderately Soluble ($\sim$ 1 - 10 g/100 g TMG):

$NH_4C_2H_3O_2$, $NaHSO_3$, KI, $K_2Cr_2O_7$, $Sr(NO_3)_2$, $CoCl_2 \cdot 6H_2O$, $CoCl_2$, Cu_2Cl_2, CuNCS, $Ni(C_2H_3O_2)_2 \cdot 4H_2O$, TMG·HBr, p-$CH_3 \cdot C_6H_4 \cdot SO_3H$

Slightly Soluble ($\sim$ 0.1 - 1 g/100 g TMG):

NH_4Br, Na_2S, $NaNO_2$, $KClO_4$, KNCO, H_3BO_3, $Ba(NO_3)_2$, $NaOCH_3$, $NaOC_2H_5$, $(C_6H_5)_4AsCl$, $(C_6H_5)_4AsClO_4$, TMG·HCl, $(CH_3)_4NOH$, $Co(NO_3)_2 \cdot 6H_2O$, $CoSO_4 \cdot 7H_2O$, $Co(ClO_4)_2 \cdot 6H_2O$, $Cu(NCS)_2$, citric acid monohydrate

Relatively Insoluble ($\sim < 0.1$ g/100 g TMG):

$(NH_4)_2S_2O_8$, NH_4Cl, NH_4HSO_4, $(NH_4)_2SO_4$, $(NH_4)_2CO_3$, NH_4F, $LiC_2H_3O_2$, Li_2SO_4, LiF, LiOH, Li_2CO_3, $Li_2C_2O_4$, NaOH, $NaHCO_3$, KNO_3, $KC_2H_3O_2$, K_2SO_4, $Ca(OH)_2$, $Ba(OH)_2$, $BaCO_3$, BaO, maleic acid

this does not neccessarily mean that the ammonium salts listed in the first line of the table are all more soluble than the lithium salts which follow in the second line. The very soluble ammonium salts (the thiocyanate, perchlorate, nitrate and iodide) have appreciably higher solubilities than the corresponding alkali metal salts while the reverse appears true for the bromides and chlorides. For the latter halides, the lithium salts are the most soluble, followed approximately by sodium, then the ammonium and potassium salts. These anomalies are likely due to a combination of opposing factors such as the high reactivity by solvolysis of NH_4^+ salts, the high polarizability of the large anions involved, and the high charge density, or solvation energy of small cations such as the lithium ion.

For the above reasons, therefore, the order of solubilities of the alkali metal and ammonium salts would have to list the ammonium and lithium salts as approximately equal, viz., $NH_4 \approx Li > Na > K$. In the case of the anions of these monopositive cations, the order of solubilities is approximately $NCS > ClO_4 > NO_3 > I > Br > C_2H_3O_2 > Cl > SO_4$, with some shifting of this order for each of the cations.

An examination of Table IX leads to a number of additional general comments: As one would expect, the order of solubility of the alkaline earth metal salts is $Ca > Sr > Ba$, although only the nitrates of these were measured. Of the hydrated transition metal salts, the acetates are the most soluble, followed by the chlorides. Perhaps surprisingly, the hydrated nitrate and perchlorate salts of cobalt are no more soluble than the sulfate. The results obtained in this case, however, may be non-equilibrium solubilities. For instance, in the preparation of stock solutions of $Co(ClO_4)_2 \cdot 6H_2O$ in tetramethylguanidine it was never possible to dissolve all the solute at any of the three concentrations 10^{-3}, 10^{-2}, or 10^{-1} molar. Apparently the resulting cobalt perchlorate-tetramethylguanidine complex, or the solvent itself, forms a coating on the solute

particles which prevents further dissolution. Since the anhydrous cobalt chloride has about the same solubility as the hexahydrate, it may be that the solvent displaces all of the water molecules from their positions around the Co^{++} ion. Further elaboration of this supposition will be made in the section on transition metal complexes.

For titrations in tetramethylguanidine the only acids found to have sufficiently high solubilities for use as standards or titrants were tetramethylguanidinium bromide and p-toluenesulfonic acid. Possible bases such as sodium methoxide, sodium ethoxide, and tetramethylammonium hydroxide were not sufficiently soluble for use in titrations. The slight solubilities of the above three bases and of chloride and perchlorate salts of the tetraphenylarsonium ion indicate that tetramethylguanidine does not tend to solvate either large organic cations or anions very well. Since the salts of the ammonium and lithium ions tend to be the most soluble, their salts listed in the relatively insoluble group of Table IX give a good indication of the inorganic anions which confer low solubility. Thus, probably all salts of peroxydisulfate, bisulfate, sulfate, fluoride, hydroxide, carbonate, and oxalate are quite insoluble. The usefulness of this list may lie in its applicability to synthetic chemistry in tetramethylguanidine as a solvent where the precipitation of an insoluble salt is used to drive a reaction to completion. Barium oxide is negligibly soluble in tetramethylguanidine. It therefore found use in this work as a drying agent since it, as well as $Ba(OH)_2$ or $BaCO_3$, formed on reaction of the oxide with water or carbon dioxide, respectively, are all insoluble. The low solubilities of citric and maleic acid may simply be an indication of the slight degree of dissolving power tetramethylguanidine has for large organic polyprotic acids.

C. Solubility and Miscibility of Organic Compounds

In the acid-base titration studies discussed later, numerous organic acids were readily dissolved in tetramethylguanidine. However, since it was most practical in these studies to titrate only dilute solutions of the acids ($\sim$0.01 molar), their solubilities were not reached and thus were not measured. It can only be stated that their solubilities are greater than approximately 0.1 g/100 g of tetramethylguanidine. Some of the compounds in question are listed below in Tables XVIII and XIX. Since these compounds dissolved readily and quite rapidly in tetramethylguanidine, it is felt that their actual solubilities may be fairly high and that many other organic compounds should also be very soluble.

Another fact that points to the high dissolving power of tetramethylguanidine for organic compounds is its complete miscibility with many of the common organic solvents. Table X lists the solvents tested for miscibility with tetramethylguanidine as a sampling of various classes of organic liquids. The table also indicates that some of the solvents undergo exothermic reaction with tetramethylguanidine, but the possible nature of these reactions will be discussed in the next section. The results in the table do show, however, that tetramethylguanidine is completely miscible with all common organic solvents, with the possible exception of saturated hydrocarbons and compounds containing long alkane groups. Apparently a number of characteristics of tetramethylguanidine contribute to its miscibility with so many liquids: the reactions noted in the table, the tendency for hydrogen-bonding to occur, and the symmetry and similarity in structure between the outer sheath of CH_3-groups in tetramethylguanidine and aliphatic or aromatic compounds.

Table X. Miscibility of 1, 1, 3, 3-Tetramethylguanidine with Organic Liquids

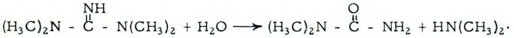
Liquid	Miscibility	Visible Reaction
Acetone	Complete	None
Carbon tetrachloride	Complete	Slow
Dichloromethane	Complete	Slow
p-Dioxane	Complete	None
Methanol	Complete	Some heat evolution
Benzene	Complete	None
Pyridine	Complete	None
Cyclohexanol	Complete	Slight heat evolution
Ethyl acetate	Complete	None
Acetic anhydride	Complete	Much heat evolution
N, N-Dimethylformamide	Complete	None
Ethyl Cellosolve	Complete	Some heat evolution
Petroleum ether	Complete	None
Cyclohexane	Complete	None
n-Pentane	Partial	None
n-Butyl ether	Partial	None
Tetramethylurea	Complete	None
Nitrobenzene	Complete	None
Ethylenediamine	Complete	None
Acetonitrile	Complete	None
Tetrahydrofuran	Complete	None
Ethyl ether	Complete	None

Reactions of 1, 1, 3, 3-Tetramethylguanidine

One of the problems associated with the use of 1, 1, 3, 3-tetramethylguanidine as a nonaqueous solvent is its reactivity with a number of compounds. Therefore, to more fully understand these problems and to circumvent them where possible, a number of reactions were studied.

A. Reaction with Water

The end product of the hydrolysis of tetramethylguanidine is 1, 1—dimethylurea which slowly precipitates out of a tetramethylguanidine-water solution at ordinary temperatures but which forms rapidly as an insoluble residue on evaporation of a similar solution. The same product, 1, 1-dimethylurea, forms as a suspension of finely divided particles on addition of a small volume of tetramethylguanidine to a large volume of water (volume ratio 1 TMG:40 H_2O). 1, 1-Dimethylurea was identified by elemental analysis, melting point, mixed melting point, and infrared spectra. The over-all hydrolysis reaction can perhaps be written:

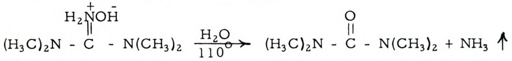


$$(H_3C)_2N - \overset{\overset{\displaystyle NH}{\|}}{C} - N(CH_3)_2 + H_2O \longrightarrow (H_3C)_2N - \overset{\overset{\displaystyle O}{\|}}{C} - NH_2 + HN(CH_3)_2. \qquad (\underline{18})$$

Although dimethylamine was not identified, it is well-known that amidines are easily hydrolyzed to carbonyl compounds (56) and that guanidine is hydrolyzed in basic solution to urea and ammonia. Thus, dimethylurea and dimethylamine appear to be reasonable tetramethylguanidine hydrolysis products.

Attempts to prepare tetramethylurea by the reaction of tetramethylguanidine and water gave only qualitative evidence for its formation. A stoichiometric mixture of tetramethylguanidine and water was refluxed for two hours and then distilled. Although only a small amount of distillate was obtained, considerable white solid collected in the air-cooled condenser. This solid was deliquescent. When heated at 110° for one

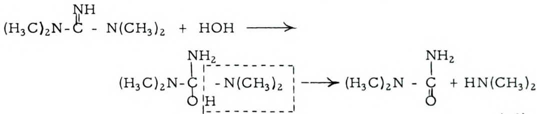
hour, it changed to a liquid having the very characteristic odor of tetramethylurea. Perhaps the white hygroscopic solid was tetramethylguanidinium hydroxide, which has never been isolated (8b). The hygroscopicity of this solid is similar to that of other tetramethylguanidinium salts prepared in this work and described below. Heating the aqueous solution may have eliminated ammonia to form tetramethylurea, as indicated in Equation 19:



$$(H_3C)_2N-\overset{\overset{H_2\overset{+}{N}O\overset{-}{H}}{\|}}{C}-N(CH_3)_2 \xrightarrow[110^{\circ}]{H_2O} (H_3C)_2N-\overset{\overset{O}{\|}}{C}-N(CH_3)_2+NH_3\uparrow$$

(19)

If this assumption is true, the mechanism of tetramethylguanidine hydrolysis may be more complicated than is indicated by Equation (18). A simpler mechanism of hydrolysis may involve addition of water to the C=N group in tetramethylguanidine followed by a rearrangement of the intermediate to 1, 1-dimethylurea and dimethylamine:



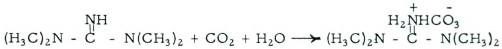
$$(H_3C)_2N-\overset{\overset{NH}{\|}}{C}-N(CH_3)_2+HOH\longrightarrow$$

$$(H_3C)_2N-\underset{\underset{O}{|}}{\overset{\overset{NH_2}{|}}{C}}\boxed{\begin{matrix}-N(CH_3)_2\\ H\end{matrix}}\longrightarrow (H_3C)_2N-\underset{\underset{O}{\|}}{\overset{\overset{NH_2}{|}}{C}}+HN(CH_3)_2$$

(20)

B. Reaction with Carbon Dioxide

Basic nonaqueous solvents readily absorb carbon dioxide to form carbonates, carbamates, etc. (57). Only the *bi*carbonate salt, on the other hand, has been identified in the reaction of tetramethylguanidine with moist carbon dioxide (see below):



$$(H_3C)_2N-\overset{\overset{NH}{\|}}{C}-N(CH_3)_2+CO_2+H_2O\longrightarrow (H_3C)_2N-\overset{\overset{H_2\overset{+}{N}H\overset{-}{CO_3}}{\|}}{C}-N(CH_3)_2$$

(21)

The need for water in the reaction was determined by measuring the relative weight increases on addition of carbon dioxide to tetramethylguanidine with or without added water. These data are plotted in

Figure 13; the upper curve shows the weight increase with time when dry carbon dioxide was bubbled into a 1:1 mole ratio of tetramethylguanidine and water. The lower curve is that for an equal amount of anhydrous tetramethylguanidine. It was possible to obtain 92 percent of the theoretical weight increase with the tetramethylguanidine:water mixture but less than two percent increase with anhydrous tetramethylguanidine. Evaporation probably caused the yield of bicarbonate to be less than theoretical in the first case. A constant weight increase of 1.9 ± 0.1% was obtained for carbon dioxide addition to various samples of tetramethylguanidine dried by different methods. It may be, therefore, that carbon dioxide is soluble to this extent in tetramethylguanidine, _i.e._, equivalent to a 1.9 percent weight increase. Another possibility would be that a like amount of the hydroxide, $TMGH^+OH^-$, was present and unremovable from the tetramethylguanidine by any dehydrating methods and simply reacted with the carbon dioxide to form the bicarbonate.

Because there is little or no difference in the conductance of pure tetramethylguanidine and of solvent saturated with tetramethylguanidinium bicarbonate, it is concluded that tetramethylguanidinium bicarbonate is essentially insoluble. Addition of carbon dioxide therefore could be used to remove water from tetramethylguanidine.

Some evidence for the identity of the bicarbonate salt was obtained by titration of its aqueous solution with acid. The shape of a typical pH titration curve (Figure 14) corresponds to that of sodium bicarbonate. Elemental analysis supports the formulation $TMGH^+HCO_3^-$ reasonably well.

Calculated: C, 40.7; H, 8.53; N, 23.7%
Found: C, 38.5; H, 8.70; N, 22.2%

It is possible that the analytical sample became wet because of the hygroscopic nature of the salt. The observed composition corresponds to

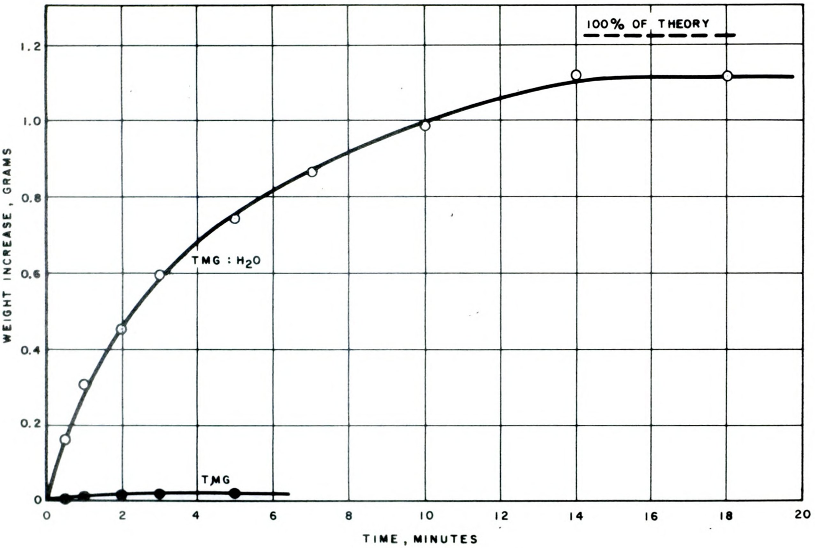


Figure 13. Carbon Dioxide Absorption by 1, 1, 3, 3-Tetramethylguanidine.

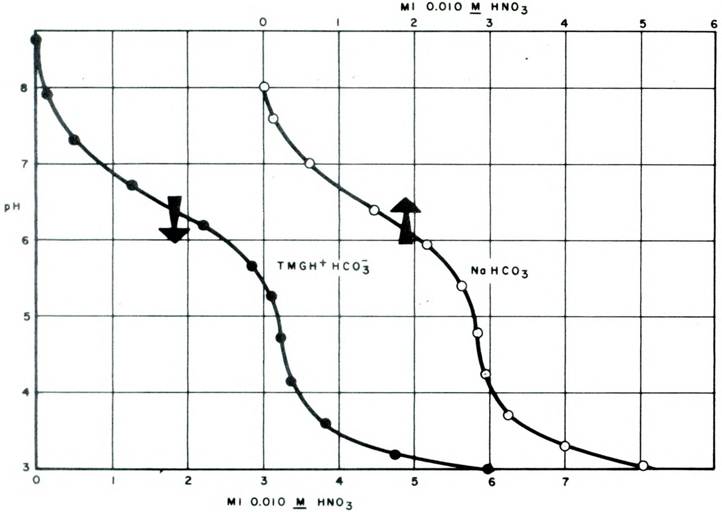


Figure 14. Titration of 1, 1, 3, 3-Tetramethylguanidinium Bicarbonate.

$TMGH^+HCO_3^- \cdot 0.6\ H_2O$ (Calculated: C, 38.3; H, 8.68; N, 22.4%). Additional physical properties of the bicarbonate are reported and discussed below.

C. Reaction with Acids

A strong base like 1, 1, 3, 3-tetramethylguanidine should react vigorously with strong acids to form $TMGH^+$ salts. (No evidence was found in this work for $TMGH_2^{++}$ salts.) The reactions proved indeed to be vigorous and strongly exothermic, but in some cases no salt could be isolated. The chloride, bromide, and acetate precipitated when formed by addition of aqueous acids to tetramethylguanidine. Reaction of gaseous HCl or HBr with tetramethylguanidine also led to precipitation of the halide salt. These white, somewhat hygroscopic solids were dried by vacuum desiccation over sulfuric acid, and their melting points were determined (Table XI). These salts are not reported in the literature. Tetramethylguanidinium iodide is reported to melt at 120° (11) and to be very hygroscopic. The chloride and bromide were analyzed by aqueous argentometric titration and found to be 1:1 TMG:HX salts. $C_5H_{14}N_3Cl$, calculated: Cl, 23.37%; found: Cl, 23.13%. $C_5H_{14}N_3Br$, calculated: Br, 40.7_5%; found: Br, 40.4_0%.

No insoluble products formed on reaction of tetramethylguanidine with such concentrated aqueous acid solutions as 98% H_2SO_4, 72% $HClO_4$, or 48% HF. Decomposition apparently occurred on addition of concentrated sulfuric acid to tetramethylguanidine as indicated by charring. No solid product was formed even on long standing of 1:1 base:acid mixtures of tetramethylguanidine and concentrated perchloric or hydrofluoric acid. It is felt, however, that the SO_4^{--}, HSO_4^-, ClO_4^-, or F^- salts could be prepared by other methods if desired.

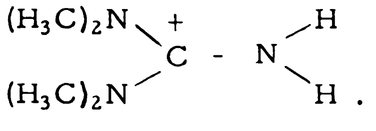
Table XI. Melting Points of Salts of 1, 1, 3, 3-Tetramethylguanidine

$TMGH^+$ Salt	Melting Point, °C
Cl^-	211-212
Br^-	184-185
HCO_3^-	110-113
$C_2H_3O_2^-$	90-93

D. Spectra and Structure of Protonated 1, 1, 3, 3-Tetramethylguanidine

Since tetramethylguanidine apparently undergoes only monoprotonation (11, this work), it is of interest to identify the basic site. Although it is not certain whether protonation of ureas and amides occurs on the oxygen or the nitrogen (58, 59), it appears that guanidines protonate predominantly at the imine nitrogen (25), with the resultant positive charge localized on the central carbon atom (23, 24).

In this study, the infrared spectrum of 1, 1, 3, 3-tetramethylguanidinium bromide (KBr pellet) was recorded (Figure 15). Comparison of this spectrum of protonated tetramethylguanidine with that for the free base (Figure 10) indicates that some frequency shifts occur on protonation. Most notable is that attributed to the N-H stretching vibration at 3311 cm^{-1} in tetramethylguanidine which is no longer found in tetramethylguanidinium bromide. The explanation may lie, therefore, in protonation of the =NH group to either an $-NH_2^+$ or a $\rangle C^+\text{-}NH_2$ group. The latter localized charge structure is analogous to that for the guanidinium ion. From the tables of Nakanishi (51) it is found that the $-NH_2^+$ group absorbs in the "ammonium band" region from 2250-2700 cm^{-1} while the triaminocarbonium ion has a broad band at approximately 3300 cm^{-1} in the free amino region. The spectrum of $TMGH^+Br^-$ in Figure 15 shows a broad band from about 2750-3250 cm^{-1}, which includes, of course, the $-CH_3$ stretching absorptions, with no bands in the 2250-2700 cm^{-1} region. Thus, the structure of the tetramethylguanidinium ion can perhaps best be represented as



Assuming that the NH absorption bands of tetramethylguanidine are the only ones which change appreciably on protonation, some tentative

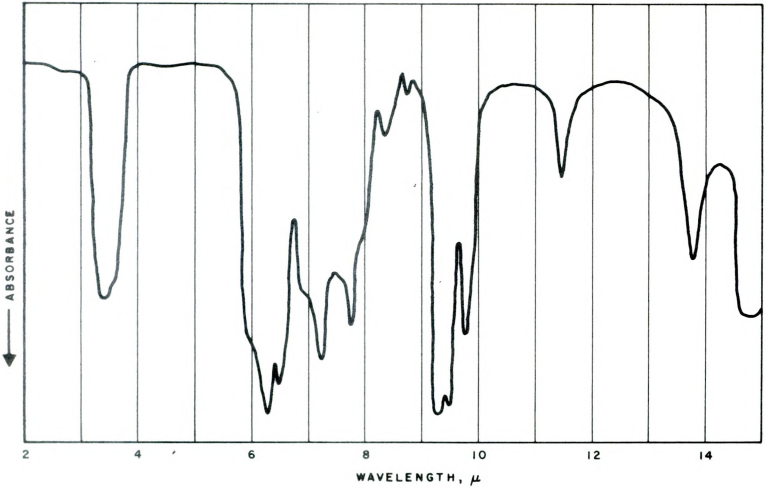


Figure 15. Infrared Spectra of 1, 1, 3, 3-Tetramethylguanidinium Bromide.

band assignments in the spectrum of the free base (Figure 10) can be made. A strong band at 1493 cm^{-1} which disappears may therefore be assigned to an NH bending vibration and the broad band from about 765-800 cm^{-1} may be due to an NH rocking deformation.

Neither tetramethylguanidine or any of its salts were found to absorb in the visible region of the spectrum, but small shoulder peaks were found in the ultraviolet below 300 mμ. However, these peaks are too small ($\epsilon_{max} \approx 1-10$) to be useful in quantitative spectrophotometric analysis.

E. Titration of 1, 1, 3, 3-Tetramethylguanidine with Acid Solutions

1, 1, 3, 3-Tetramethylguanidine can be titrated potentiometrically with standard acid solutions in either aqueous or nonaqueous media using a glass-calomel electrode system. A typical titration of tetramethylguanidine in water solution with aqueous standard acid is shown in Figure 16. In this case, 1.00 ml of tetramethylguanidine was dissolved in water and titrated with 0.1027 M $HClO_4$ using a Beckmann Model G pH meter. Tetramethylguanidine titrates like a strong monoprotonic base with one steep inflection in the curve. Over a series of six titrations, the end points were constant within ± 2% of 1:1 stoichiometry.

Titrations of tetramethylguanidine in water as a solvent must be done with a freshly prepared solution to avoid hydrolysis (see Equation 18). Evidence supporting Equation 18, and especially dimethylamine as a product, is found in the titration of a tetramethylguanidine-water solution after allowing it to stand for several hours. In this case a second break at pH ~ 5 is obtained which can be attributed to the presence of dimethylamine.

Additional evidence for only monoprotonation of 1, 1, 3, 3-tetramethylguanidine was obtained by potentiometric titrations in nonaqueous

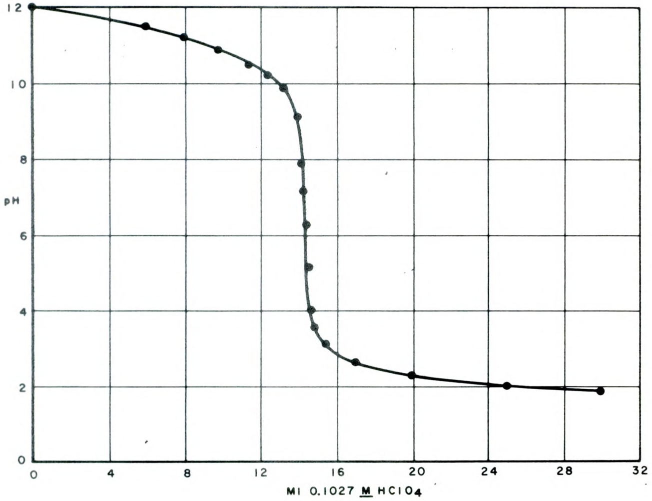


Figure 16. Titration of 1, 1, 3, 3-Tetramethylguanidine in Aqueous Solution with Standard Acid.

media. Two typical titrations are shown in curves 1 and 2 of Figure 17. Curve 1 is the titration in glacial acetic acid with perchloric acid as titrant; curve 2 is similar except for use of acetonitrile as a solvent. In each case, the steep potentiometric inflection is only about two percent lower than the calculated 1:1 acid:base ratio. Addition of excess acid in each of these titrations gave no second inflections in the titration curves.

Perhaps even better evidence for tetramethylguanidine undergoing only monoprotonation is the titration of pure, undiluted tetramethylguanidine with 4.0 M aqueous HCl (Figure 17, curve 3). Again, there is only one potentiometric inflection with the measured end point about one percent below calculated 1:1 stoichiometry. Initially in this titration, $TMGH^+Cl^-$ precipitated, but on further addition of titrant sufficient water was present to keep the salt in solution.

F. Qualitative Study of Miscellaneous Reactions of 1, 1, 3, 3-Tetramethylguanidine

A number of other substances were found (Table XII) to react with tetramethylguanidine but in general were studied only on a qualitative or semiquantitative basis.

Some gas evolution occurs on addition of metallic sodium or potassium to tetramethylguanidine but even in the presence of a large excess of solvent, the alkali metal was not consumed. Although the evolved gas was not identified, there appeared to be little or no reaction. Lithium metal, lithium amide, and sodium amide, on the other hand, decompose the solvent to give unknown red-brown and orange solid products. Sodium amide was also treated with tetramethylguanidine in liquid ammonia with similar results. Little evidence is found in the literature for alkali metal guanidide salts. The one reference found, that of a 1927 British patent (60), claims the formation of the mono- and di-sodium compounds of urea and of guanidine by reaction with

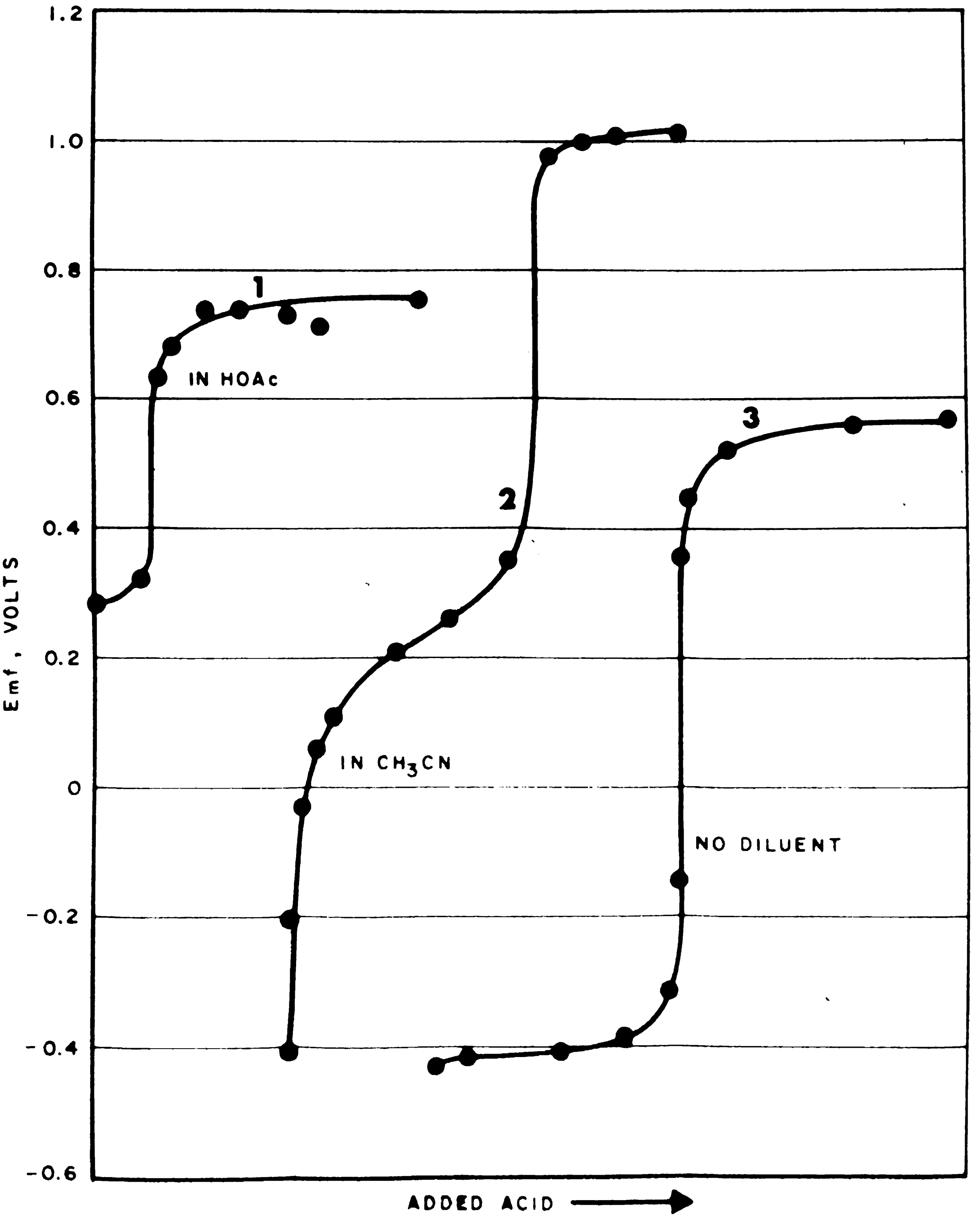


Figure 17. Potentiometric Titrations of 1, 1, 3, 3-Tetramethylguanidine.

Table XII. Miscellaneous Reactions of 1, 1, 3, 3-Tetramethylguanidine

Reactant	Results, products
Na; K	No reaction (?)
Li; $LiNH_2$; $NaNH_2$	Decomposition, orange solid
$LiAlH_4$	Vigorous reaction
LiH; CaH_2	Slow reaction
$KMnO_4$	K_2MnO_4(?) + MnO_2 (vigorous, pyrophoric)
$K_2Cr_2O_7$	Cr^{+3} (slow)
$NaIO_4$	Yellow solution
Ag^+	Ag^o
Hg_2^{++}	$Hg^o + Hg^{++}$
NH_4^+	NH_3
CCl_4; $CHCl_3$; CH_2Cl_2	$TMGH^+Cl^-$
CS_2	Decomposition; orange solid

sodium hydride, but the work has apparently never been substantiated. The reactions of tetramethylguanidine with the hydrides listed in the table again gave gas evolution but no products were isolated.

The reaction of tetramethylguanidine with $KMnO_4$ is pyrophoric if the permanganate is finely ground. A mixture of green and brown solids is formed which suggested the reduction of MnO_4^- to MnO_4^{--} and MnO_2. Potassium dichromate also oxidized tetramethylguanidine as indicated by the resultant green (Cr^{+3}) solution, but the reaction is quite slow at room temperature. Sodium periodate apparently oxidizes tetramethylguanidine and may itself be reduced to I_2 as evidenced by the yellow solution which is formed.

Silver(I) salts, if soluble in tetramethylguanidine, are reduced to free silver, especially when heated. On first addition of a solution such as aqueous silver nitrate to tetramethylguanidine, however, a brown precipitate resembling silver hydroxide is formed. When heated, this mixture forms a silver mirror on the walls of the container. The disproportionation of Hg(I) in tetramethylguanidine to Hg and Hg(II) is not surprising since a similar disproportionation occurs in the case of mercury(I) chloride in the analogous solvent, ethylenediamine (61).

Ammonium salts on dissolution in tetramethylguanidine invariably evolve ammonia gas. This shows that tetramethylguanidine is a stronger base than ammonia and that the ammonium ion acts as an acid in tetramethylguanidine:

$$\text{TMG} + NH_4^+ \longrightarrow \text{TMGH}^+ + NH_3 \cdot \qquad (\underline{22})$$

However, the presence of the solvo-cation, TMGH^+, was not directly demonstrated in any of the ammonium salt solutions in tetramethylguanidine. In fact, if the solvo-cation does form, one should obtain similar solubilities for the NH_4^+ and TMGH^+ salts of the same anion. This, however, does not hold true in this work where it was found that

the solubilities of NH_4Br and NH_4Cl were about an order of magnitude greater than the solubilities of corresponding $TMGH^+$ salts. These solubility differences are essentially unexplainable but it must be recalled that the solubility measurements in question here were made only semiquantitatively.

Reactions analogous to that of tetramethylguanidine with chlorinated hydrocarbons to form tetramethylguanidinium chloride are also found with other basic nonaqueous solvents. For instance, ammonium chloride is one of the products in the reaction of anhydrous ammonia with dichloromethane (62). It is also known (63) that such organic chlorides as chloroform, carbon tetrachloride, ethylene dichloride, butyl chloride, and dichloroethyl ether react at 100° C with an excess of ethylenediamine to form secondary amines and amine hydrochlorides.

The decomposition reaction of carbon disulfide with tetramethylguanidine is vigorous and exothermic. For instance, on addition of carbon disulfide to tetramethylguanidine, an immediate reaction takes place in which a yellow gas is evolved, the tetramethylguanidine becomes yellow-red, and a red-orange solid is formed. The complexity of this reaction is obvious and thus was not investigated further.

The reactions of 1, 1, 3, 3-tetramethylguanidine which were studied qualitatively and listed in Table XII can perhaps best be summarized in terms of some of the problems which they cause in the study of tetramethylguanidine as a solvent. Thus, it was not possible to prepare alkali metal salts of tetramethylguanidine by reaction with the elements, their amides, hydrides, etc. If any of these reactions had been successful, the strongest possible base in the solvent would, of course, have been prepared. The reactions of tetramethylguanidine with permanganate, dichromate, periodate, and silver(I) indicate that the solvent can be oxidized readily. The reduction of Ag^+ to free silver by tetramethylguanidine precludes the use of silver salts in titrations,

syntheses, etc. in tetramethylguanidine. The reaction of tetramethylguanidine with Hg(I) as well as Ag(I) could also cause problems in the use of salts of these species in construction of electrodes for use in the solvent. The reaction of tetramethylguanidine with carbon tetrachloride, carbon disulfide, etc. rule out their use as spectrophotometric solvents in the presence of tetramethylguanidine.

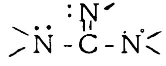
Transition Metal Complexes of 1, 1, 3, 3-Tetramethylguanidine

A. Isolation and Analysis of Complexes

As has been mentioned previously and shown in Table IX, it was found that a number of the common transition metal salts, both hydrated and anhydrous, exhibit appreciable solubility in tetramethylguanidine. This was especially true with the hydrated acetate salts of Co(II), Cu(II), and Cr(III), which all formed highly colored solutions in the solvent. Therefore, in order to identify the complex species giving rise to the colors, various attempts were made to isolate solid material from tetramethylguanidine solutions of these metal acetates and of some other transition metal salts listed in Table IX. Isolation of tetramethylguanidine complexes was attempted by solvent evaporation, addition of another solvent to precipitate an insoluble complex, addition of another solvent to extract a soluble complex, etc. However, all these methods were generally unsuccessful. Some limited success was achieved by evaporation of excess solvent in a vacuum oven at temperatures 10-20° below the predetermined atmospheric melting points of the products ultimately obtained. The resulting solids were ground in a mortar under anhydrous conditions and were analyzed commercially. In this manner, the following tetramethylguanidine "complexes" (or solvates) of some of the transition metal acetates were isolated: $Co(C_2H_3O_2)_2 \cdot 0.33TMG$; $Ni(C_2H_3O_2)_2 \cdot 0.5TMG$; and $Cr(C_2H_3O_2)_3 \cdot 1.0TMG$. No "complex" of copper(II) acetate could be isolated due to

decomposition below its melting point. Analytical and other data for the materials which were obtained are given in Table XIII. Except for the analytical percentages for carbon, the observed analyses correspond to the given formulas reasonably well. Analytical discrepancies probably can be ascribed to uncertainties in the amount of solvent removal in the isolation of these compounds.

B. Structure of Complexes

In addition, and subsequent to the above studies, the more definite complexes of tetramethylguanidine mentioned in the historical section of this thesis were prepared and analyzed. Thus, in work in this laboratory and elsewhere (29, 30, 31), the following complexes have been reported: $[Co(TMG)_4](ClO_4)_2$, $[Cu(TMG)_4](ClO_4)_2$, $[Zn(TMG)_4](ClO_4)_2$, $[Cu(TMG)_2]HCO_3$ or $[Cu(TMG)_2CO_3]$, and $[Co(TMG)_3H_2O](NO_3)_2 \cdot H_2O$. It appears that a maximum of four molecules of tetramethylguanidine can be arranged as ligands around a first row transition metal ion, but other complexes having lower tetramethylguanidine:metal ratios than 4:1 also can be isolated. The analytical formulas of these complexes definitely show that tetramethylguanidine is monodentate in behavior, which is not surprising since a four-membered ring would have to form for it to be bidentate. The  $>\ddot{N}-\overset{:N\diagup}{\overset{\|}{C}}-\ddot{N}<$ backbone of tetramethylguanidine, however, should lend a tendency for it to function as a bridging ligand.

The infrared spectra of one or more of the tetramethylguanidine complexes should indicate whether coordination is at the imine or amine nitrogen, but results are inconclusive. From infrared spectra of their $[M(TMG)_4](ClO_4)_2$ complexes, Longhi and Drago (29) claim that the imine nitrogen is the donor site because the C=N band of tetramethylguanidine is shifted toward lower wave numbers (e.g., 1609 to 1548 cm^{-1}) in complexes. Infrared spectra of the complexes obtained in this work (Table XIII) showed no corresponding shift of the C=N absorption band.

Table XIII. Transition Metal Complexes Obtained by Evaporation of Solvent

	$Co(OAc)_2 \cdot 0.33TMG$		$Ni(OAc)_2 \cdot 0.5TMG$		$Cr(OAc)_3 \cdot 1.0TMG$	
Color	blue-violet		light green		dark green	
Approx. m.p.	159°		176°		108°	
	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
% C	26.9	31.6	30.3	33.3	34.1	38.4
% H	4.28	4.84	5.41	5.38	6.47	6.44
% N	6.90	6.50	9.60	8.97	13.9	12.2
% Metal	26.9	27.4	25.3	25.0	14.7	15.1

C. Visible Absorption Spectra

To obtain further information on the complexing ability of 1, 1, 3, 3-tetramethylguanidine, the visible absorption spectra of tetramethylguanidine solutions of transition metal salts were studied. This work was confined mainly to cobalt(II) salts because of the relatively high solubility (> 0.1 M) of cobalt(II) acetate tetrahydrate in tetramethylguanidine, the intense color ($\epsilon_{max} \approx 500$) of cobalt(II) solutions, etc. Other metal acetate hydrates were not as soluble as the cobalt salt and did not produce as intense a color. For instance, for $Cu(C_2H_3O_2)_2 \cdot H_2O$, $\epsilon_{max} \approx 75$. Spectra of tetramethylguanidine solutions of the latter salt were studied by Kennedy (30) in this laboratory in cooperation with the author. She found that the spectra of copper(II) acetate solutions were Gaussian-shaped with $\lambda_{max} = 680$ mμ and that deviations from Beer's law between 0.002 M and 0.008 M were positive.

An additional argument favoring the selection of the cobalt(II) ion for spectral study in tetramethylguanidine is that it probably has been investigated more than any other system in other nonaqueous solvents. Notable among these investigations is the work of Katzin and co-workers (64a-d) dealing with the absorption spectra of cobalt(II) salts in alcohols and acetone. Other studies include the series of papers by Libuś, *et al.* (65a-c) using alcohols and acetonitrile as solvents for cobalt complexes as well as the spectral studies by Buffagni and Dunn (66) of the $CoCl_2$ and $CoCl_4^{--}$ species in nitromethane, N, N-dimethylformamide, and other solvents. Considerable success has been achieved by the above authors in the characterization of various complex species in these solvents by visible absorption spectroscopy.

D. Effect of Anions on the Spectrum of Cobalt(II) Acetate

Absorption spectra in tetramethylguanidine of several hydrated cobalt(II) salts show a maximum around 600 mμ (Figure 18).

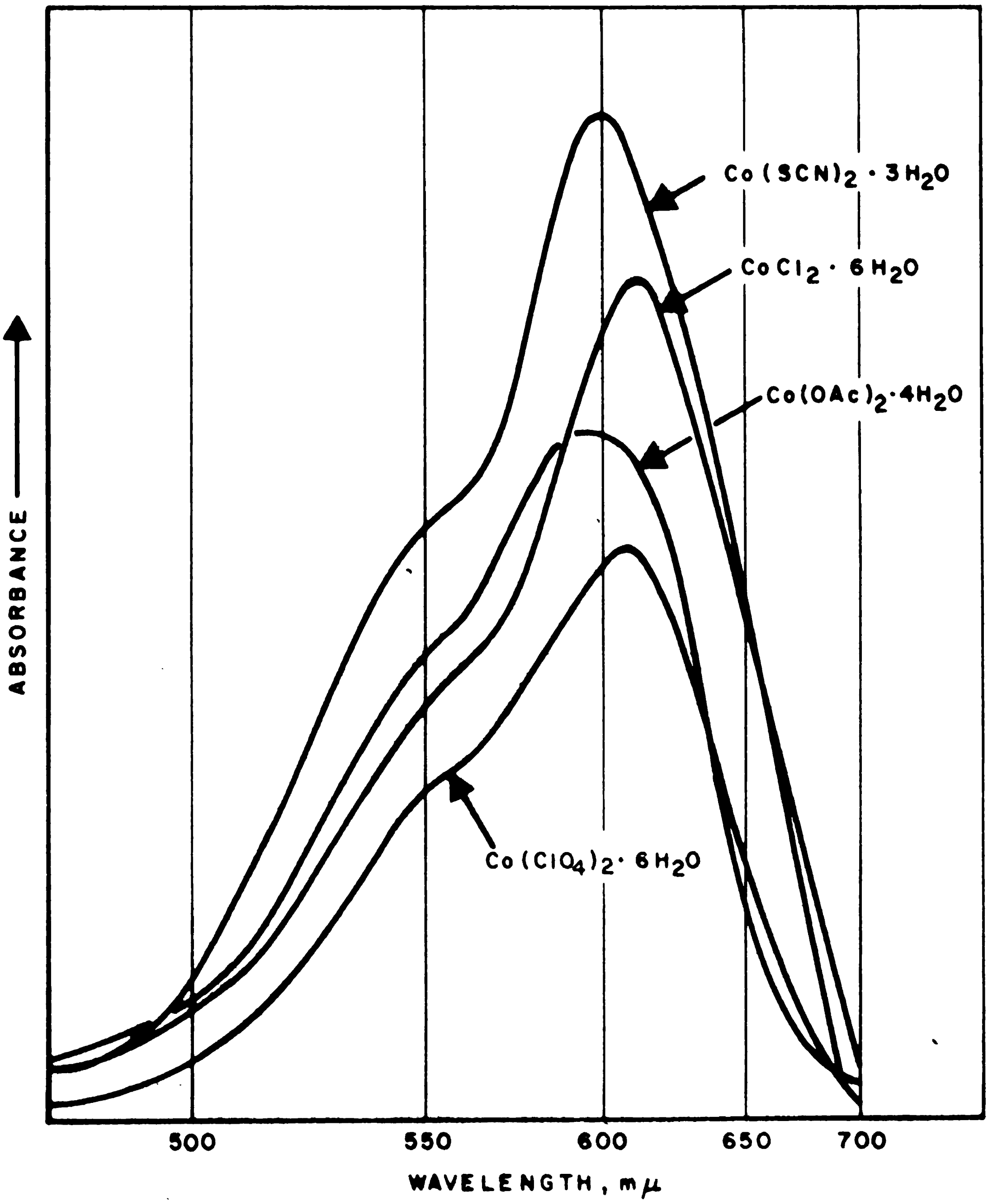


Figure 18. Visible Absorption Spectra of Hydrated Cobalt(II) Salts in 1, 1, 3, 3-Tetramethylguanidine.

The similarities in these spectra appear to indicate that tetramethylguanidine forms a stable complex with cobalt(II) which is little influenced by the particular anion present. Further illustration of this is given in Table XIV which shows the rather small wavelength and absorbance changes in the spectrum of 10^{-3} $\underline{M}$ $Co(C_2H_3O_2)_2 \cdot 4H_2O$ solution in tetramethylguanidine on addition of a ten-fold excess of an anion. For solubility reasons, the anions were added as their lithium salts except for acetate ion, in which case ammonium acetate was used. Anions are listed in Table XIV in order of decreasing effect on the position of the absorption maximum.

E. Effect of Water on the Spectrum of Cobalt(II) Acetate

The effect of water of hydration on the spectra of the cobalt(II) salts was determined by recording the spectra of the anhydrous acetate and chloride in tetramethylguanidine. These spectra are shown in Figure 19, and a comparison with the spectra of the corresponding hydrated salts in Figure 18 shows no difference in curve shape. There is, however, a small shift of the maxima (< 5 mμ) to lower wavelengths in the case of the anhydrous salts and an increase in absorbance.

In contrast to water of hydration, large amounts of added water greatly alter the absorbance in tetramethylguanidine of cobalt(II) salts. Figure 20 illustrates this effect for a 10^{-3} $\underline{M}$ solution of $Co(C_2H_3O_2)_2 \cdot 4H_2O$. From the figure it is seen that something above three percent H_2O is necessary to change significantly the absorption spectrum; at nine percent H_2O the absorbance has decreased by nearly one-half and the curve shape has changed; finally, at 25 per cent H_2O there was zero absorbance and the solution was colorless. Because of the known hydrolysis of tetramethylguanidine, it is not surprising that the 25 percent H_2O solution was colorless since this is more than enough water to hydrolyze all the tetramethylguanidine present.

Table XIV. Effect of Anions in a Tenfold Excess on the 600 mμ Absorption of $Co(C_2H_3O_2)_2 \cdot 4H_2O$ in Tetramethylguanidine

Anion	$\Delta\lambda_{max}$	ΔA_{max}
Cl^-	+15 mμ	+0.147
NO_3^-	+13	+0.147
Br^-	+12	+0.186
ClO_4^-	+11	+0.030
SCN^-	+ 3	+0.128
$C_2H_3O_2^-$	-10	-0.016

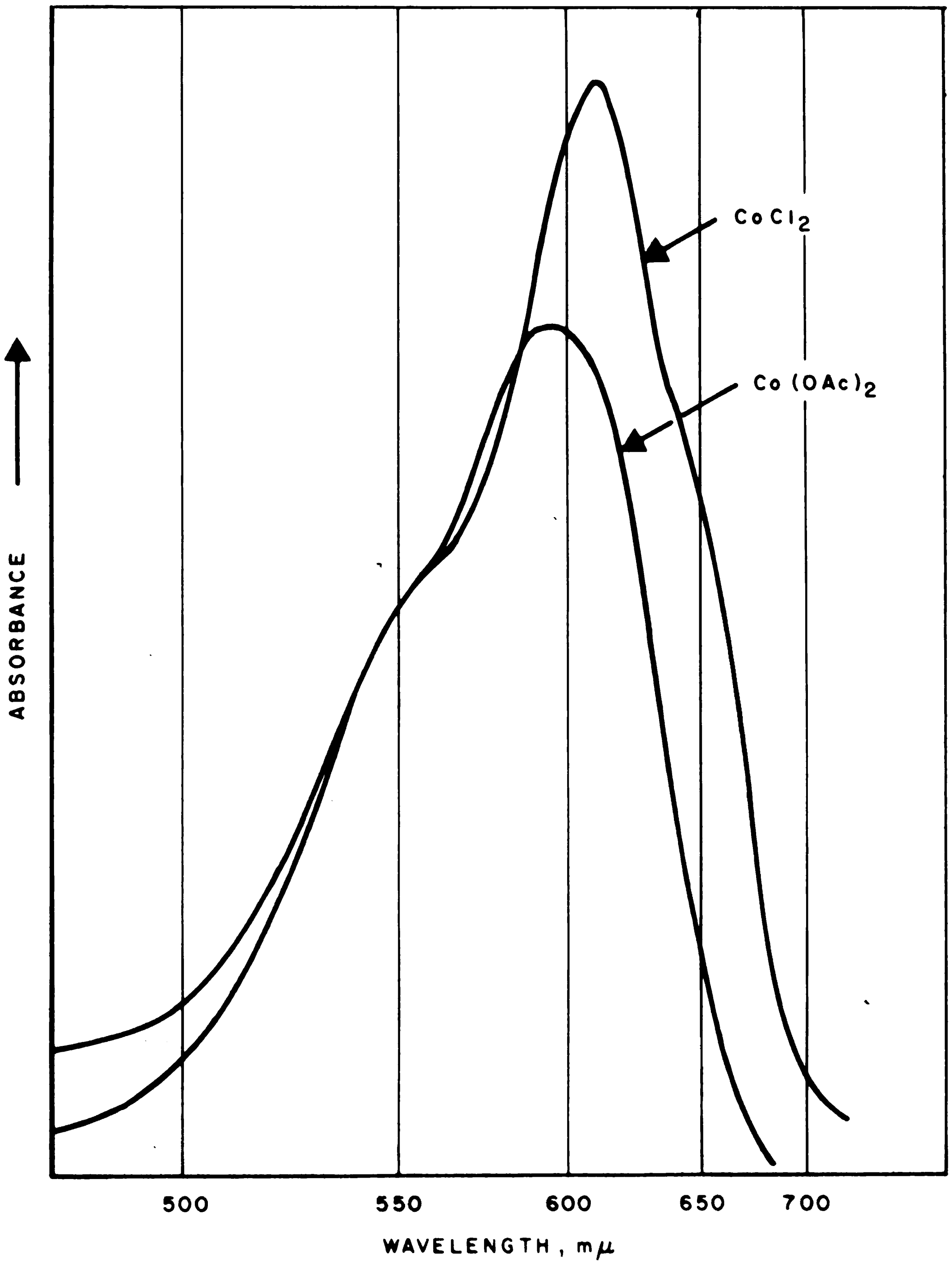


Figure 19. Visible Absorption Spectra of Anhydrous Cobalt(II) Salts in 1, 1, 3, 3-Tetramethylguanidine.

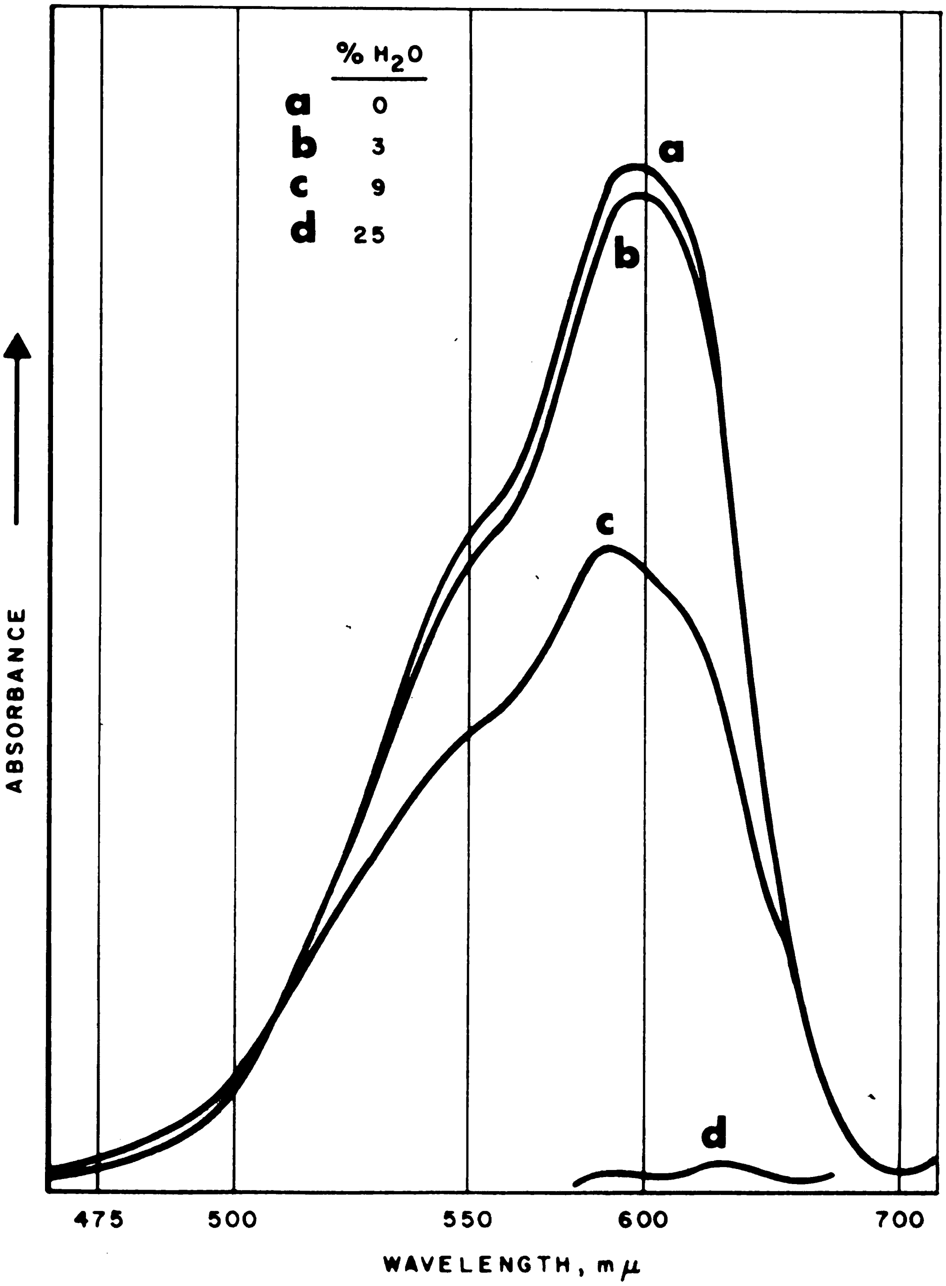


Figure 20. Effect of Water on the Absorption Spectrum of $Co(C_2H_3O_2)_2 \cdot 4H_2O$.

F. Beer's Law Study of Cobalt(II) Salts

A Beer's law study of cobalt(II) salts in tetramethylguanidine was made to obtain information on solvent-solute interaction. Hydrated and anhydrous cobalt salts were investigated over concentration ranges of approximately 10^{-4} to 10^{-3} M. Only in the case of 0 to 5×10^{-4} M anhydrous $CoCl_2$ did any of the salts obey Beer's law. The Beer's law plot for anhydrous cobalt chloride is shown in Figure 21, at a wavelength near the main peak at 600 mμ and near the shoulder at 550 mμ. Deviation may occur at concentrations higher than 5×10^{-4} M $CoCl_2$.

A typical Beer's law plot for other cobalt(II) salts in tetramethylguanidine, all of which showed deviation, is given in Figure 22. At 590 mμ, Beer's law appears to be obeyed up to $\sim 4 \times 10^{-4}$ M $Co(C_2H_3O_2)_2$, with negative deviations at higher concentrations. However, at wavelengths on either side of the main peak, 550 and 620 mμ, the deviations occur over the entire concentration range. Thus the Beer's law studies are a good indication of reaction between most cobalt(II) salts and tetramethylguanidine.

G. Possible Cobalt(II) Complex Species in Tetramethylguanidine Solution

Since the nature of the anion present has some influence on the absorption spectrum of cobalt(II) in tetramethylguanidine (Table XIV), it was decided to study this effect in greater detail. Iodide ion was selected for study because of the high solubility of NaI (Table VII). The effect of increasing concentrations of iodide ion on the spectrum of $Co(C_2H_3O_2)_2 \cdot 4H_2O$ and $CoCl_2 \cdot 6H_2O$ solutions in tetramethylguanidine is shown in Figures 23 and 24.

The figures show that: (1) there are no major changes in the spectrum of either cobalt salt even at a thousandfold excess of iodide ion, (2) all spectra have a left-shoulder inflection near 550 mμ but only the cobalt chloride spectrum at 0 and 10^{-3} M I^- shows a right-shoulder

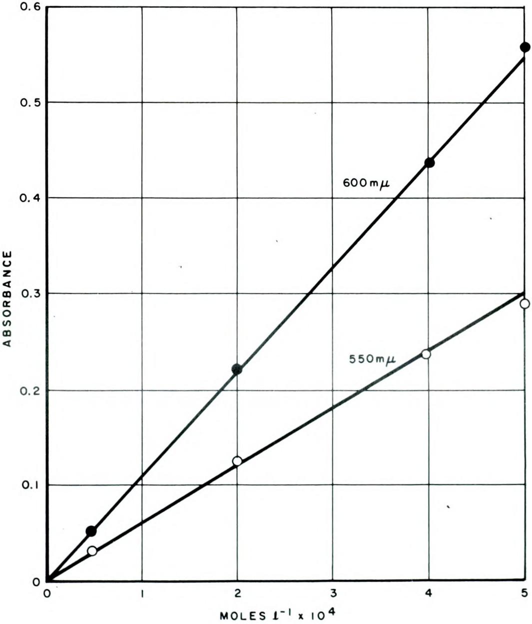


Figure 21. Beer's Law Plot for Anhydrous $CoCl_2$ Solutions.

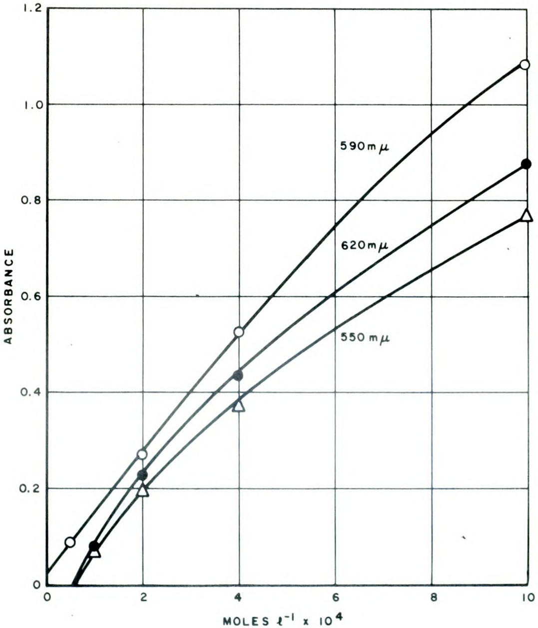


Figure 22. Beer's Law Plot for Anhydrous $Co(C_2H_3O_2)_2$ Solutions.

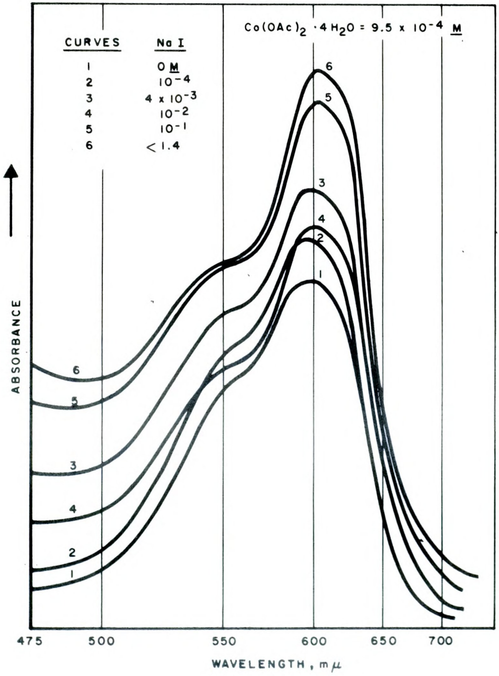


Figure 23. Effect of Iodide Ion on the Spectrum of $Co(C_2H_3O_2)_2 \cdot 4H_2O$.

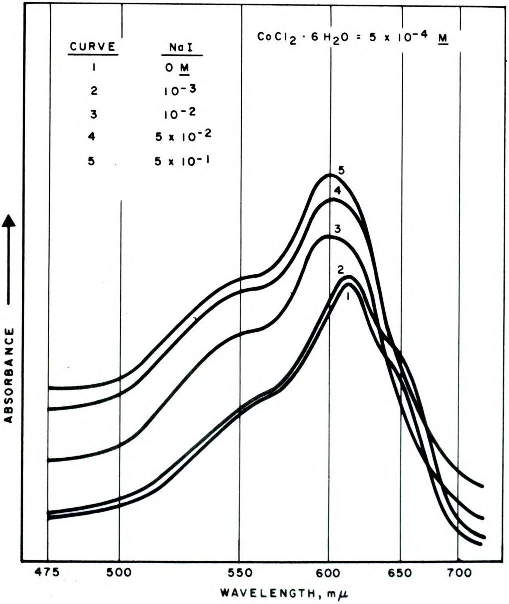


Figure 24. Effect of Iodide Ion on the Spectrum of $CoCl_2 \cdot 6H_2O$.

inflection near 650 mμ, and (3) there are no isosbestic points in either series of spectra. The latter fact indicates that these systems may be quite complicated, e.g., there may be three or more complex species in equilibrium with each other. These complications are perhaps not surprising when one considers the number of possible ligands in either of the systems: TMG, I^-, H_2O, and Cl^- or $C_2H_3O_2^-$. It is unfortunate that low solubilities in tetramethylguanidine limited these studies at the time to so few possible Co(II) salt:added salt combinations. Hindsight now indicates, however, that solubilities may have been sufficiently large for analogous spectral studies of such systems as anhydrous cobalt chloride plus lithium chloride or anhydrous cobalt iodide plus sodium iodide. Conversely, inorganic halides such as lithium chloride probably form ion pairs (66) in a low dielectric-constant solvent like tetramethylguanidine. To avoid ion-pairing, chloride ion can be added as the salt of a large organic cation such as tetramethylammonium- or tetraphenylarsonium chloride, but these compounds also possess low solubility in tetramethylguanidine (Table IX).

Despite the above mentioned difficulties in interpretation of such spectra as those of Figures 23 and 24, it is felt that some additional comments can be made in regard to possible cobalt(II) complex species present in tetramethylguanidine solution. There is little doubt that only tetrahedral, or four-coordinate, complexes of cobalt(II) are involved; all cobalt(II) complexes exhibiting strong absorption bands ($\epsilon = 10^2$ to 10^3) in the spectral region above about 550 mμ are those of four-coordinated cobalt (67, 68).

Longhi and Drago (29) have published the visible absorption spectrum of the complex salt, $[Co(TMG)_4](ClO_4)_2$ as obtained in dichloromethane solution and by solid reflectance (Figure 25). There is considerable similarity between their $[Co(TMG)_4]^{++}$ spectra and those observed in this work (Figures 18-20, 23, 24). Small differences in

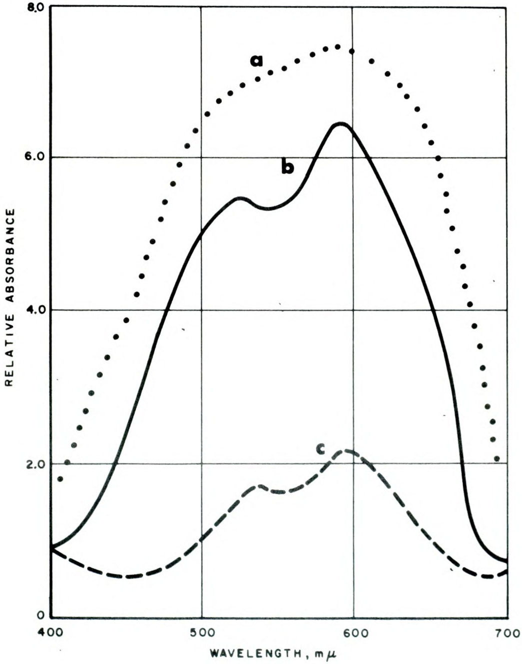


Figure 25. Visible Absorption Spectra of $[Co(TMG)_4] \cdot (ClO_4)_2$.
a. Solid Reflectance
b. 1.0×10^{-2} M in CH_2Cl_2
c. 1.65×10^{-3} M in CH_2Cl_2

λ_{max} values may be instrumental errors; the fact that Drago obtained a second maximum near 530 mμ as opposed to the shoulder inflections of this work may be due to the solvent effect of dichloromethane on the one hand and tetramethylguanidine on the other. In the absence of a solvent (the reflectance spectrum of solid $[Co(TMG)_4](ClO_4)_2$, Figure 25), only a shoulder inflection is found near 550 mμ.

It is felt that the spectra recorded in this study of cobalt(II) in tetramethylguanidine under varying conditions indicate that the principal complex species present is the completely solvated cation, $[Co(TMG)_4]^{++}$. The small wavelength shifts and absorbance changes which were found (Table XIV) on addition of anions to $Co(C_2H_3O_2)_2 \cdot 4H_2O$ can perhaps be rationalized in terms of different degrees of ion-pairing depending on the anion X^-:

$$[Co(TMG)_4]^{++} + X^- \rightleftharpoons [Co(TMG)_4]^{++};X^- \qquad (\underline{23})$$

$$[Co(TMG)_4]^{++};X^- + X^- \rightleftharpoons [Co(TMG)_4]^{++};2X^- \qquad (\underline{24})$$

The spectra used to obtain the data of Table XIV would therefore represent varying concentrations of the three species, $[Co(TMG)_4]^{++}$, $[Co(TMG)_4]^{++};X^-$, and $[Co(TMG)_4]^{++};2X^-$.

The spectra of Co(II) solutions with added iodide ion (Figures 23 and 24) perhaps also can be explained in terms of ion-pairing (Equations <u>23</u> and <u>24</u>). Although small, still the biggest spectral changes in these experiments are found in the cobalt chloride plus iodide systems shown in Figure 24. Here it is seen that there are two and only two types of spectra. A summary of the principal wavelengths is given in Table XV. The spectra of low I^-/Co^{++} ratios may therefore be due to the $[Co(TMG)_4]^{++};2Cl^-$ or $[Co(TMG)_4]^{++};Cl^-$ species since chloride ion readily undergoes ion-pairing. As the ratio of I^- to Co^{++} is increased to twenty and above, the right shoulder inflection disappears and the

Table XV. Spectra of Cobalt(II) Chloride-Sodium Iodide Solutions in Tetramethylguanidine

Initial Concentration = 5×10^{-4} $\underline{M}$ $CoCl_2 \cdot 6H_2O$

I^-/Co^{++}	Wavelength, mμ		
	Shoulder	Maximum	Shoulder
0	564	612	640
2	564	614	643
20	553	602	None
100	553	600	None
1000	553	600	None

spectra become constant in shape and quite similar to that reported (29) for $[Co(TMG)_4](ClO_4)_2$. Therefore it is felt that curves 3-5 in Figure 24 represent the $[Co(TMG)_4]^{++}$ species. Conductivity measurements as a function of added iodide ion concentration could perhaps shed some light on degrees of ion-pairing in these solutions.

The fact that anhydrous $CoCl_2$ obeys Beer's law up to 5 x 10^{-4} M (Figure 21) supports the postulation of a single ion-paired complex, probably $[Co(TMG)_4]^{++};2Cl^-$, at these concentrations. Perhaps in the case of the other Co(II) salts in tetramethylguanidine the deviation from Beer's Law is a measure of the dissociation or association equilibria represented by Equations 23 and 24 (69).

Acid-Base Titrations in 1, 1, 3, 3-Tetramethylguanidine

A. Selection of Useful Indicators

At the time this work was done, nothing was known of the possibility of using visual indicators to detect end points in acid-base titrations in tetramethylguanidine. Williams and co-workers (17a) had already demonstrated that potentiometric acid-base titrations could be made in tetramethylguanidine, but they did not report use of indicators until later (17b). They found that alizarin yellow and azoviolet gave visual end points in agreement with potentiometric values in the titration of benzoic acid. Less satisfactory indicators were o-nitroaniline, thymol blue, phenolphthalein, and o-cresolphthalein. In the work reported in this thesis, phenolphthalein was found to be a useful visual indicator. None of the other indicators mentioned by Williams were studied here.

Some twenty-one indicators were tested in the present work, each in pure (neutral) tetramethylguanidine as well as in acidic and basic solutions. The acidic solutions were 10^{-3} M in $TMGH^+Br^-$, although the colors of each of the potentially useful indicators were also verified in 0.01-0.02 M $TMGH^+$ solutions. The basic solutions used were $\sim 10^{-2}$ M

in tetrabutylammonium hydroxide, added to tetramethylguanidine as a twenty-five percent methanol solution. The presence of the small amount of resultant methanol had no effect on the color of the indicators.

The indicators and their colors are listed in Table XVI. Eight of them, marked with an asterisk in the table, are potentially useful in acid-base titrations. Agreement between the color changes of some of these indicators and the end points in conductometric titrations will be discussed below. Metacresol purple and 2, 4-dinitrophenylhydrazine are listed in the table as having questionable colors because of changes in these colors with time and non-reproducibility of the colors. Perhaps these two indicators react with the solvent.

The indicators from crystal violet to basic fuchsin in Table XVI cover the aqueous pH transformation range from about pH 1 to pH 13. The remaining compounds, all nitro-containing dyes, have pKa values from about 14 to 18.5 as determined in mixed aqueous-nonaqueous systems (70). Thus it is seen that except for tropeoline 00, the useful indicators all have high pKa values (or possess isoelectric points above pH 7 in aqueous solution). This usefulness is likely due to the strongly basic nature of the solvent itself. In fact, practically all the indicators that undergo any color change in tetramethylguanidine show this change only on addition of base (see Table XVI) with the corresponding acidic and neutral solutions possessing the same color.

B. Visible Absorption Spectra of Indicators

Two indicators that gave an appreciable visual color change even at 10^{-3} $\underline{M}$ OH^- were curcumin and clayton yellow. Visible absorption spectra of acidic, neutral, and basic solutions of these indicators are reported in Figures 26 and 27. As is evident, when an indicator solution in tetramethylguanidine is made acidic there is little or no change in its absorption spectrum. When made basic, however, a marked

Table XVI. Colors of Indicators in 1, 1, 3, 3-Tetramethylguanidine

Indicator	Acidic ($TMGH^+$)	Neutral (TMG)	Basic (OH^-)
Crystal Violet	Yellow	Yellow	Orange-yellow
*Tropeoline 00	Yellow	Yellow	Violet
p-Aminoazobenzene	Yellow	Yellow	Yellow
Bromphenol Blue	Blue	Blue	Blue
Alizarin Red S	Blue-Violet	Blue-Violet	Blue
Bromthymol Blue	Blue	Blue	Blue
Neutral Red	Yellow	Yellow	Yellow
Metacresol Purple	?	?	?
*Phenolphthalein	Colorless	Colorless	Pink-Violet
*Thymolphthalein	Pale green	Pale green	Blue
*Curcumin	Red-Violet	Blue-Violet	Yellow
Alkali Blue	Red-Brown	Orange-Brown	Green-Black
Methyl Blue	Colorless	Colorless	Yellow-Black
*Clayton Yellow	Orange-Red	Orange-Red	Red-Violet
Basic Fuchsin	Orange-Yellow	Orange-Yellow	Orange-Yellow
2, 4-Dinitrodiphenylamine	Red-Orange	Red-Orange	Orange-Brown
*2, 4-Dinitroaniline	Orange-Pink	Pink	Red-Violet
2, 4-Dinitrophenylhydrazine	?	?	?
*2-Nitroacetanilide	Pale Yellow	Pale Yellow	Orange
*2-Nitrodiphenylamine	Yellow	Yellow	Violet
4-Nitroaniline	Green-Yellow	Green-Yellow	Yellow

*Useful visual indicator.

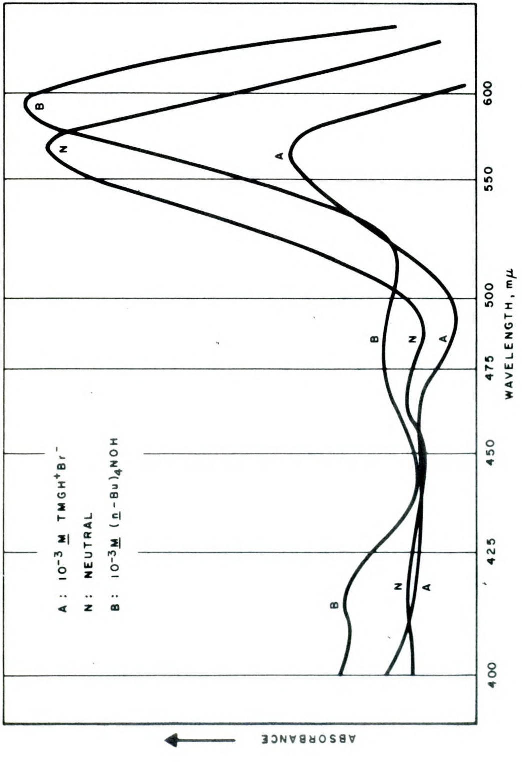


Figure 26. Visible Absorption Spectra of Curcumin, An Acid-Base Indicator.

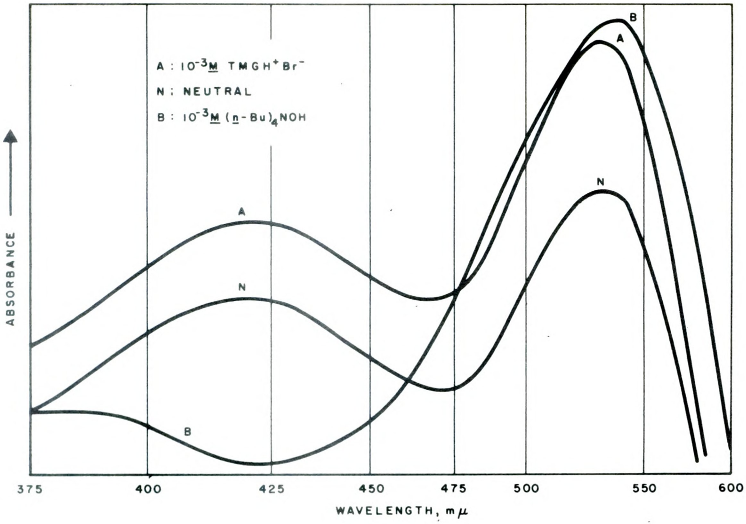


Figure 27. Visible Absorption Spectra of Clayton Yellow, An Acid-Base Indicator.

spectral change occurs. Absorption maxima for curcumin and clayton yellow are given in Table XVII. It is therefore believed that acid-base behavior in tetramethylguanidine could be studied spectrophotometrically by proper selection of indicators such as curcumin, clayton yellow, etc. It should be added that the spectra of Figures 26 and 27 were recorded using indicator concentrations which were unknown but sufficient to give reasonable absorbance readings.

C. Conductometric Titrations of Organic Acids

Conductometric methods were used to study the applicability of tetramethylguanidine in the titration of substances which are very weak acids or even weak bases in water solution.

Organic acids which can be titrated in water should be even stronger acids in a basic solvent like tetramethylguanidine. This indeed appears to be the case with such representative acids as p-toluenesulfonic, benzoic, and salicylic acids. The latter two acids have been titrated potentiometrically in tetramethylguanidine by Williams et al. (17b).

Conductance titration curves are shown in Figure 28 for p-toluenesulfonic acid at two different sets of acid-base concentrations. The end points are exceedingly sharp and appear within experimental error of 1:1 stoichiometry. Quantitative acid recovery percentages for this and some succeeding titrations will be given below (Table XIX) subsequent to discussion of the remainder of the titrations. Figure 28 also contains the color transformation range for the three indicators phenolphthalein, 2-nitrodiphenylamine, and curcumin which were used in separate titrations of p-toluenesulfonic acid.

The first change in indicator color corresponds almost exactly with the conductometric end point. Apparently the base reacts first with the strong acid p-toluenesulfonic acid (or $TMGH^+$, in this case) and then with the weaker indicator acid. Thus, in the acid solution the equilibrium

Table XVII. Absorption Maxima: Visible Absorption Spectra of Indicators

Indicator	Wavelength Maxima, mμ Acid	Neutral	Base
Curcumin:	563	565	592
	461	467	479
	--	417	409
	362	368	369
Clayton Yellow:	529	533	542
	423	421	388

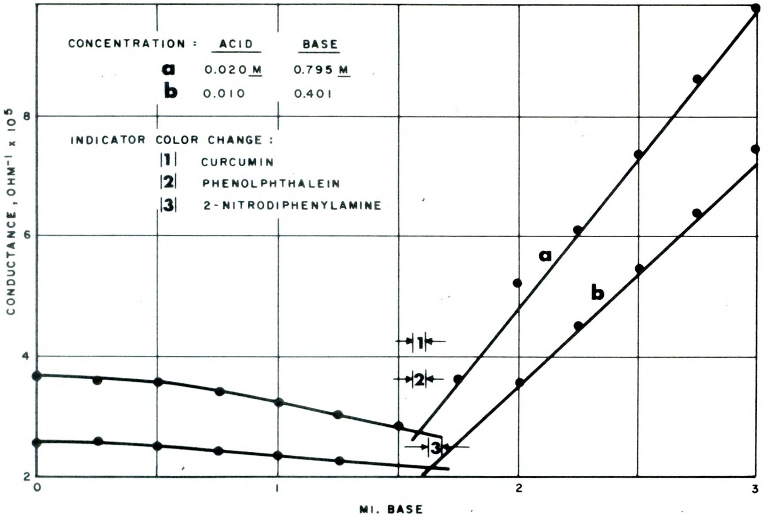


Figure 28. Conductometric Titration of p-Toluenesulfonic Acid.

$$CH_3C_6H_4SO_3H + TMG \longrightarrow CH_3C_6H_4SO_3^- + TMGH^+ \qquad (25)$$

is believed to lie far to the right with all of the sulfonic acid ionized to form the solvo-cation. On titration with base prior to the end point the reaction

$$TMGH^+ + (C_4H_9)_4NOH \longrightarrow TMG + HOH + (C_4H_9)_4N^+ \qquad (26)$$

occurs. After the last $TMGH^+$ is consumed at the end point, the indicator acid reacts with the base:

$$HIn + (C_4H_9)_4NOH \longrightarrow HOH + In^- + (C_4H_9)_4N^+ \qquad (27)$$

and the color changes from that of HIn to that of In^-. Beyond the end point, the rapidly increasing conductance of the solution must be due to addition of base, which is ionized as

$$(C_4H_9)_4NOH \longrightarrow (C_4H_9)_4N^+ + OH^- \qquad (28)$$

Thus, the base could probably be written simply as the OH^- ion in Equations 26 and 27 since the large $(C_4H_9)_4N^+$ cation does not take part in the reactions and probably contributes little to the total conductance of a given solution.

The conductometric titration curve for benzoic acid is given in Figure 29. This particular titration was actually one in which a solution of the base was standardized using a weighed quantity of the acid. In addition, the concentration of the base was determined by an aqueous titration and found to agree with the titration in tetramethylguanidine. Figure 29 also shows the behavior of the two indicators thymolphthalein and clayton yellow in separate titrations of benzoic acid. Apparently clayton yellow is a stronger acid than benzoic acid since its color change occurs immediately upon addition of base. Thymolphthalein, on the other hand, could be used as a visual indicator for benzoic acid,

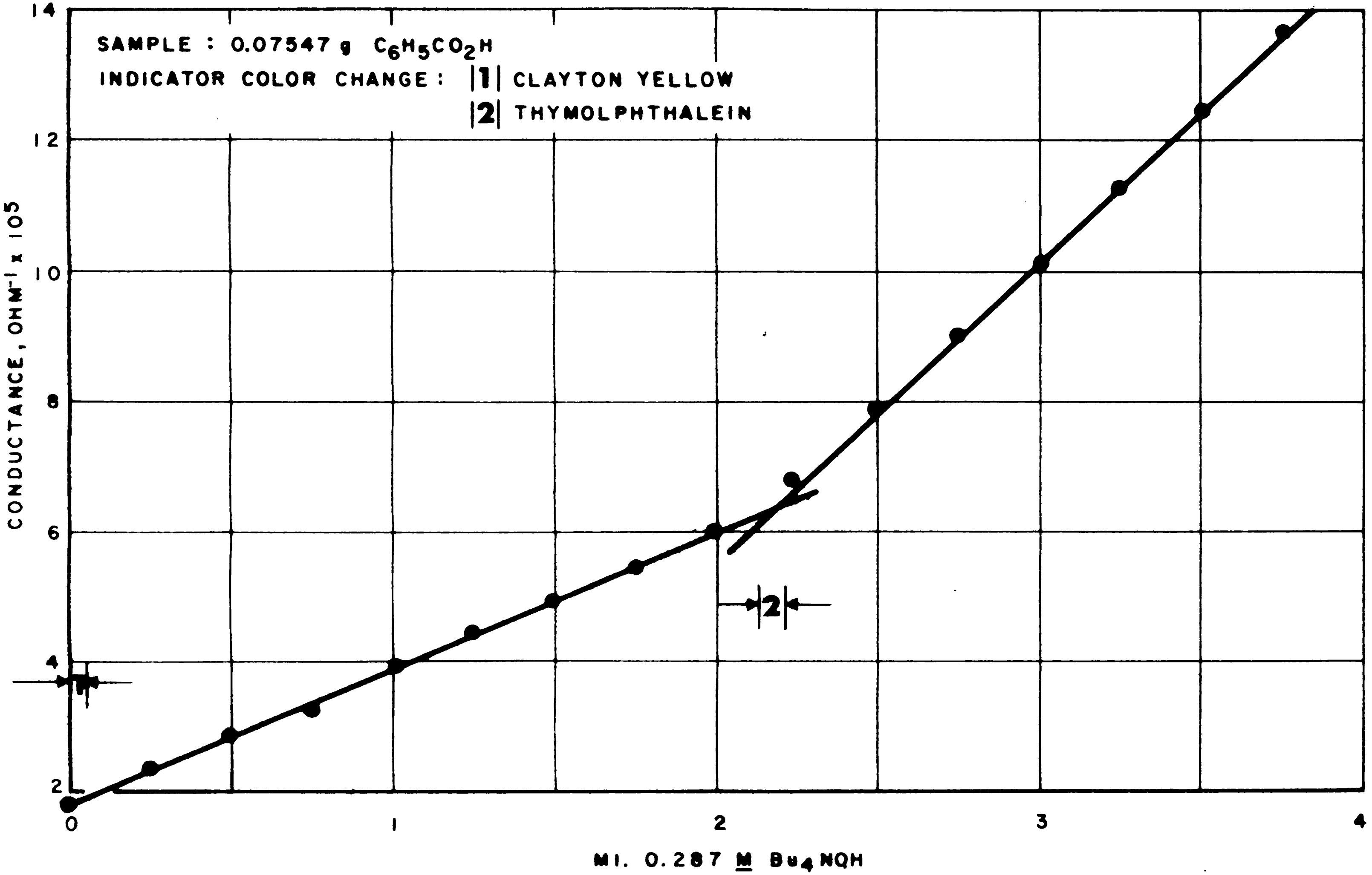


Figure 29. Conductometric Titration of Benzoic Acid.

although the initial color change occurs slightly before the measured conductometric end point. A separate experiment extending the addition of base beyond a 2:1 base:acid ratio showed no additional break in the conductance curve. This single end point is important in connection with the titration of nitroaromatic compounds described below.

Salicylic acid was of interest because of the possibility of titrating both the first [$K_1(aq) \approx 10^{-3}$] and second [$K_2(aq) \approx 10^{-13}$] protons in a strongly basic solvent such as tetramethylguanidine. Figure 30 shows that this was not possible; only the first strong-acid proton was definitely titratable. The curvature in the conductance plot after the end point was reproducible, but it was not possible to draw this curve as two straight lines intersecting at a second end point.

D. Titrations of Nitroaromatic Compounds

Since a nitro group on an aromatic ring is electron-withdrawing, protons on the benzene ring itself or on the substituents tend to be acidic. This acidity should be even more pronounced in basic solvents, and Williams and Custer (17a) have already found 2, 4-dinitrophenol as well as p- and m-nitrophenol to behave as acids in tetramethylguanidine.

In the present work o-nitrophenol was titrated conductometrically (Figure 31). The expected end point occurs at a 1:1 mole ratio, but there is also a second sharp break in the curve at a 1:2 acid-base stoichiometry. That the second end point is real was shown by reproducible results using titration cells with different constants (see Figure 6) and by variation of the concentration of basic titrant. Possibly, after titration of the hydroxyl hydrogen, one of the ring protons is sufficiently acidic to be titrated. A better explanation is believed to lie in the addition of a hydroxyl ion to the ring. The reasoning behind this comes primarily from some of the work of Fritz et al. (71), in which it was found that some nitroaromatic amines gave two end points in titrations

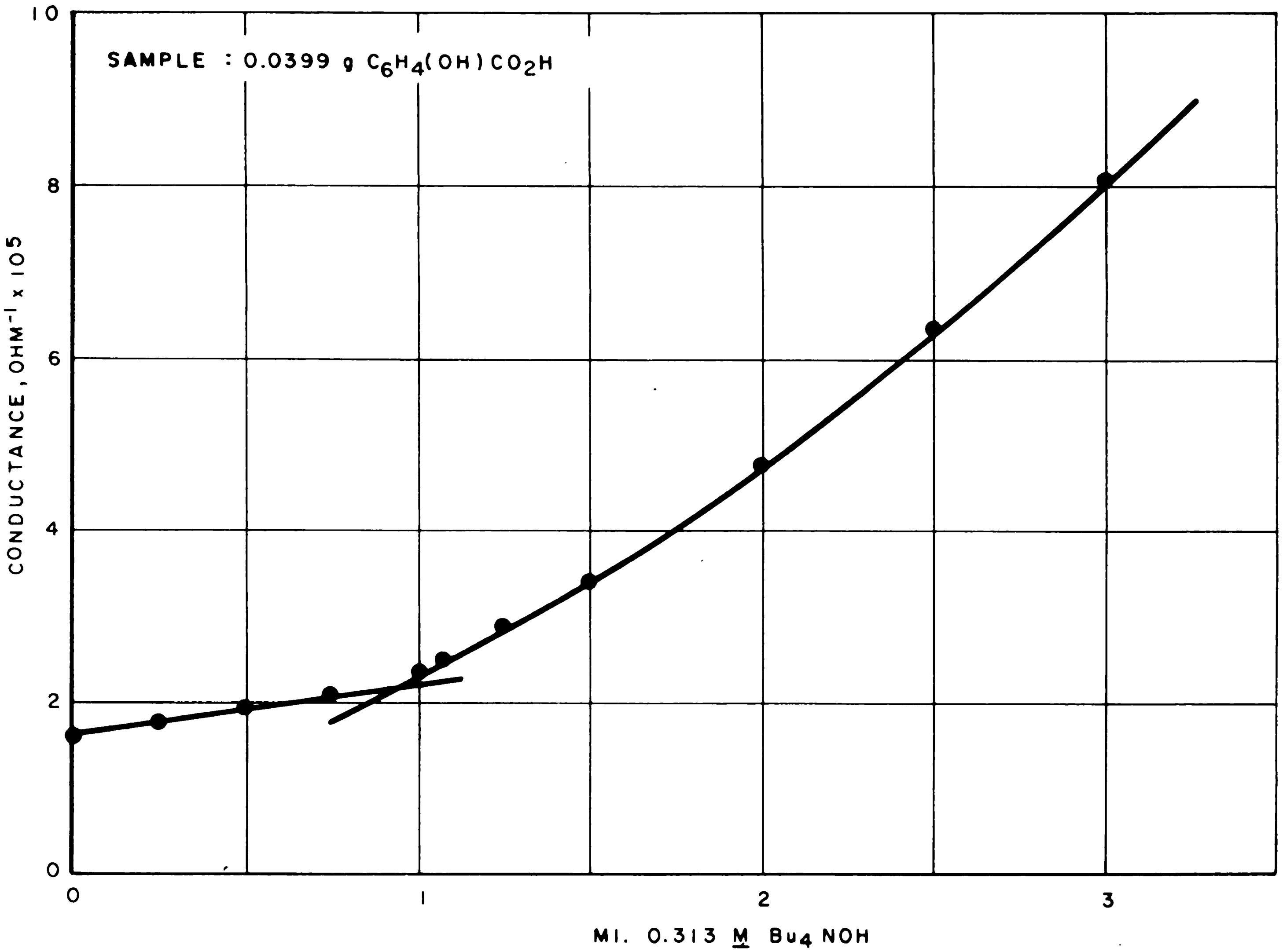


Figure 30. Conductometric Titration of Salicylic Acid.

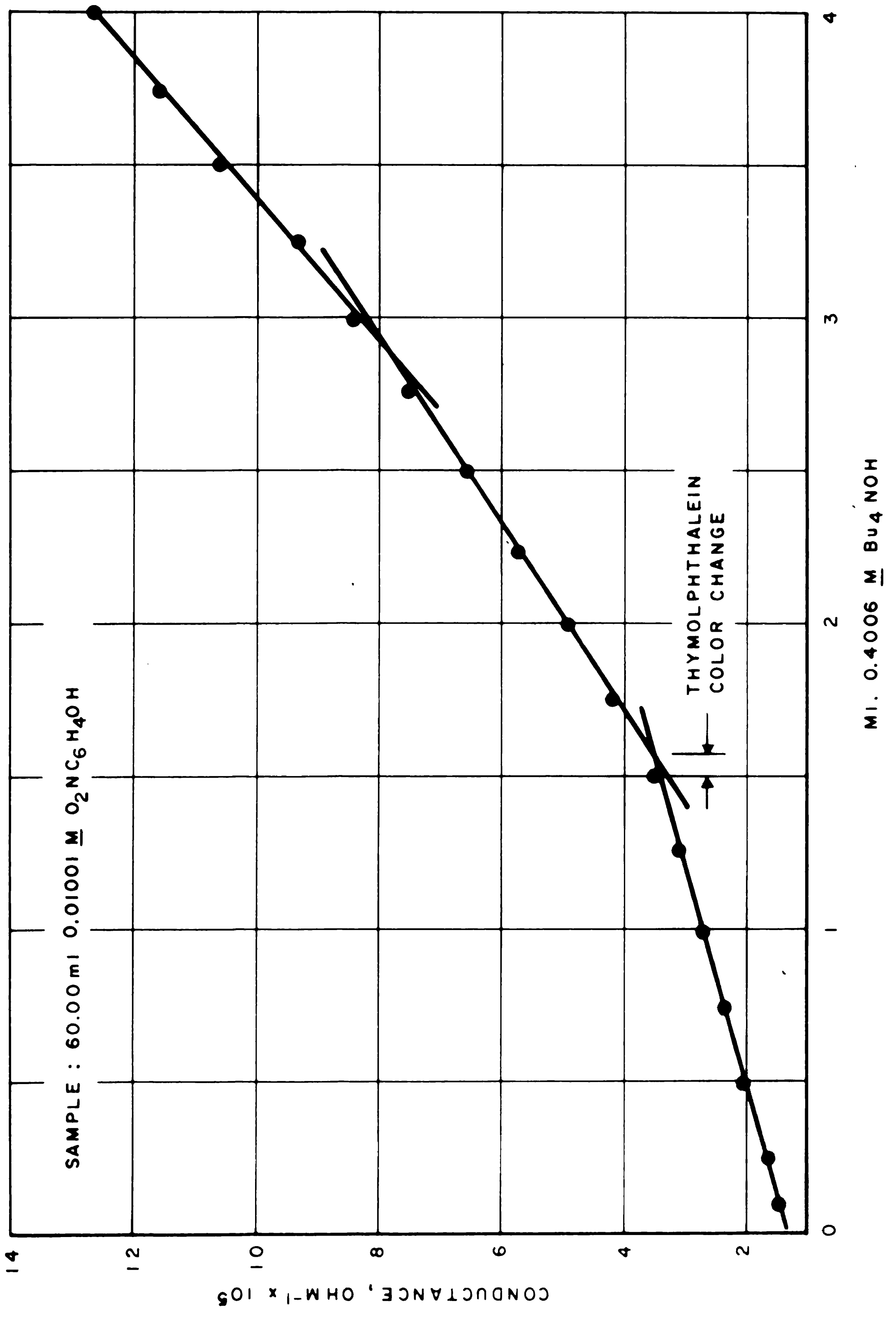
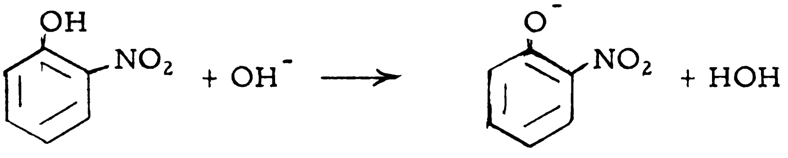


Figure 31. Conductometric Titration of o-Nitrophenol.

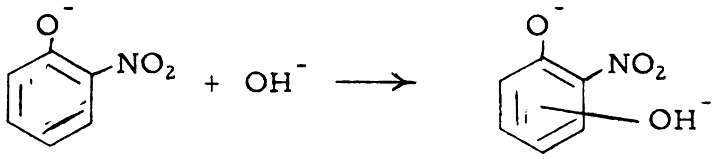
in pyridine with the base triethylbutylammonium hydroxide. With 1, 3, 5-trinitrobenzene, for example, they attribute the second end point to OH^- addition to the benzene ring.

Referring again to Figure 31, it is seen that the color change for thymolphthalein corresponds to the first end point of o-nitrophenol. The consecutive reactions occurring in the titration can be written as follows:



(29)

$$HIn + OH^- \longrightarrow In^- + HOH \qquad (30)$$



(31)

Further insight into reactions such as Equation 31 may be possible through ultraviolet or visible absorption studies. The fact that water is a product in titrations of acids with $(C_4H_9)_4NOH$ apparently is not a problem due to the slowness of the tetramethylguanidine hydrolysis reaction.

Further validation of the second break in the conductance titration of o-nitrophenol was obtained by titration of phenol where only a single end point at 1:1 stoichiometry was found. Titration data are given in Figure 32 and, within experimental error, the conductance is linear from the 1:1 end point to as high as a 1:3 acid:base ratio. Thus, ring addition is more facile in the case of nitro-substituted aromatics. Perhaps the potentiometric titrations of the nitrophenols by Williams (17a) would have given second end points had base addition been continued.

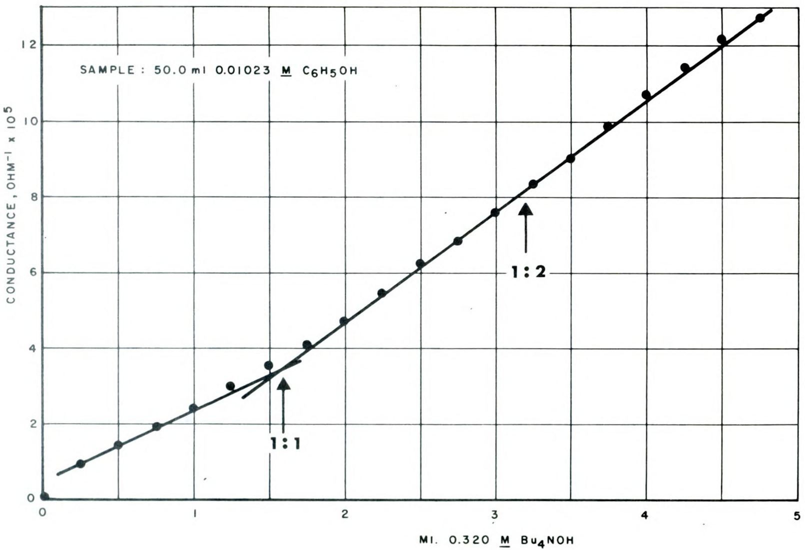


Figure 32. Conductometric Titration of Phenol.

An attempt to compare the titration of o-nitrophenol with that of nitrobenzene met with little success. Apparently nitrobenzene is too weak an acid in tetramethylguanidine to give a satisfactory conductometric titration.

Two polynitrobenzenes, 1, 3-dinitro- and 1, 3, 5-trinitrobenzene, were titrated. Two conductometric titrations of 1, 3-dinitrobenzene were carried out under different conditions (Figure 33). The marked slope changes at 1:1 and 1:2 acid:base ratios are evidence for the reaction of each mole of the dinitrobenzene with two moles of hydroxyl ion. Since there likely are no acidic protons in 1, 3-dinitrobenzene, the hydroxyl ion may again be adding to the ring or perhaps there is reaction of hydroxyl ion with each of the nitro groups.

That the latter may very well be true is shown by the titration of 1, 3, 5-trinitrobenzene in Figure 34. Although the constructed end points in this titration do not agree very well with the integral acid: base ratios, there are three breaks in the conductance curve near the 1:1, 1:2 and 1:3 ratios. Thus, the number of nitro groups substituted on a benzene ring corresponds to the number of end points which obtain in these titration systems.

The literature is helpful here in interpreting the titration behavior of the polynitrobenzenes. Similar multiple end points have been found using ethylenediamine as a solvent. Favini and Bellobono in both potentiometric (72a) and conductometric (72b) titrations with sodium aminoethoxide in ethylenedimaine found 1, 3-dinitrobenzene to have two end points and 1, 3, 5-trinitrobenzene to exhibit three. They also studied other polynitrobenzenes and toluenes and obtained generally similar results. It is also of interest that only single end points were found for phenol and for benzoic acid, as in the present work. By combination of the titration results with some spectrophotometric studies on the same systems, Favini and Bellobono (72a) interpret the titration behavior as

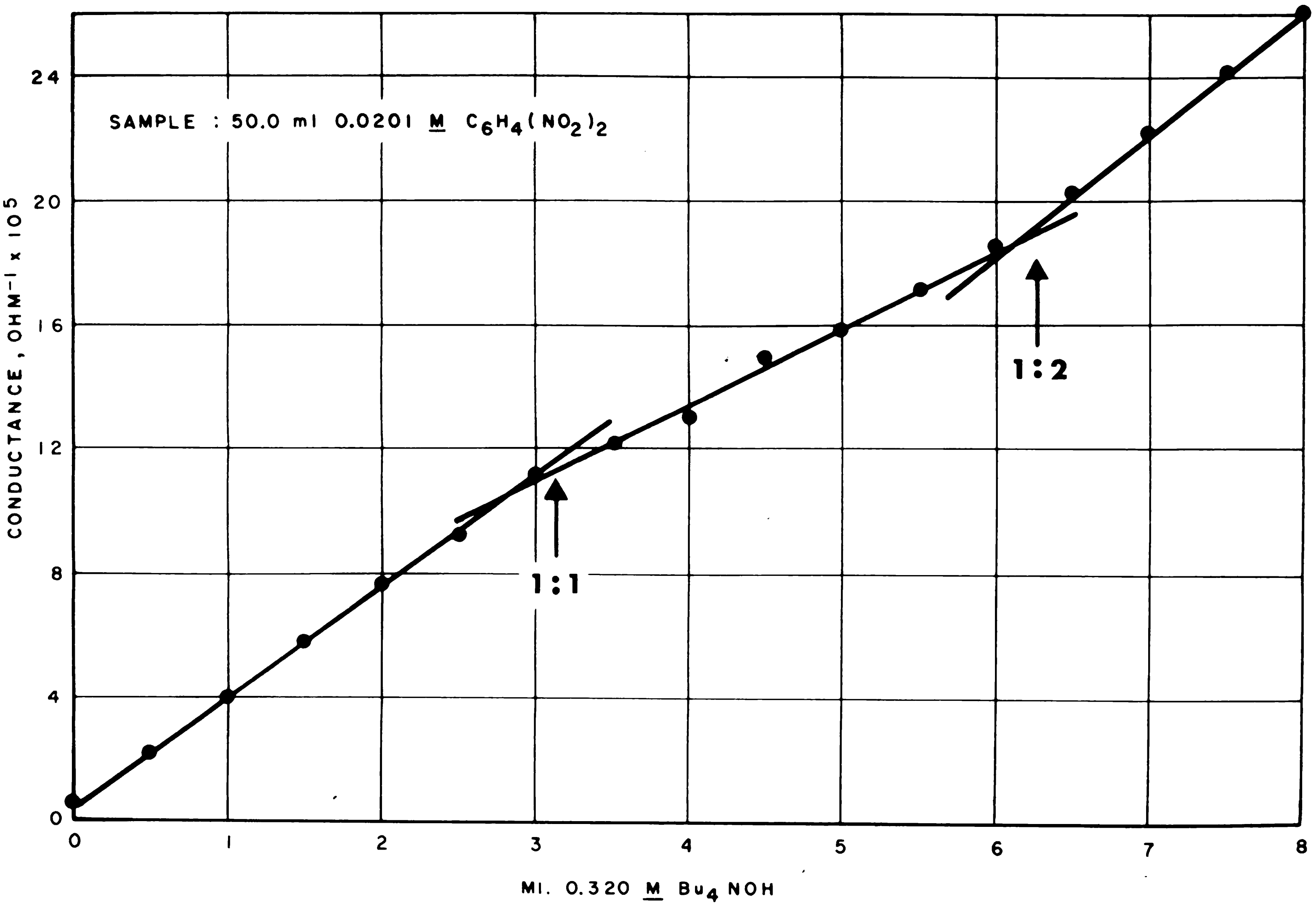


Figure 33. Conductometric Titration of 1, 3-Dinitrobenzene.

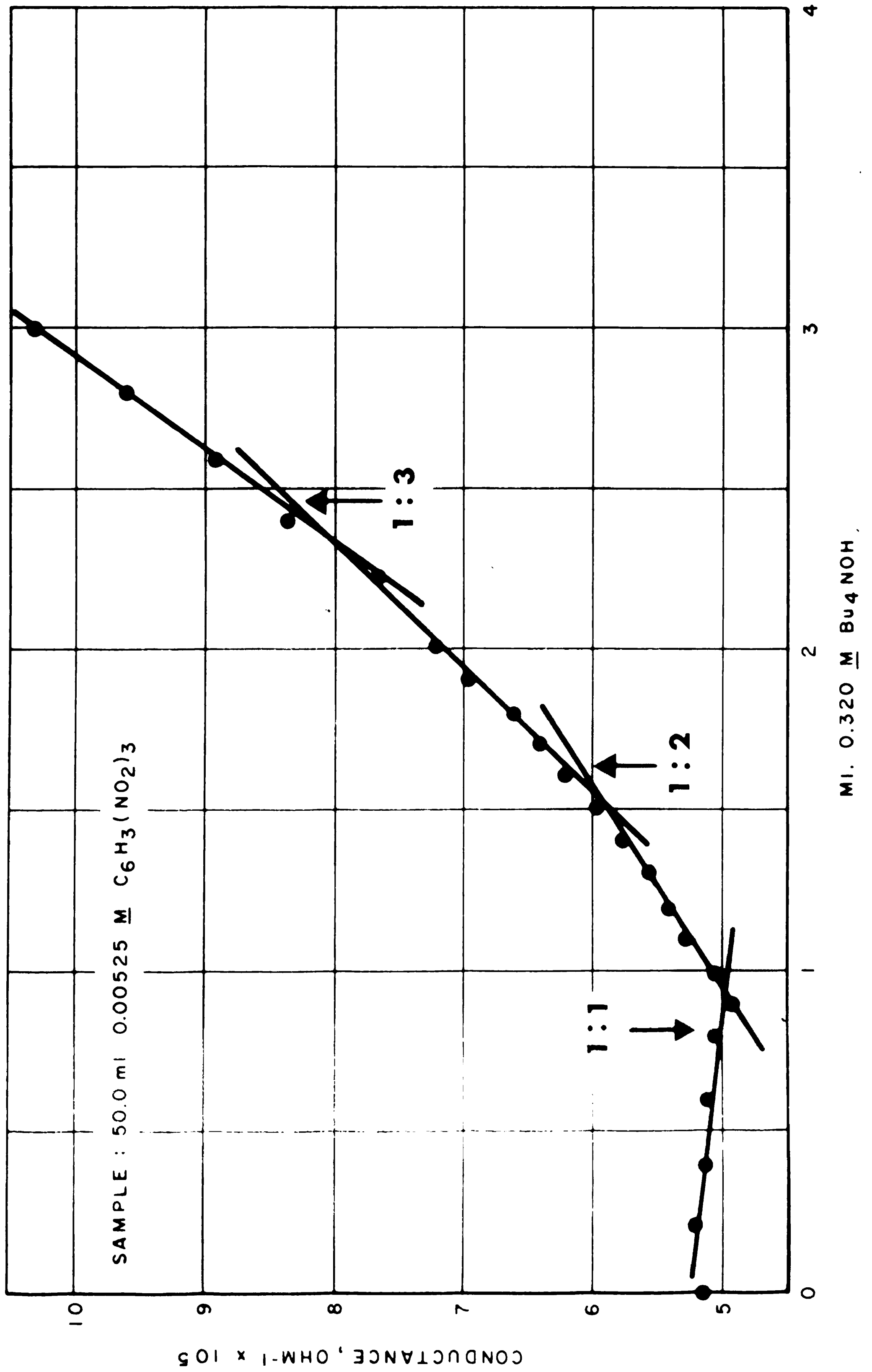
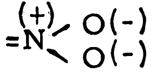


Figure 34. Conductometric Titration of 1, 3, 5-Trinitrobenzene.

consistent with ring addition. This addition, in turn, gives rise to polarization of the individual nitro groups, as  $=\overset{(+)}{N}\genfrac{}{}{0pt}{}{\diagup O(-)}{\diagdown O(-)}$. Therefore it is believed that analogous mechanisms can also be postulated for the titrations of polynitrobenzenes in tetramethylguanidine.

E. Titrations of Inorganic Acids

Previous results indicate that ammonium salts function as acids in tetramethylguanidine according to Equation 22. Solutions of ammonium salts therefore should be titrated readily. That this is so is shown by Figure 35a, the conductance titrations for two different concentrations of ammonium bromide. Single sharp breaks are obtained at ~ 1:1 mole ratios. Tetramethylguanidinium bromide, as one would expect, also titrates as an acid as indicated in Figure 35b.

F. Titrations of Polycarboxylic Acids

It was desired to titrate some representative polyprotic acids in tetramethylguanidine to determine if multiple end points could be obtained. For this purpose, citric acid and maleic acid were selected. Citric acid, a triprotic acid, may give some indication of the possibility of differential titration of mixed acid solutions. This should be true since the consecutive dissociation constants of citric acid in aqueous solution differ only by about single orders of magnitude from each other. The pKa (aq) values for citric acid are 3.06, 4.74, and 5.40.

On attempted dissolution of citric acid monohydrate in tetramethylguanidine it was not possible to obtain complete solution of a given sample, despite the dilution. Apparently the solvent forms a film of liquid around the solute to prevent solubility equilibrium. Nevertheless, two titrations of citric acid were made at two different acid concentrations. These conductance curves are given in Figure 36, where it is easily seen that three end points were obtained for each concentration of acid. Assuming the first conductance break to occur at the 1:1 acid:base ratio,

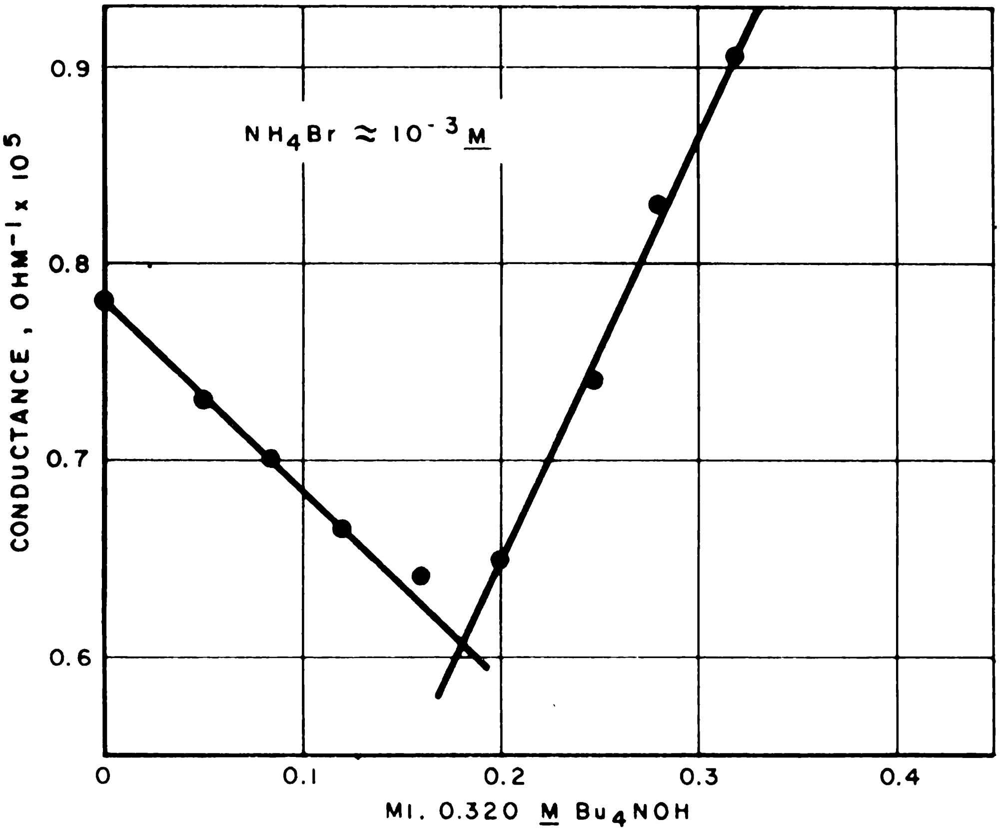


Figure 35a. Conductometric Titration of Ammonium Bromide.

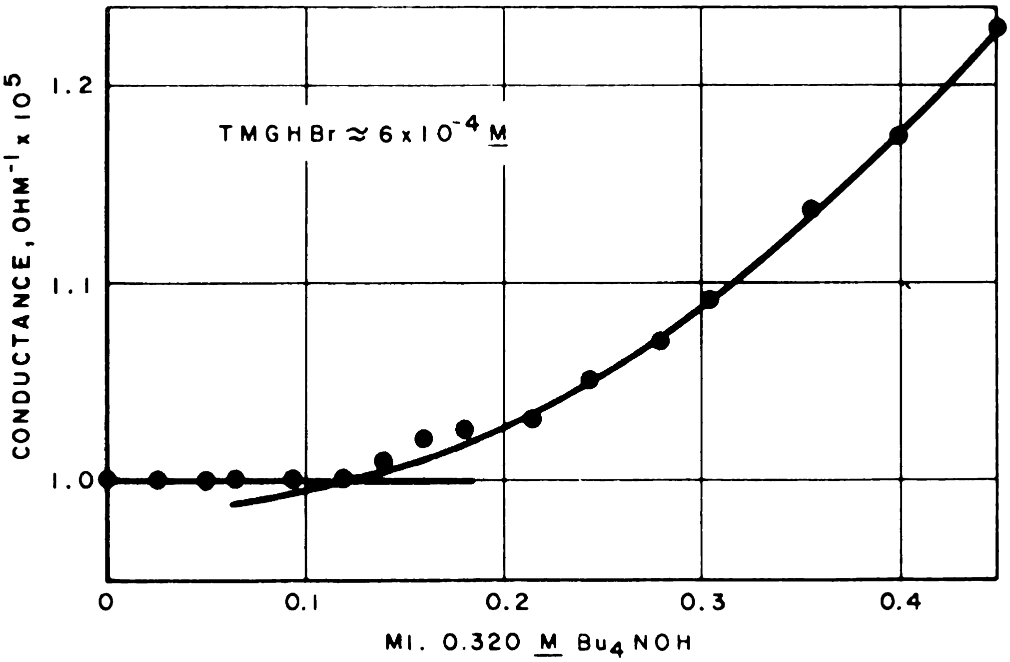


Figure 35b. Conductometric Titration of Tetramethylguanidinium Bromide.

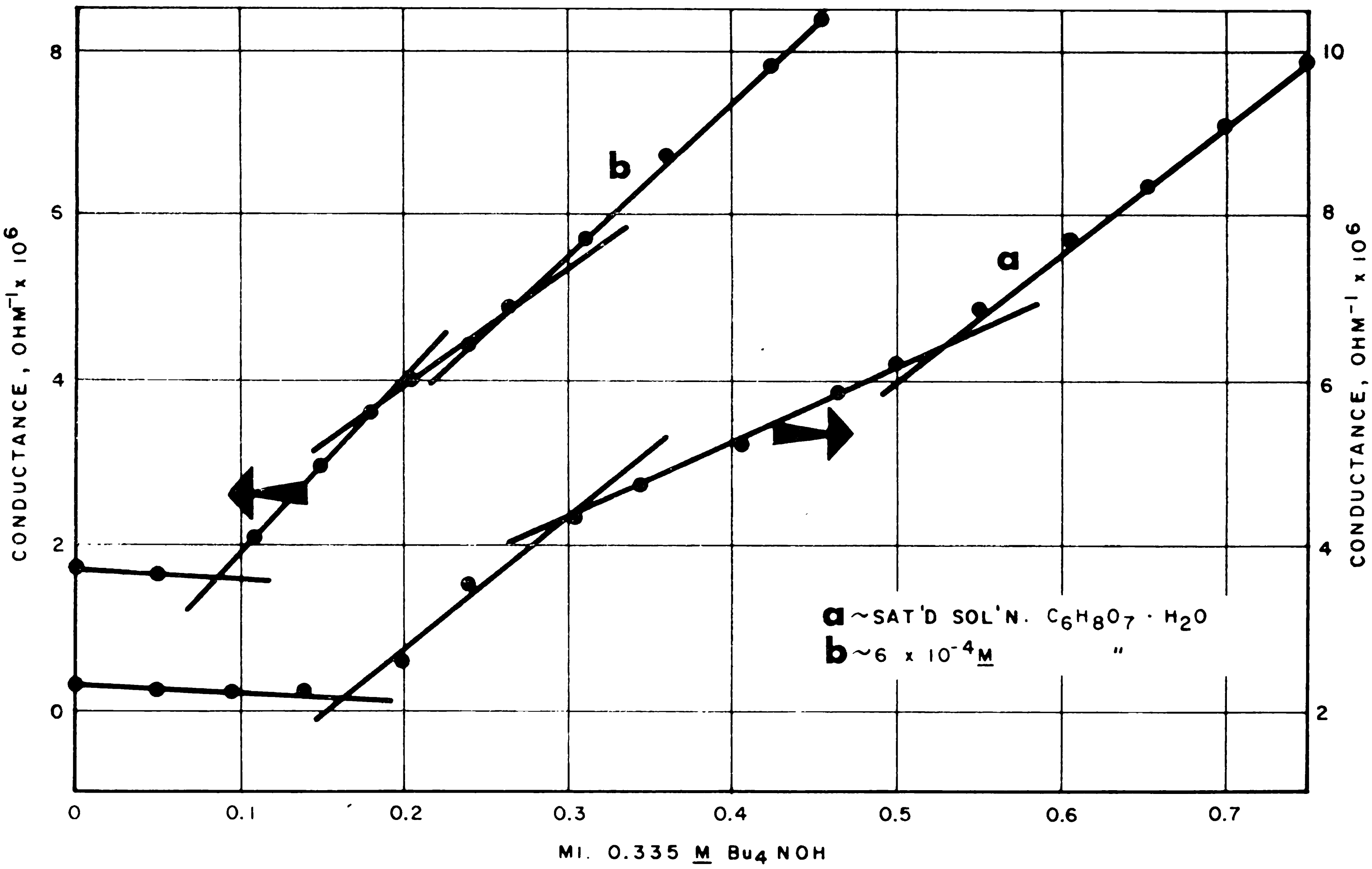


Figure 36. Conductometric Titration of Citric Acid.

the others fall within experimental error of 1:2 and 1:3. That there are three and only three end points is shown by the completely linear conductance behavior well beyond a theoretical 1:4 acid:base stoichiometry.

It is interesting that each of the three acidic protons in citric acid can be titrated with base in tetramethylguanidine. Similar behavior would probably be obtained in other basic solvents. In fact, quite analogous conductometric titrations of many carboxylic and phenolic acids have been reported by van Meurs and Dahmen (73a, b). Their titrations were done in pyridine and N, N-dimethylformamide.

Maleic acid is a diprotic acid whose aqueous dissociation constants are separated by several orders of magnitude. The pKa (aq) values are 1.83 and 6.07. As expected, two easily distinguishable end points are found in a conductance titration in tetramethylguanidine (Figure 37). As with citric acid, solubility equilibrium was not achieved, so that the exact maleic acid concentration was unknown. The end points, however, are in relative agreement with each other.

G. Unsuccessful Conductometric Titrations

A number of materials, generally weak acids or weak bases in aqueous solution, could not be titrated satisfactorily as acids in tetramethylguanidine. These compounds are listed in Table XVIII. The titration curves for these compounds were essentially indistinguishable from "blank" titrations.

It had been hoped that weak bases like urea and acetamide would have some acidic properties in tetramethylguanidine. However, no acidity was detectable by the present system of conductometric titration. Perhaps urea is also a weak base in tetramethylguanidine as recently has been indicated for it in liquid ammonia (69), contrary to the older literature (74). The fact that water does not possess acidic properties may indicate that the initial reaction product is $TMGH^+OH^-$, a salt of a strong acid and a strong base.

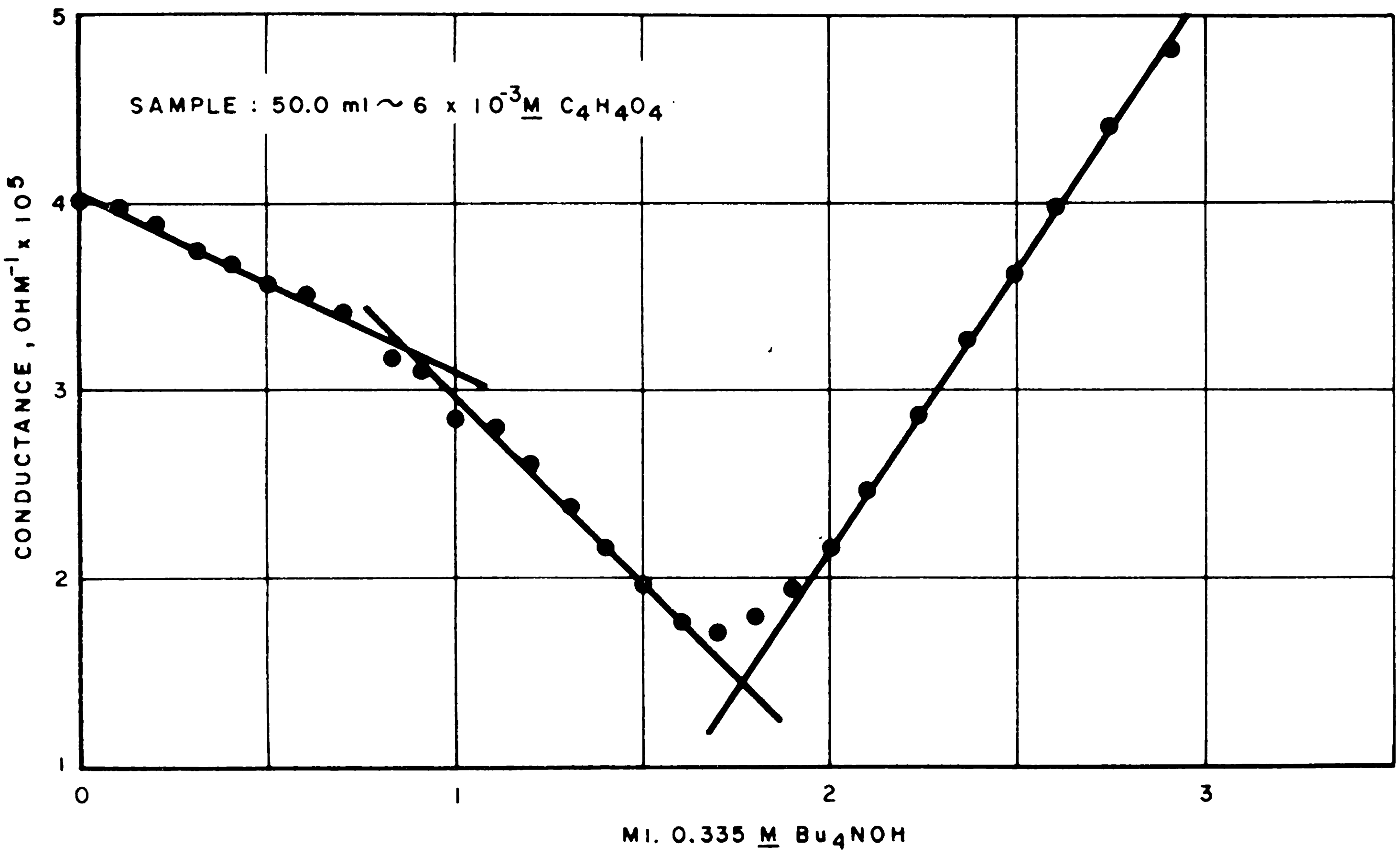


Figure 37. Conductometric Titration of Maleic Acid.

Table XVIII. Compounds Incapable of Titration as Acids in 1, 1, 3, 3-Tetramethylguanidine

Name	Formula
Urea	H_2NCONH_2
Acetamide	H_3CCONH_2
Water	H_2O
Benzene	C_6H_6
Nitrobenzene	$C_6H_5NO_2$
2-Nitroacetanilide	$H_3CCONHC_6H_4NO_2$
Two Acetylureas,	R = cyclo-$C_6H_{11}CH_2$-
 $R\text{-}\overset{O}{\overset{\Vert}{C}}\text{-}\overset{H}{N}\text{-}\overset{O}{\overset{\Vert}{C}}\text{-}NH_2$	R = $C_6H_5CH(C_2H_5)$-

The titration of nitrobenzene was mentioned previously. It has been shown here and by others (71, 72) that at least two nitro groups or one nitro and one other substituent are necessary for these aromatic compounds to exhibit acidic behavior in basic solvents. The neutrality of unsubstituted benzene is therefore quite predictable. o-Nitroacetanilide was titrated to determine whether it would be a self-indicator and whether its color changes corresponded to any conductance breaks. On titration with base, however, the color change from yellow to a deep red was gradual.

The acetylureas listed in Table XVIII have possible barbiturate applications (75). Correlation of any acidic behavior with structure and physiological properties was therefore of interest but they apparently are not acidic in tetramethylguanidine.

H. Quantitative Reliability of Titrations

Most of the conductometric titrations discussed above lend themselves to determination of the percentage recovery of the acid. These percentages are listed in Table XIX, in terms of millimoles of acid taken and found. As can be seen, the recoveries are reasonably good in most cases. It is felt that a major cause of error could have been in the value for the concentration of base in some of the titrations. Since the base, tetrabutylammonium hydroxide, was in a methanol solution, solvent evaporation may have resulted in some error in the base molarities used in the calculations. Perhaps the given basic titrant solutions should have been checked against standard aqueous acid (potassium acid phthalate was used) immediately prior to each of the nonaqueous titrations.

Impure acid samples may have led to errors in some titrations. For instance, the accurate titration values obtained for o-nitrophenol may very well have been the result of using a freshly sublimed sample. Most of the other acids were dried, reagent grade materials.

TABLE XIX. Recovery of Acids by Conductometric Titrations

Acid	Millimoles		Recovery
	Taken	Found	
p-Toluenesulfonic	1.21	1.25	103.$_{3}$%
	0.624	0.611	97.9
Benzoic	0.617	0.624	101.$_{1}$
Salicylic	0.289	0.285	98.6
o-Nitrophenol	0.6006	0.6009	100.0
	0.6006	0.5969	99.38
Phenol	0.512	0.515	100.$_{6}$
1, 3-Dinitrobenzene	0.608	0.614	101.$_{0}$
	1.01	0.989	97.9

An inherent error in conductometric titrations is that of obtaining good graphical end points. This can be obviated reasonably well, however, by securing as many data points as is practical; this latter was done in the titration of maleic acid (see Figure 37).

With reference to Figure 34, no acid recovery calculations were made for 1, 3, 5-trinitrobenzene because of the rather large errors involved in each of the end points. These errors may be partially due to impurities but, on the other hand, they differ markedly for each end point.

No acid recovery values could be obtained for those titrations in which saturated solutions of uncertain concentration were used. These include the titrations of ammonium and tetramethylguanidinium bromide, and citric and maleic acid.

CONCLUSIONS

A. Physical Constants

The relatively high values of the heat of vaporization and Trouton constant for 1, 1, 3, 3-tetramethylguanidine indicates considerable association in the liquid, very likely through intra- and intermolecular hydrogen bonding. "Glass" formation rather than crystallization on cooling the liquid likewise indicates association. The wide liquid range of tetramethylguanidine is convenient. Although its dielectric constant is rather low ($\epsilon = 11.5$), it is not out of the range of usefulness for an ionizing solvent. The following infrared band assignments (cm^{-1}) for the compound have been made: ν N-H, 3311; ν C=N, 1594; δ N-H, 1493; N-H rock, 765-800. The proton magnetic resonance spectrum of 1, 1, 3, 3-tetramethylguanidine is consistent with the expected structure.

B. Solubilities

Solubilities of inorganic salts in tetramethylguanidine parallel those in liquid ammonia but are generally lower. Except for semi-quantitative evidence for the hemisolvate $LiCl \cdot 0.5TMG$, little indication was found for any enhancement of solubilities through cation or anion solvation. Some orders of solubilities are $NH_4 \gtrsim Li > Na > K$, $Ca > Sr > Ba$, and $NCS > ClO_4 > NO_3 > I > Br > C_2H_3O_2 > Cl > SO_4$. Many organic compounds possess reasonable solubility in tetramethylguanidine and complete miscibility is found with most common organic solvents.

C. Reactions

Tetramethylguanidine undergoes slow hydrolysis at room temperature to 1, 1 –dimethylurea and dimethylamine. Carbon dioxide is

readily absorbed by tetramethylguanidine in the presence of water or atmospheric moisture to form tetramethylguanidinium bicarbonate. Water could perhaps be removed from tetramethylguanidine by addition of carbon dioxide to form the insoluble bicarbonate salt.

Reactions of tetramethylguanidine with acids are vigorous and exothermic; the chloride, bromide, acetate, and bicarbonate salts have been isolated. Protonation of tetramethylguanidine occurs at the imine nitrogen followed by a localization of charge on the central carbon atom, $[(CH_3)_2N]_2C^+NH_2$. Only monoprotonation is possible, however. Alkali metal guanidide salts such as $Na^+NC[N(CH_3)_2]_2^-$ could not be isolated.

Tetramethylguanidine is oxidized by agents such as $KMnO_4$ but none of its oxidation products have been characterized. Reaction of tetramethylguanidine with ions such as Ag^+ and Hg_2^{++} may limit the use of silver(I) or mercury(I) salts in electrode construction for electrochemical studies. Reaction of tetramethylguanidine with CCl_4 and CS_2 preclude their use as solvents in spectrophotometry.

D. Metal Complexes

A maximum of four molecules of tetramethylguanidine can coordinate with a typical transition metal ion such as cobalt(II). Tetramethylguanidine is monodentate but could function, perhaps, as a bridging ligand. Insufficient evidence was obtained in this study to determine whether tetramethylguanidine coordinates via the imine or amine nitrogen, but coordination at the imine position recently has been claimed (29).

Tetramethylguanidine is a strong donor ligand as indicated partially by the minor spectral changes with added anions, water, etc. Beer's law studies of cobalt(II) systems in tetramethylguanidine indicate considerable solvent-solute interaction. The visible absorption spectra in

these systems are consistent with the presence of one or more of the species $[Co(TMG)_4]^{++}$, $[Co(TMG)_4]^{++};X^-$, or $[Co(TMG)_4]^{++};2X^-$ in tetramethylguanidine solution. The latter two species are ion-pairs between the fully complexed cobalt(II) ion and a mononegative anion such as chloride ion. Only tetrahedral Co(II) complexes seem to be formed in tetramethylguanidine.

E. Acid-Base Titrations

Acids can be titrated conductometrically in tetramethylguanidine as a solvent using $(\underline{n}\text{-}C_4H_9)_4NOH$ in methanol as titrant. Several visual indicators (see Table XVI) exhibit color changes in tetramethylguanidine which could lead to their use in spectrophotometric studies of acid-base behavior in the solvent. The indicator color changes agree with the conductometric end points providing the indicator acid is weaker than the sample acid.

Acids likely are leveled to the acidity of the solvo-cation, tetramethylguanidinium ion, but no measure of the degree of leveling was made. In addition, the degree of dissociation of any of the resultant $TMGH^+A^-$ salts formed on acid addition were not determined.

Titration of nitroaromatic compounds in tetramethylguanidine results in multiple end points through hydroxyl ion addition to the aromatic ring. Thus, o-nitrophenol and m-dinitrobenzene gave two conductometric end points, while the titration of 1, 3, 5-trinitrobenzene resulted in three breaks in the conductance curve.

Excellent conductometric titration of all three protons in citric acid was obtained. Since the consecutive ionization constants for citric acid in aqueous solution only differ by about tenfold from each other (8.7×10^{-4}, 1.8×10^{-5}, and 4.0×10^{-6}), differential titration of mixed acids in tetramethylguanidine should be possible.

Ammonium ion titrates as an acid in tetramethylguanidine; in other words, tetramethylguanidine is a stronger base than ammonia. A number of compounds such as urea, water, acetamide, and nitrobenzene, however, do not possess sufficiently acidic properties to be titrated conductometrically in tetramethylguanidine.

F. General

In the introduction it was stated that an over-all purpose of this work was to determine the utility of 1, 1, 3, 3-tetramethylguanidine as a solvent. The above conclusions have demonstrated a number of potential areas of usefulness for tetramethylguanidine in terms of its properties. However, despite the findings of the present studies, a great deal more study is necessary before tetramethylguanidine will become a commonly used nonaqueous solvent. It is hoped that this thesis will generate new interest in 1, 1, 3, 3-tetramethylguanidine.

RECOMMENDATIONS

As mentioned in the conclusions, additional research on 1, 1, 3, 3-tetramethylguanidine would be helpful indeed. Some of the more important studies are:

1. Determination of the self-ionization constant.
2. Thermodynamics and kinetics of reactions in or of tetramethylguanidine.
3. Comparison of potentiometric and conductometric titrations with high-frequency, thermometric, and coulometric methods.
4. Differential titrations of two or more acids.
5. Ion-pair formation studies.

REFERENCES

1. American Cyanamid Company, Market Development Department Report, IC-0219R-500, May, 1960.

2. J. Kleinberg, W. G. Argersinger, Jr., and E. Griswold, Inorganic Chemistry, D. C. Heath and Co., Boston, 1960, pp. 218-220.

3. L. F. Audrieth and J. Kleinberg, Nonaqueous Solvents, John Wiley and Sons, Inc., New York, 1953, pp. 33-34.

4. H. H. Sisler, Chemistry in Nonaqueous Solvents, Reinhold Publishing Corp., New York, 1961, pp. 6-10.

5. A. Berg, Compt. rend., 116, 887 (1893).

6. M. Schenck, Z. physiol. Chem. 77, 328 (1912).

7. M. Schenck and F. von Graevenitz, Z. physiol. Chem. 141, 132 (1924).

8. (a) H. Lecher and F. Graf, Ber. 56B, 1326 (1923).
   (b) H. Lecher and F. Graf, Ann. Chem. 438, 154 (1924).
   (c) H. Lecher, F. Graf, and F. Gnädinger, ibid. 445, 61 (1925).

9. C. K. Cain, U. S. 2,898,369, Aug. 4, 1959. C. A. 54, 4395i.

10. H. Z. Lecher, E. M. Hardy, and C. L. Kosloski, U. S. 2,845,459, July 29, 1958. C. A. 53, 231e.

11. S. J. Angyal and W. K. Warburton, J. Chem. Soc. 1951, 2492.

12. N. F. Hall and M. R. Sprinkle, J. Am. Chem. Soc. 54, 3469 (1932).

13. T. H. Wirth and N. Davidson, J. Am. Chem. Soc. 86, 4325 (1964).

14. T. E. Mead, J. Phys. Chem. 66, 2149 (1962).

15. R. Kitawaki, Nippon Kagaku Zasshi, 78, 1435 (1957). C. A. 54, 4382b.

16. American Cyanamid Company, Market Development Department Report, ICO234-R-1000, Sept., 1960.

17. (a) T. R. Williams and J. Custer, Talanta 9, 175 (1962).
    (b) T. R. Williams and M. Lautenschleger, ibid. 10, 804 (1963).

18. H. M. Randall, R. G. Fowler, N. Fuson, and J. R. Dangle, *Infrared Determination of Organic Substances*, D. Van Nostrand Co., Inc., New York, 1949.

19. J. Fabian, M. Legrand, and P. Poirier, Bull. soc. chim. France 1956, 1499.

20. Sadtler Spectrum No. 16115, S. P. Sadtler and Son, Inc., Philadelphia, 1962.

21. R. S. Drago, private communication.

22. G. Williams and M. L. Hardy, J. Chem. Soc. 1953, 2560.

23. T. Goto, N. Nakanishi, and M. Ohashi, Bull. Chem. Soc. Japan 30, 723 (1957).

24. L. Paoloni, Gazz. chim. ital. 89, 957 (1959).

25. A. Kotera, T. Morita, S. Aoyagi, Y. Kakiuchi, S. Nagakura, and K. Kume, Nippon Kagaku Zasshi 82, 302 (1961). C. A. 55, 15128g.

26. P. Rây, Chem. Revs. 61, 313 (1961).

27. P. S. Gentile and L. H. Talley, J. Am. Chem. Soc. 79, 4296 (1957).

28. S. Akihama and S. Toyoshima, Chem. Pharm. Bull. (Tokyo) 10, 1254 (1962). C. A. 58, 12885c.

29. R. Longhi and R. S. Drago, Inorg. Chem. 4, 11 (1965).

30. B. A. Kennedy, unpublished data.

31. J. H. Bloor, unpublished data.

32. P. Job, Ann. chim. 9, 113 (1928).

33. R. L. Shriner and R. C. Fuson, The Systematic Identification of Organic Compounds, John Wiley and Sons, Inc., New York, 1948, p. 27.

34. A. Weissberger and E. Proskauer, Organic Solvents, Oxford University Press, London, 1935, p. 94.

35. F. Daniels, J. H. Mathews, J. W. Williams, and Staff, Experimental Physical Chemistry, McGraw-Hill Book Co., Inc., New York, 1949, p. 557.

36. A. A. Maryott and E. R. Smith, Table of Dielectric Constants of Pure Liquids, National Bureau of Standards Circular 514, U. S. Government Printing Office, Washington, D. C., 1951, pp. 5-13.

37. W. J. Mader, R. D. Vold, and M. J. Vold, in A. Weissberger, ed., Physical Methods of Organic Chemistry, 3rd ed., Vol. 1, Interscience Publishers, Inc., New York, 1959, pp. 655-688.

38. H. H. Willard, L. L. Merritt, Jr., and J. A. Dean, Instrumental Methods of Analysis, 3rd ed., D. Van Nostrand Co., Inc., New York, 1958, pp. 218-257.

39. K. T. Wilke and W. Opferman, Z. Physik. Chem. (Leipzig) 224, 237 (1963).

40. A. I. Popov and J. C. Marshall, J. Inorg. Nucl. Chem. 19, 340 (1961).

41. A. Weissberger, E. S. Proskauer, J. A. Riddick, and E. E. Toops, Jr., Organic Solvents, Interscience Publishers, Inc., New York, 1955, pp. 289-295.

42. G. L. Putnam and K. A. Kobe, Trans. Electrochem. Soc. 74, 609 (1938).

43. B. E. Geller, Zh. Fiz. Khim. 35, 2210 (1961).

44. F. Daniels, *Outlines of Physical Chemistry*, John Wiley and Sons, Inc., New York, 1948, p. 182.

45. F. Daniels, *loc. cit.*, p. 71.

46. John Deere Chemical Company, Product Data Bulletin, *Tetramethylurea*.

47. A. Luettringhaus and H. W. Dirksen, Angew. Chem. Internat. Ed. *3*, 260 (1964).

48. A. I. Popov in H. B. Jonassen and A. Weissberger, eds., *Techniques of Inorganic Chemistry*, Vol. 1, Interscience Publishers, Inc., New York, 1963, p. 45.

49. L. F. Audrieth and J. Kleinberg, *loc. cit.*, pp. 119, 123.

50. S. Glasstone, *Textbook of Physical Chemistry*, D. Van Nostrand Co., Inc., New York, 1946, p. 502.

51. K. Nakanishi, *Infrared Absorption Spectroscopy--Practical*, Holden-Day, Inc., San Francisco, 1962, pp. 38-39.

52. E. Lieber, D. R. Levering, and L. J. Patterson, Anal. Chem. *23*, 1594 (1951).

53. K. Nakamoto, *Infrared Spectra of Inorganic and Coordination Compounds*, John Wiley and Sons, Inc., New York, 1963, pp. 71, 145.

54. J. H. Hibben, J. Chem. Phys. *5*, 166 (1937).

55. L. F. Audrieth and J. Kleinberg, *loc. cit.*, p. 120.

56. V. Grignard, G. Dupont, and R. Locquin, *Traité de Chimie Organique*, Masson et cie, ed., Paris, Vol. 13, 1941, pp. 901-902.

57. C. A. Jacobson, ed., *Encyclopedia of Chemical Reactions*, Reinhold Publishing Corp., New York, Vol. 2, 1948, pp. 355, 365-369.

58. R. Huisgen and H. Brade, Chem. Ber. *90*, 1432 (1957).

59. E. Spinner, J. Phys. Chem. *64*, 275 (1960).

60. Anonymous, Brit. 293,040, July 1, 1927, C. A. 23, 1418^5.

61. W. B. Schaap, A. E. Messner, and F. C. Schmidt, J. Am. Chem. Soc. 77, 2683 (1955).

62. C. A. Jacobson, ed., loc. cit., pp. 227-238.

63. L. F. Audrieth and J. Kleinberg, loc. cit., p. 122.

64. (a) L. I. Katzin and J. R. Ferraro, J. Am. Chem. Soc. 72, 5451 (1950).
    (b) L. I. Katzin and E. Gebert, ibid. 72, 5455, 5464 (1950).
    (c) L. I. Katzin, J. R. Ferraro, and E. Gebert, ibid. 72, 5471 (1950).
    (d) L. I. Katzin and J. R. Ferraro, ibid. 74, 2752, 6040 (1952).

65. (a) W. Libuś, A. Ugniewska, and S. Minc, Roczniki Chem. 34, 29 (1960).
    (b) W. Libuś, ibid. 35, 411 (1961).
    (c) W. Libuś, ibid. 36, 999 (1962).

66. S. Buffagni and T. M. Dunn, J. Chem. Soc. 1961, 5105.

67. C. J. Ballhausen and C. K. Jørgensen, Acta Chem. Scand. 9, 397 (1955).

68. L. I. Katzin, J. Inorg. Nucl. Chem. 4, 187 (1957).

69. R. D. Hill, Ph. D. Thesis, Michigan State University, East Lansing, Michigan, 1962.

70. R. Stewart and J. P. O'Donnell, J. Am. Chem. Soc. 84, 493 (1962).

71. J. S. Fritz, A. J. Moye, and M. J. Richard, Anal. Chem. 29, 1685 (1957).

72. (a) G. Favini and I. R. Bellobono, Ann. chim. (Rome) 50, 825 (1960).
    (b) G. Favini and I. R. Bellobono, ibid. 51, 841 (1961).

73. (a) N. van Meurs and E. A. M. F. Dahmen, Anal. Chim. Acta 19, 64 (1958).
    (b) N. van Meurs and E. A. M. F. Dahmen, ibid. 21, 443 (1959).

74. L. F. Audrieth and J. Kleinberg, *loc. cit.*, p. 77.

75. A. I. Popov, private communication.

APPENDICES

APPENDIX I

Toxicological Investigation of 1, 1, 3, 3-Tetramethylguanidine

Range finding toxicological tests on 1, 1, 3, 3-tetramethylguanidine have been done by courtesy of the Biochemical Research Laboratory of Dow Chemical Company, Midland, Michigan. The following conclusions are quoted verbatim from the report of the tests:

"1, 1, 3, 3-Tetramethylguanidine has a moderate acute oral toxicity, but should present no problem from ingestion incidental to industrial handling. It should be borne in mind, however, that serious injury may occur from the accidental or willful swallowing of relatively small amounts. Containers should be clearly and carefully labeled so that accidental swallowing due to mistaken identity cannot occur.

"The undiluted material is severely irritating to the eye. Direct eye contact would likely result in extensive conjunctival and corneal injury sufficient to produce at least some permanent impairment of vision and possibly total loss of sight. Washing, if it is to be effective, must be immediate and thorough. Unless first aid measures and precautionary handling recommendations suggested in this report are followed, permanent impairment of vision may be sustained. Chemical workers goggles are recommended for safe industrial handling whenever the likelihood of eye contact exists.

"1, 1, 3, 3-Tetramethylguanidine is also severely irritating to the skin. Short exposures of 15 seconds or so are likely to produce a severe burn. Precautions must be taken to avoid all skin contact. Protective clothing should be worn whenever the likelihood of skin contact exists.

"Inhalation studies conducted on rats indicate that single exposures to the vapors of 1, 1, 3, 3-tetramethylguanidine at room temperature should present no problem. The effect of vapors of the material maintained at elevated temperatures were not studied.

"These conclusions are based on range finding toxicological tests and are limited to precautions for industrial handling of the material. Development of specific uses will require consideration of the health problems presented and of the need for further toxicological studies."

APPENDIX II

Data and Calculations: Solubility of $NaHSO_4$

Data: Weighings

Sample No.	(a) Wt. Satd. Soln. for Flame Anal.
7	4.49399 g
8	4.46883
9	4.46882

Data: Flame Photometry

ppm Na	Scale Divisions (ave.)
1.00	82.8
0.80	66.4
0.60	52.1
0.40	38.9
0.20	14.2
0.10	7.9

These data are plotted in Figure 5.

No.	Scale Div.	(b) ppm Na	ppm Na minus Blank
7	56.7	0.653	0.524
8	49.6	0.612	0.483
9	53.1	0.698	0.569
Blank	10.4	0.129	0.00

Calculations: Flame Photometry

	(b)	(c)	(d)
No.	mg Na/l	mg Na/sample vol.	mg $NaHSO_4$
7	0.524	0.0131_0	0.0684_0
8	0.483	0.0120_8	0.0630_7
9	0.569	0.0142_2	0.0742_4

Calculations: Solubility

	(d)	(e) = (a-d)	(d/10e)
No.	Wt. Solute	Wt. Solvent	g Solute/100 g Solvent
7	0.0684_0 mg	4.49392 g	0.00152_2
8	0.0630_7	4.46877	0.00141_1
9	0.0742_4	4.46875	0.00166_1
		Ave. Solubility	0.0015_3