

HIGH RESOLUTION PROTON MAGNETIC RESONANCE STUDY  
IN HYDROGEN BONDED SYSTEMS

by

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## ABSTRACT

The keto-enol tautomeric systems of cyclic 1,3 diones have been studied by the proton magnetic resonance method. The presence of both keto and enol forms were confirmed in chloroform and acetonitrile solutions. From the concentration dependence of OH proton chemical shift, the equilibrium among the three forms has been suggested:  $(\text{Enol})_2 \xrightleftharpoons{K_1} 2\text{Enol} \xrightleftharpoons{K_2} 2\text{Keto}$

A linear relationship was found between the OH proton chemical shift and  $1/\sqrt{C}$ . The chemical shift of the hydrogen bonded OH proton was found to be -740 cps from T.M.S. at 60 M.c. by extrapolation to infinite concentration. That of the non-hydrogen bonded OH proton was found to be -440 cps, which gave the most reasonable equilibrium constant,  $K_1$ , for all concentrations.

The equilibrium constants were obtained from the observed OH chemical shift and from the ratio of the areas under the specific peaks for each species. Measurements were also made in the temperature range 302°K to 357°K for cyclohexane 1,3 dione in chloroform. The overall heat of conversion from the dimer enol form to the monomer keto form was found to be 2.05 Kcal/mole.

The proton magnetic resonance spectra of methyl pyridines have been investigated both in carbontetrachloride and trifluoroacetic acid. The broad triplets which were observed at the

pyridine concentration of 6~8 mole % in trifluoroacetic acid confirmed the presence of the pyridine cations. Almost all the signals shifted to low field on protonation. The factors which affect the chemical shift were split into several terms on the basis of Pople's theory.<sup>125</sup> The chemical shifts of the pyridine and pyridinium systems were compared with the benzene system. Dominating factors were found to be; the inductive and anisotropic effects of the nitrogen atom or the protonated nitrogen atom, the mesomeric effect of the above, and the inductive and anisotropic effects of the methyl groups. Using these values, which were obtained from the simple compounds, the chemical shifts were calculated and compared with the observed values. They agreed in most of the cases within  $\pm 5$  cps at 60 M.c.

The ortho coupling constants between the 2 and 3 ring protons in the pyridine system are much smaller than those in the benzene system. The slight increases in coupling constants on protonation were only understandable considering the pyridinium cations as odd sequences from the benzene and pyridine systems.

It was observed that the  $C^{13}$ -H' coupling constants increased on protonation as a result of the increase in the electronegativity of the nitrogen atom. That is the s character in the carbon atomic orbital increased on protonation.

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## I. INTRODUCTION

### A. Study of Keto-Enol Tautomerism by N.M.R.

Keto-enol tautomerism involves the motion of a proton to a carbonyl oxygen from an  $\alpha$ -carbon. This is illustrated in the following equation.



The existence of two forms was first recognized from the behavior in chemical reactions.<sup>3</sup> Presence of these isomers ~~was~~ also seen from the studies of I.R.<sup>4</sup>, U.V.<sup>4</sup>, and N.M.R.<sup>5,6,7</sup> spectra.

In general, the carbonyl compounds exist almost exclusively in the keto form unless there is any stabilizing factor for the enol form. The keto form is about 17 kcal/mole more stable<sup>7</sup> than the enol form from bond energy calculations. The relative stability of these two forms is affected by factors such as resonance, conjugation of C=C and C=O double bonds, the formation of hydrogen bonds to the enol proton and other structural features.<sup>8</sup>

Equilibrium position also changes with different solvents. The keto form is almost invariably more polar than the enol form and the keto-enol ratio for a given pair of tautomers at equilibrium ~~in~~ solution depends markedly on the polarity of the solvent, and this ratio tends to be the greatest in the least

polar solvents.<sup>9</sup> Acidic and basic solvents also vary the position, both favouring the formation of the enol form. The hydrogen bond to the solvent molecule is also important.

Tautomeric systems have been analyzed by chemical,<sup>10,11</sup> refractive index<sup>12</sup> and light absorption<sup>13,14</sup> methods.

Proton magnetic resonance has been a useful method for studying tautomeric systems<sup>5,6,7,15,16,17,18,19,20,21</sup> because it doesn't perturb the system during measurements. The enolization of carbonyl compounds, in particular,  $\beta$ -diketones and  $\beta$ -triketones, etc., are well known and much work has been done on the factors which influence the position of equilibrium.<sup>5,6,7,15,16,17,18,20</sup> The first enolic compound studied by N.M.R. was the liquid acetylacetone.<sup>5,6</sup> The spectrum of liquid acetylacetone show five peaks which were assigned to two different methyls due to the keto and to the enol forms, to  $\text{CH}_2$  protons between the two carbonyls in the keto form, to olefinic protons  $\text{C}=\text{CH}$  in the enol, and to the  $\text{OH}$  protons in the enol. The ratio of the keto to the enol forms were determined from the measurements of signal intensities (= ratio of area under the peaks). The heat of conversion has also been obtained from the measurement of the keto-enol ratio over a range of temperatures. The enthalpy,  $\Delta H$ , was thus found from the slope of a graph of  $\log K_E$  versus  $1/T$ . Similar work has been done in different solvents to study the effect of solvents on the system.

With certain assumptions<sup>1</sup> the condition for coalescence of two peaks  $\nu_A$  and  $\nu_B$  arising from two non-equivalent protons which

may undergo exchange can be written:

$$\tau \leq \frac{\sqrt{2}}{2\pi} (\nu_A - \nu_B)$$

$$\text{where } 2\tau = \tau_A = \tau_B$$

$\tau_x$  = average lifetime of the proton at the site  $x$ .

From the above equation we can estimate the average lifetime of the keto and enol forms to be at least 0.07 sec.

Triketones, such as cyclic  $\beta$ -triketones,<sup>15</sup> dehydroacetic acid,<sup>17</sup> diacetic and cinnamoyl acetoacetic esters<sup>16</sup> and usnic acid<sup>16</sup> were found to be completely enolized in solutions and to form intramolecular hydrogen bonds with unsymmetrical diketones, such as  $\alpha$ -formyl ketones, with various substituents, several enolic forms are possible, and there will also be a tautomerism between the two enol forms.<sup>6</sup>

The study of the temperature dependence of the chemical shifts and spin-spin coupling constants<sup>19,20,21</sup> in these compounds will give additional information on the energetics of the proton transfer in the enolic systems.

The large coupling constants observed between the hydrogen bonding proton and the other protons in Schiff Bases<sup>19,22</sup> provides strong evidence that the compounds exist exclusively in the enaminoketone forms:  $\left[ \begin{array}{c} \phi - N - H \cdots O \\ | \quad \quad \quad || \\ C = C - C \end{array} \right]$ . Similarly some  $\alpha$ -formyl ketones have been shown to exist in only one specific enol form.<sup>20</sup>

## B. Hydrogen Bond by N.M.R.

### 1. General Descriptions

The following definition is suggested for hydrogen bond by Pimentel and McClellan.<sup>2</sup>

"A hydrogen bond exists between a functional group A-H and an atom or a group of atoms B in the same or a different molecule when (a) there is evidence of bond formation (association or chelation), (b) there is evidence that this new bond linking A-H and B specifically involves the hydrogen atom already bonded to A." Or in other words, the hydrogen bond is the interaction which involves two functional groups in the same or different molecules. One of these groups must be a proton donor and the other an electron donor. Most commonly the proton is donated by a carboxyl, hydroxyl, amine, or amide groups to oxygen in carbonyls, ethers, and hydroxyls, to nitrogen in amines and in N-heterocyclic compounds, and to halogen atoms in particular molecular environments."

The strength of the hydrogen bond lies between that of chemical bonds and Van der Waals interactions, and the energy of breaking is the order of a few kilocalories.<sup>2</sup>

The formation of a hydrogen bond in a compound, either in solution or in the pure form, modifies a great many physical and a few chemical properties: molecular weight, shape, arrangement of atoms, frequency of I.R. and Raman bands, change of freezing point and boiling point, solubility, N.M.R. shift, etc...

The hydrogen bond can be detected fairly easily by

practically any physicochemical method. Other than spectroscopic studies, dielectric measurements and gas imperfections are the most frequently used to give the maximum information.

Together with N.M.R. spectroscopy, I.R. and Raman spectroscopy are excellent methods of detecting hydrogen bonds. Since the restraining forces are simply related to chemical bond orders, the vibrational spectra are significantly disturbed by hydrogen bond formation. Evidences for this are; frequency shift of OH peak, broadening of the peak by hydrogen bond formation; intensity change; and temperature, concentration, and solvent dependence of these changes.

Other spectroscopic studies such as U.V., visible, fluorescence, and nuclear quadrupole resonance spectroscopy also give information about the hydrogen bond.<sup>2</sup>

## 2. Hydrogen Bonding Involving OH by N.M.R.

When a proton experiences a different magnetic shielding by forming hydrogen bond, the chemical shift will vary from the unassociated state to associated state.

Marshall<sup>23</sup> gave a crude equation for the chemical shift of protons considering an intermolecular electric field E:

$$\delta = - \frac{881}{216} \frac{a^3 E^2}{mc^2}$$

where

$\delta$  = the chemical shift

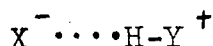
m = mass of the proton

c = velocity of light

a = the Bohr radius

According to this equation, an electric field of 0.14 atomic units, which would arise from a single electron at a distance of about 1.4 Å, gives a shift of 4 ppm.

In addition to its primarily electrostatic character, the hydrogen bond has some covalent character, such as:



and the donation of electrons from Y molecule into the  $X \cdots H$  bond leads to increased electron density on the hydrogen and a shift to high field. However, usually, the electrostatic character is more dominant and masks such effects, the result being that the observed chemical shifts are usually to lower field when a hydrogen bond is formed.<sup>1</sup>

The N.M.R. method is superior to the I.R. method in that it is more sensitive to frequency shift and that water may be used as a solvent. If the lifetime of the hydrogen bond is very short, we observe in the N.M.R. spectrum the time averaged chemical shift of associated and unassociated protons<sup>24,25</sup> instead of the two overlapping, different absorptions, as in the I.R. spectrum.

The changes in proton chemical shift in ammonia and water were first demonstrated by Ogg<sup>26,27</sup> by measuring the proton shifts in the liquid and gaseous states. A number of studies have also been done, on the association of alcohols and phenols.<sup>6,23,28,29,30,31,32,33,34,35,36,37,38</sup> Some of the results of dilution chemical shift measurements were correlated with the data obtained by the I.R. spectroscopy.<sup>29,35,36</sup>

Huggins, Pimentel and Shoolery<sup>29</sup> have studied the hydrogen bonding of phenol and substituted phenols. At the equilibrium of rapid exchange of monomer-dimer system, the following equation was applied to the observed chemical shift of OH proton.

$$\delta = \frac{x}{m} \delta_M + \frac{\frac{1}{2}(X - m)}{x} 2 \delta_D$$

where  $x$  = total moles of phenol

$m$  = moles of monomer

$\delta_M$  = chemical shift of monomer

$\delta_D$  = chemical shift of dimer

Knowing  $\delta_M$  and  $\delta_D$ , and measuring  $\delta$ , the equilibrium constants of the monomer-dimer system of phenol derivatives have been obtained.

The concentration dependence of OH shift in dilute solution was interpreted in terms of a dimer-monomer equilibrium and the following relation between the slope and the equilibrium constant was derived:

$$\left(\frac{d\delta}{dx}\right)_0 = 2K\Delta_D$$

where  $\left(\frac{d\delta}{dx}\right)_0$  = the limiting slope

$K$  = equilibrium constant

$$\Delta_D = \delta_D - \delta_M$$

## C. Proton Exchange

### 1. General Description

The shape and the width of N.M.R. signals are sensitive to



a time dependent process. For a slow process on the time scale of the Larmor frequency difference in distinct environments, spectra appear as separate lines for each environment. For rapid processes, the spectra are determined by the time average environment of the nuclei under investigation. When the lifetime in distinct sites is of the order ;

$$\sqrt{2}/2\pi(\nu_A - \nu_B) \times 10^{-2} < \tau < \sqrt{2}/2\pi(\nu_A - \nu_B) \times 10^{-1}$$

where  $(\nu_A - \nu_B)$  is the frequency difference in two sites, N.M.R. spectroscopy can be a valuable tool in quantitative rate investigations.

The Bloch equations,<sup>39</sup> which describe the appearance of a resonance signal, have been modified by Gutowsky<sup>40</sup> to obtain a quantitative relation between the line shape and the rapid exchange rate for a number of chemical systems. This method of solving the Bloch equations under the influence of chemical exchange has been extended<sup>41,42,43</sup> to a number of reaction-rate problems. McConnell<sup>44</sup> has generalized the Bloch equations to include the effect of chemical exchange and reduced the equations<sup>39,41,42,43</sup> to simple algebraic form. They considered a simple chemical exchange system in which a nucleus X is transferring back and forth between two molecular environments A and B. The components of the X nuclear magnetization were written as the sum of those in A and B systems.

$$u = U_A + U_B$$

$$v = V_A + V_B$$

$$M_x = M_x^A + M_x^B$$

where  $u$  = components in phase with the effective rotating component of the r.f. field

$v$  = component of out of phase with the above rotating r.f. field

$M_z$  = component in the direction of the large stationary field

Then the modified equations are:

$$\begin{aligned}\dot{U}_A + \Delta\omega_A V_A &= -U_A/T_{2A} + U_B/T_B \\ \dot{U}_B + \Delta\omega_B V_B &= -U_B/T_{2B} + U_A/T_A \\ \dot{V}_A - \Delta\omega_A U_A &= -V_A/T_{2A} + V_B/T_B - \omega_1 M_z^A \\ \dot{V}_B - \Delta\omega_B U_B &= -V_B/T_{2B} + V_A/T_A - \omega_1 M_z^B \\ \dot{M}_{zA} - \omega_1 V_A &= M_0^A/T_{1A} - M_z^A/T_{1A} + M_z^B/T_B \\ \dot{M}_{zB} - \omega_1 V_B &= M_0^B/T_{1B} - M_z^B/T_{1B} + M_z^A/T_A\end{aligned}$$

where

$\tau_A$  and  $\tau_B$  = the first order lifetimes of X in A and B

$M_0^A$  and  $M_0^B$  = equilibrium z magnetizations of X in A and B

$$\omega_1 = \gamma H$$

$$\frac{1}{\tau_{A(B)}} = \frac{1}{T_{1A(B)}} + \frac{1}{\tau_{A(B)}}$$

$$\frac{1}{\tau_{2A(B)}} = \frac{1}{T_{2A(B)}} + \frac{1}{\tau_{A(B)}}$$

$T_{1A}$  and  $T_{1B}$  = the longitudinal relaxation times of X in A and B

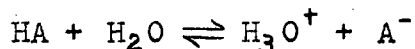
$T_{2A}$  and  $T_{2B}$  = the transverse relaxation times of X in A and B

The modified equations are easily solved in the slow passage case, with negligible r.f. saturation, and were used to show how

rapid exchange rates can be measured in solutions where the X relaxation times are relatively long in one system, A, and short in the other, B.

One example of a rate process which modifies the nuclear resonance spectrum is a system in which the individual nuclei are moving from one position to another. Some of the protons in a mixture of water and alcohol will be exchanging between water molecules and the hydroxyl position of the alcohol.<sup>45</sup> The proton exchange has been found to be greatly accelerated in the presence of strong acids or bases in this system. In aqueous solutions of mineral acids, a very rapid exchange occurs between the protons of acid and those of the solvent-water molecules, resulting in a single sharp proton signal.

Studies on dissociation equilibria in solutions of aqueous electrolytes have been done. Gutowsky and Saika<sup>41</sup> were the first to apply N.M.R. to dissociation and chemical exchange in some mineral acids and bases. Room temperature spectra of these acids show a single proton resonance peak whose chemical shift is an average for all species in solution. The equilibrium in aqueous solutions of these acids may be written as:



And the observed chemical shift is given by

$$\delta = x_1 \delta_{\text{H}_3\text{O}^+} + x_2 \delta_{\text{H}_2\text{O}}$$

where  $x_1$  and  $x_2$  are the fraction of protons in  $\text{H}_3\text{O}^+$  and  $\text{H}_2\text{O}$  respectively. The concentration dependence of the chemical shift is determined by the dissociation of the acid. A linear

relation has been found in dilute acid solutions between the chemical shift and the fraction of protons present as  $\text{H}_3\text{O}^+$ .<sup>25,41,46,47,48,49</sup> The slopes of the lines have been used to evaluate the dissociation constants of acids.<sup>41,46,47</sup>

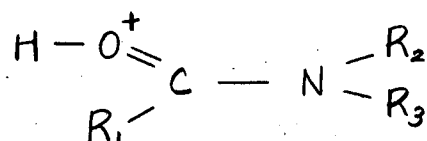
A similar study has also been done on trifluoroacetic acid as an example of a moderately strong acid.<sup>50</sup> The proton and fluorine resonances of the acid in different water concentrations show the influence of electrolytic dissociation if the acid mole fraction is below 0.5 and of hydration if it is above 0.5. The dissociation constant of the acid was estimated to be about 1.8. Hood and Reilly<sup>51</sup> have extended these investigations on the ionization of strong electrolytes to considering the temperature coefficients of dissociation of  $\text{HNO}_3$  and  $\text{HClO}_4$ . Grunwald, Loewenstein and Meiboom<sup>42</sup> have carefully studied the rates and mechanisms of protolysis of the methyl ammonium ion in aqueous solution. From the exchange broadening of the water signal they measured the mean lifetime of a proton on a water molecule. Therefore it is possible to estimate the fraction of protolysis that proceeds by proton transfer via water molecules compared to the direct proton transfer between methyl ammonium groups. Similar studies of the unsubstituted, dimethyl and trimethyl ammonium ion have also been investigated.<sup>52,53,54,55,56</sup>

## 2. Protonation by Strong Acids

Structure of the ion formed when compounds are protonated

has been the subject of discussion since Hantzsch<sup>57</sup> first presented evidence for oxygen protonation of benzamide in concentrated  $H_2SO_4$  from ultra violet absorption spectra studies. All this previous work has been summarized by Katritzky and Jones,<sup>58</sup> who concluded that amides are predominantly protonated at the oxygen atom.

The N.M.R. spectrum of pure liquid dimethyl formamide shows two peaks of equal area for the N-methyl groups.<sup>59,60</sup> It was concluded that the two methyl groups have different environments because of restricted rotation about the OC-NMe<sub>2</sub> bond. Frankel and Nieman<sup>61,62</sup> have shown that these two peaks remain unchanged in aqueous solutions of strong acids and in 100% H<sub>2</sub>O and 100% D<sub>2</sub>SO<sub>4</sub>. From this fact they concluded that the O-protonated form:



dominates in these strong acid solutions from the evidence that the protonated molecule is still restricted in rotation around OC-NMe<sub>2</sub> bond. Similar results have been obtained for N-methyl acetamide.<sup>63</sup>

The rate of exchange of the captured proton with the solvent has been slowed down sufficiently using fluorosulfuric acid,<sup>64,65</sup> which has the advantages of being a strong acid with a low freezing point of  $-89^{\circ}\text{C}$ , so that a separate signal for this proton could be observed in the spectra at low temperatures.

The protonation of pyridine has been studied by Smith and

Schneider.<sup>66</sup> They observed the signals of the proton bonded to nitrogen in the presence of excess trifluoroacetic acid. They found that the largest low field shift of ring protons occurs for the  $\gamma$ -proton, and that for the  $\beta$ -protons the low field shift is almost as large, while the corresponding shift for  $\alpha$ -proton is much smaller as a result of protonation. Assuming a simple proportionality between the resonance shift and the electron charge deficiency on the carbon and nitrogen atom to which the proton is bonded they estimated the local charge density in the pyridinium ion.

Danyluk and Schneider<sup>67,68</sup> have studied azulenes and their conjugate acids in trifluoroacetic acid. They confirmed that the protonation occurs at one position in every case and found the coupling constants between the methylene proton and the protons at two and three positions by first order analysis. They also found that the protonation of the azulenes brings about pronounced changes in the chemical shifts and coupling constants.

Protonation mechanisms involving simple benzene derivatives<sup>69,70</sup> have also been studied in  $\text{HF}/\text{BF}_3$  mixtures at low temperature. Structures of protonated purine and pyrimidine derivatives have also been studied in trifluoroacetic acid,<sup>71</sup> and the order of basicity was found to decrease as  $\text{N ring} > \text{N amino} > \text{oxygen}$ .

#### D. Carbon 13 - Proton Coupling

Although the ordinary carbon nuclei have no magnetic moment, the isotope carbon 13 which has the spin quantum number  $\frac{1}{2}$  and has a natural abundance of 1.1%. This abundance is sufficient to observe the coupling between  $C^{13}$  and protons. Many coupling constants have now been obtained.<sup>72,73,74,75,76,77</sup>

Lauterbur<sup>72</sup> demonstrated the possibility of observing the  $C^{13}$  resonance directly in natural abundance.  $C^{13}$  coupling constants are related to s character<sup>73,74,75,78,79,80,81</sup> and are also sensitive to electronegativity of the substituents on the carbon.  $Sp^3$  hybridization at the carbon which has 25% s character in each bond, gives a  $J C^{13} - H^1$  approximately 120 cps,  $sp^2$  gives  $\sim 160$  cps and  $sp$ ,  $\sim 240$  cps. From the studies of  $J C^{13} - H^1$  in substituted methanes an interpretation has been given that the distribution of s character among the carbon orbitals of the four substituents lead to an additivity relation based on the assumption that the total s character is conserved.<sup>78,82</sup>

Gutowsky gave the equation shown below:

$$J_{CH}(CHXYZ) = J_{CH}(CH_3X) + J_{CH}(CH_3Y) + J_{CH}(CH_3Z) - 2J_{CH}(CH_4)$$

The  $C^{13} - H^1$  multiplets have been effectively used to obtain the spin-spin coupling constants between equivalent hydrogen atoms<sup>83,84</sup> which are not normally observed.

The long-range coupling between protons and carbon has also been observed in compounds containing a natural abundance of  $C^{13}$  and in enriched compounds,<sup>85,86,87,88</sup> and the linear relationship between the percentage s character of  $C^{13}$  atomic orbital and

$J_{C^{13}-C-H}$  has been found.<sup>87</sup> For the longer range coupling constant ( $J_{C^{13}-C-H}$ ) a linear relationship to  $J_{H-C-C-H}$  has been found. This indicates an analogy with the conformational dependence of  $J_{H-C-C-H}$  vicinal coupling constants.<sup>89</sup>



## II. OBJECT OF THE PRESENT STUDY

### A. Keto-Enol Tautomerism of Cyclic 1,3 Diones

Cyclohexane 1,3 dione and 5,5' dimethyl cyclohexane 1,3 dione have been shown by I.R.<sup>90,91</sup> and U.V.<sup>92</sup> measurements to exist almost entirely in the enol form both in solid and in concentrated solutions. From the structural considerations of the cyclohexane ring, the molecules must exist mostly in the hydrogen bonded dimer form when they are enolized.

Polarity and some other solvent properties have also been shown to affect the position of keto-enol equilibrium.<sup>92</sup> For example, cyclohexane 1,3 dione has been found to associate with the solvent molecule in dioxane by I.R. measurements.<sup>90</sup>

The present study is mainly concerned with the tautomeric study of cyclohexane 1,3 diones in chloroform and acetonitrile by N.M.R. measurements which have the advantages of distinct signals for both tautomers and of sensitivity of proton chemical shift change to formation of hydrogen bonds.

### B. Protonation of Pyridines

N.M.R. spectra of some methyl substituted pyridines<sup>93,94,95,96,97,98,99</sup> and pyridine itself<sup>100</sup> have been analyzed and proton chemical shifts and coupling constants have been obtained. Methyl groups do not appreciably affect the chemical shifts and coupling constants in the aromatic ring.<sup>94,98,99</sup> The strong solvent dependence of ring proton chemical shifts in heterocyclic compounds have been studied<sup>101</sup> and the  $\beta$ -proton chemical

shift is the most sensitive to solvent change. The solvent dependence of methyl protons has also been studied.<sup>102</sup>

In the present study an investigation of the effect of protonation on chemical shifts and coupling constants in methyl pyridines has been made.

### III. EXPERIMENTAL

#### A. Preparation of Samples

Commercially available cyclohexane 1,3 dione, 5,5' dimethyl cyclohexane 1,3 dione, and cyclohexane 1,4 dione (L.Light & Co., Ltd.; Eastman Organic Chemicals) were purified by recrystallization from benzene. Spectroscopic grade chloroform was, one day before use, shaken with concentrated sulfuric acid, washed with distilled water, and fractionally distilled in order to remove ethanol. It was kept over  $\text{CaCl}_2$  in a dark place. Reagent grade acetonitrile was fractionally distilled and kept over  $\text{CaCl}_2$ . All the commercially available pyridines (K&K Laboratories Inc.) of reagent grade were fractionally distilled from over  $\text{BaO}$ , which had been baked twenty-four hours under vacuum, onto  $\text{BaO}$  and kept under refrigeration and in a nitrogen atmosphere. Trifluoroacetic acid was purified by fractional distillation immediately before use and a few drops of trifluoroacetic anhydride were added to remove the trace of water. Reagent grade carbon tetrachloride was fractionally distilled and kept over  $\text{CaCl}_2$ . All the other solvents were reagent grade and used without further purification.

All solutions for both keto-enol study and protonation study were prepared by weighing out into small vials and sealed in 5 mm O.D. N.M.R. tubes after thoroughly degassing by freezing with liquid nitrogen under vacuum.

A small amount of magnesium perchlorate for the chloroform

solutions, and sodium sulfate for acetonitrile solutions were added to keep the solutions dry throughout the measurements.

#### B. Measurements

Varian A-60 N.M.R. Spectrometer was used for all measurements. For chemical shift and coupling constant measurements, accurate calibrations were obtained by using a Hewlett-Packard Wide Range Audio Oscillator externally connected to a model 522B Electronic Frequency Counter and to the A-60 Spectrometer.

For high temperature regulation, a V-6057 Variable Temperature Instrument was attached to the A-60. The temperatures were calibrated from the separation of ethylene glycol signals.

For the reference standard, a small amount of internal tetramethylsilane (T.M.S.) was used for chloroform, acetonitrile, and carbon tetrachloride solutions, and external T.M.S. in carbontetrachloride was used for acid solutions. The corrections for volume diamagnetic susceptibility were made afterwards.

To obtain the ratio of keto to enol, the signals (see Table 1) were swept at the slowest rate (500 sec/50 cm), on the narrowest width (50 cps/50 cm), and with the spectrum amplitude not exceeding the linear response region of the instrument. The absorption signals were integrated by carefully tracing the signals onto good quality bond paper and then weighing the cut-outs of these tracings.

Table 1

## The Signals Used for the Analysis

1,3 cyclohexane dione in  $\text{CHCl}_3$ 

$$\left\{ \begin{array}{l} \text{keto: } \text{CH}_2 \text{ between the carbonyls} \\ \text{enol: } \text{OH} \end{array} \right.$$
1,3 cyclohexane dione in  $\text{CH}_3\text{CN}$ 

$$\left\{ \begin{array}{l} \text{keto: } \text{CH}_2 \text{ between the carbonyls} \\ \text{enol: } \text{olefinic proton} \end{array} \right.$$

5,5' dimethyl cyclohexane 1,3 dione

4 and 6  $\text{CH}_2$  signals for both the keto and the enol.

The volume susceptibilities were corrected by applying the method, proposed by Bernstein,<sup>48</sup> as follows: A tube with a sphere of about 2.5 mm in diameter and a cylindrical capillary which contain cyclohexane were inserted in an ordinary N.M.R. tube as shown in Figure 1, and the outer tube was filled with solvents of which magnetic susceptibilities were required. From the separation of the two signals, which is linearly dependent on the volume susceptibility of the sample contained in the tube, as expressed by the following equation:

$$\delta_{\text{cyl(ref)}} - \delta_{\text{sph(ref)}} = [\rho_{\text{cyl}} - \rho_{\text{sph}}][\chi_v(\text{ref}) - \chi_v(\text{sample})]$$

The volume susceptibilities were obtained for acid solutions of pyridines.

where  $\delta$  = chemical shift in ppm

$\chi_v$  = volume susceptibility in cgs units

$\mathcal{G}$  = geometrical constant depending on the shape of the common interface of reference and surrounding sample tube. This constant was determined by calibration using such solvent whose susceptibilities are known and the value of 2.7 was obtained for  $(\mathcal{G}_{\text{cyl}} - \mathcal{G}_{\text{sph}})$ .

$\text{C}^{13}$  - $\text{H}^1$  coupled multiplets in dilute solutions were detected by sweeping slowly, with high gain and lowest noise damping, several times and varying the spinning rate of the samples. The sweep width was 250 cps per 50 cm.

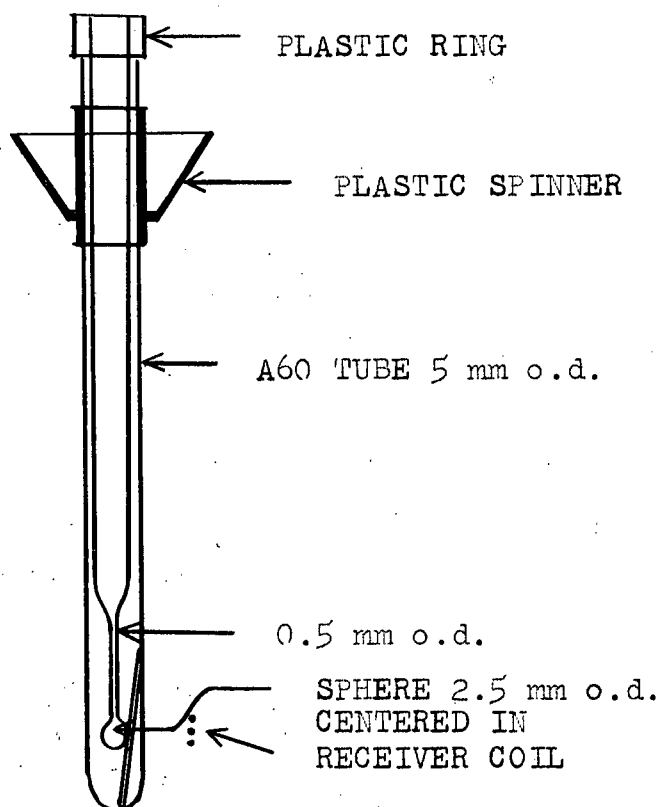


FIGURE 1

Sample Tube Containing a Cylindrical and a Spherical Reference Tube

#### IV. RESULTS

##### A. Keto-Enol Tautomerism of Cyclic 1,3 Diones

###### 1. Cyclohexane 1,3 Dione in Chloroform

The solubility limit in chloroform was found to be approximately 16 mole %. Figure 2 shows a spectrum of cyclohexane 1,3 dione in chloroform at a concentration of 16.0 mole %.

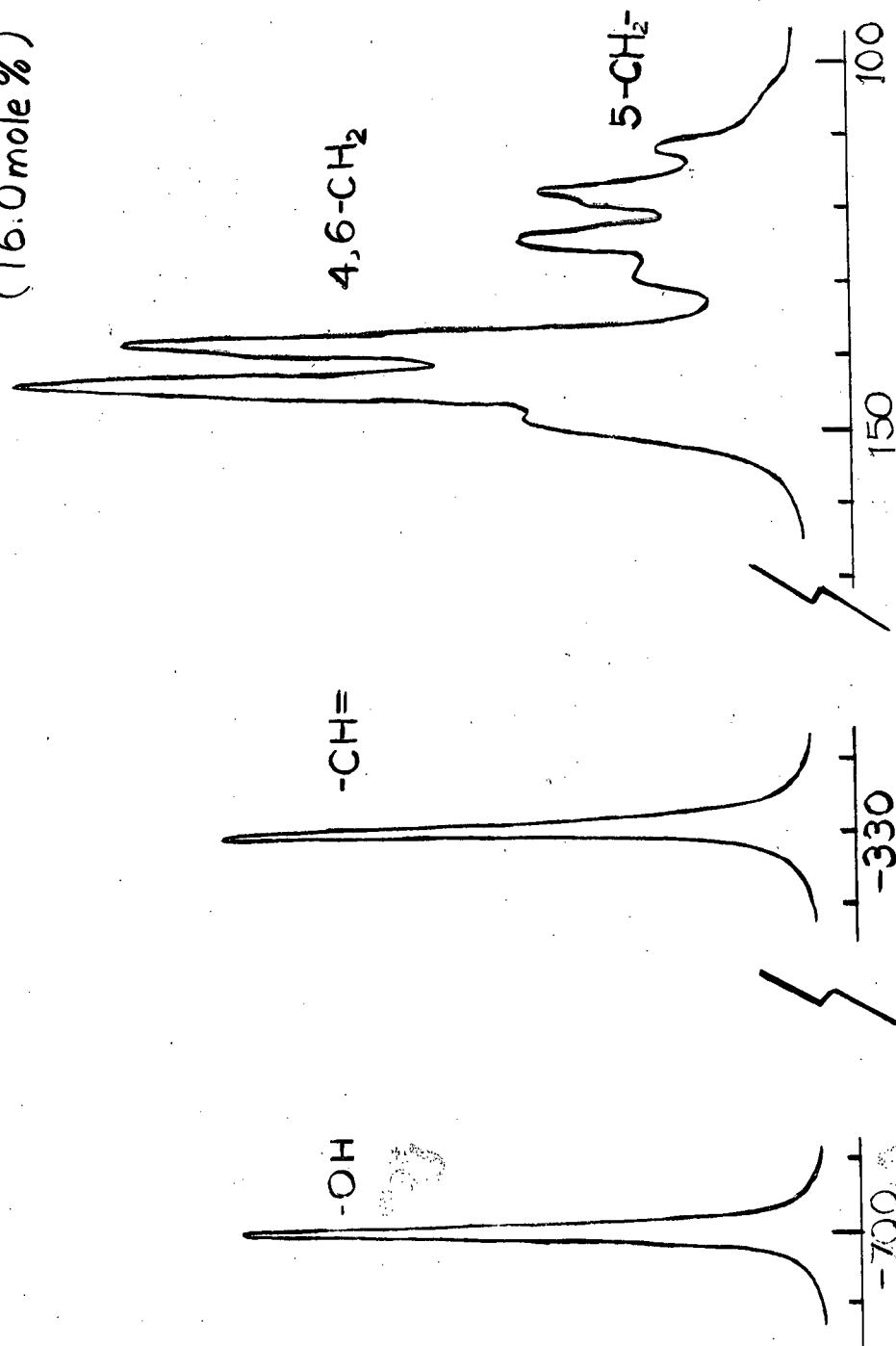
Apart from the solvent signal, there were observed two peaks, each of unit intensity, at -703 cps and -329 cps respectively; and a complex series of signals at high field between -110 and -155 cps with respect to T.M.S. with total intensity six. As the concentration was decreased, there appeared, as is shown in Figure 3, a new peak at -205 cps. The low field signal, circa -703 cps was found to be concentration dependent, shifting to high field on dilution. This was not found to be so for the other signals. The concentration dependence of the chemical shift of this signal is shown in Figure 4.

The concentration dependence of this signal indicated the presence of a hydrogen bond and the signal ca. -703 cps was assigned to the OH-proton. The signal at -329 cps, in a region where olefinic protons are usually found, was assigned to the olefinic proton in the enol form. The intensity of this signal was the same as that of OH proton signal. The signal which was found only in dilute solution at -196 cps was assigned to the methylene proton between the two carbonyl groups in the keto form. This signal was not found in either hydrochloric acid or

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FIGURE 2

Spectrum of Cyclohexane 1,3 dione in  $\text{CHCl}_3$   
(16.0 mole %)

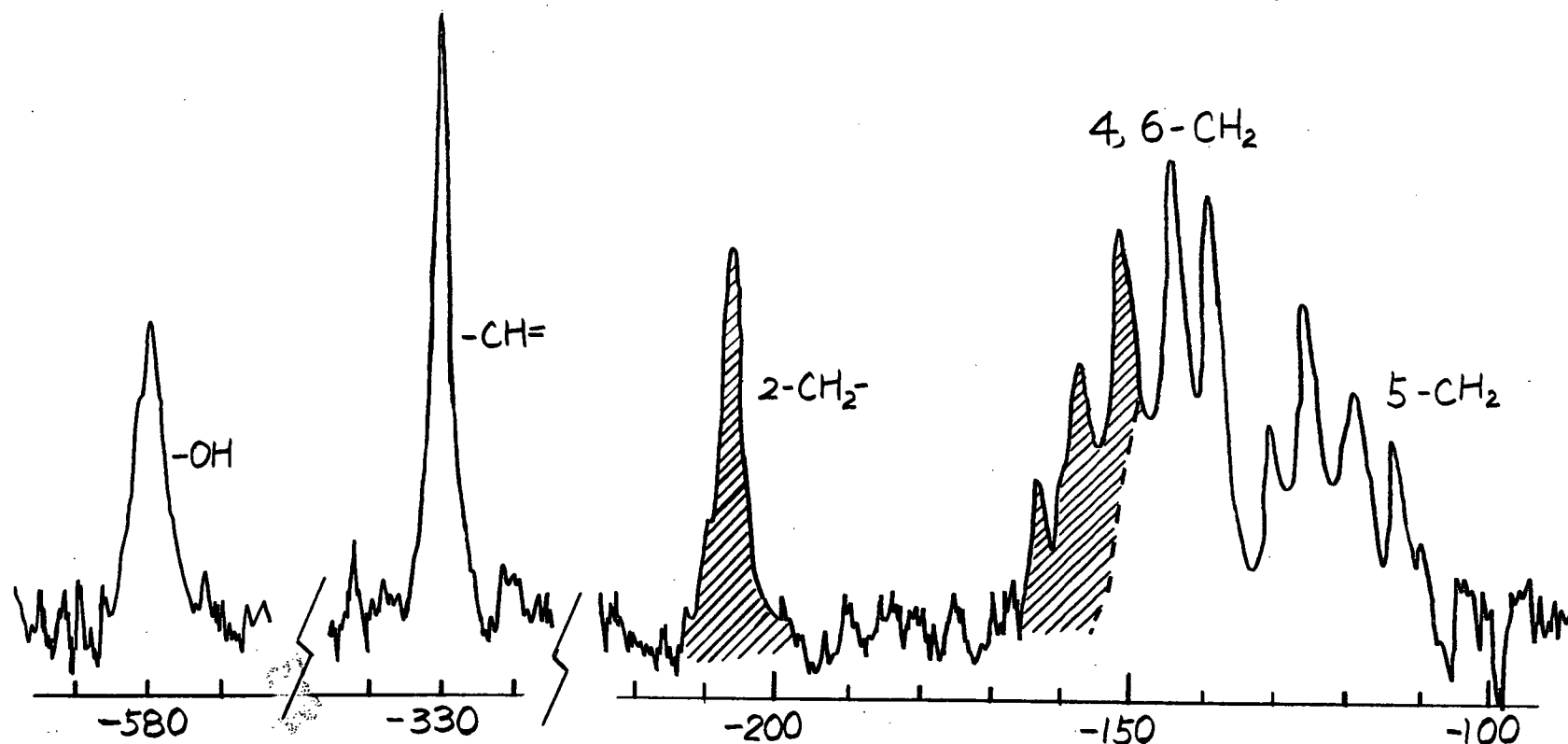




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# FIGURE 3

Cyclohexane 1,3 dione in  $\text{CHCl}_3$  1.05 mole %



CHEMICAL SHIFT cps from T.M.S. at 60 M.c.

TO FOLLOW PAGE 22

FIGURE 4

Change of OH-Proton Chemical Shift with Concentration.

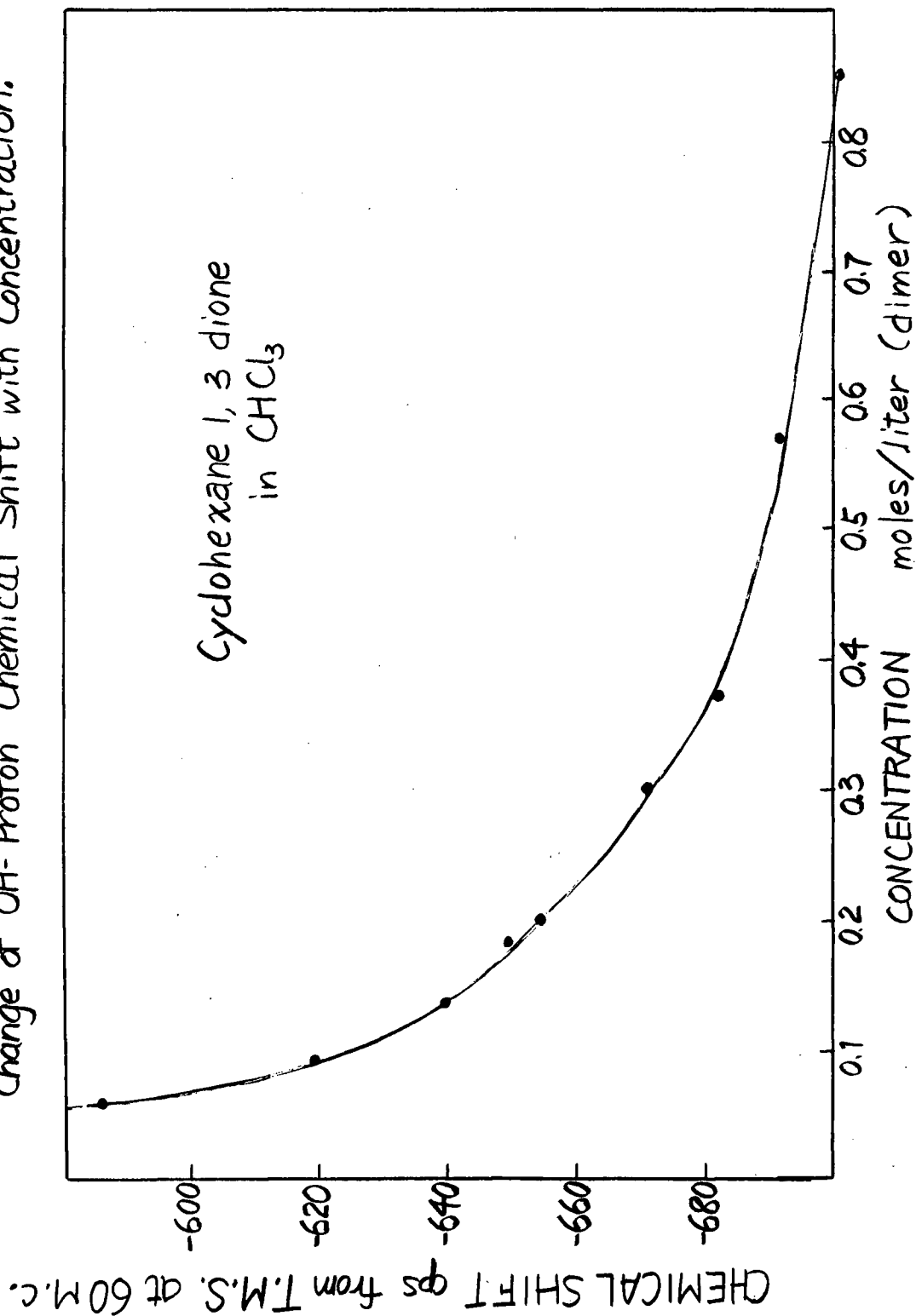


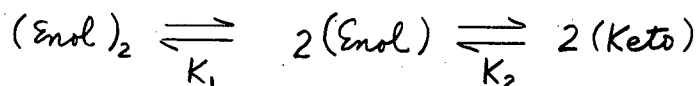
Table 2

## Cyclohexane 1,3 Dione in Chloroform

C	R	C <sub>D</sub>	obs <sup>***</sup>	$\alpha$	C <sub>M</sub>	2(C-C <sub>D</sub> )	K <sub>1</sub>	K <sub>2</sub>
(x10)		(x10)			(x10 <sup>3</sup> )	(x10 <sup>3</sup> )	(x10 <sup>3</sup> )	
0.75	0.905	0.494	602	0.460	4.54	5.11	7.80	1.13
0.77	0.800	0.473	605	0.450	4.25	5.9	7.00	1.40
0.92	1.10	0.632	616	0.414	5.24	6.0	7.44	1.14
1.18	1.42	0.870	631	0.363	6.31	6.2	7.24	0.983
1.34	1.96	1.05	635	0.350	7.35	6.0	7.88	0.818
1.40	2.02	1.12	640	0.333	7.47	5.6	7.44	0.750
1.85	2.81	1.57	654	0.286	8.98	5.6	7.28	0.625
2.05	3.90	1.82	657	0.277	10.1	4.6	7.72	0.455
2.71	4.05	2.39	669	0.237	11.3	6.4	7.04	0.565
3.03	4.69	2.74	673	0.224	12.3	5.8	7.04	0.472
3.10	4.53	2.79	675	0.217	12.1	6.2	6.76	0.513
3.72	5.86	3.43	679	0.203	13.9	5.8	<u>7.12</u>	0.418

Average  $7.31 \times 10^{-2}$ 

C = Concentration in unit of moles per liter

 $\delta$  = Chemical shift in unit of cps from T.M.S. at 60 M.C.

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# FIGURE 5

-OH Proton Chemical Shift of  
Cyclohexane 1,3 dione in Chloroform

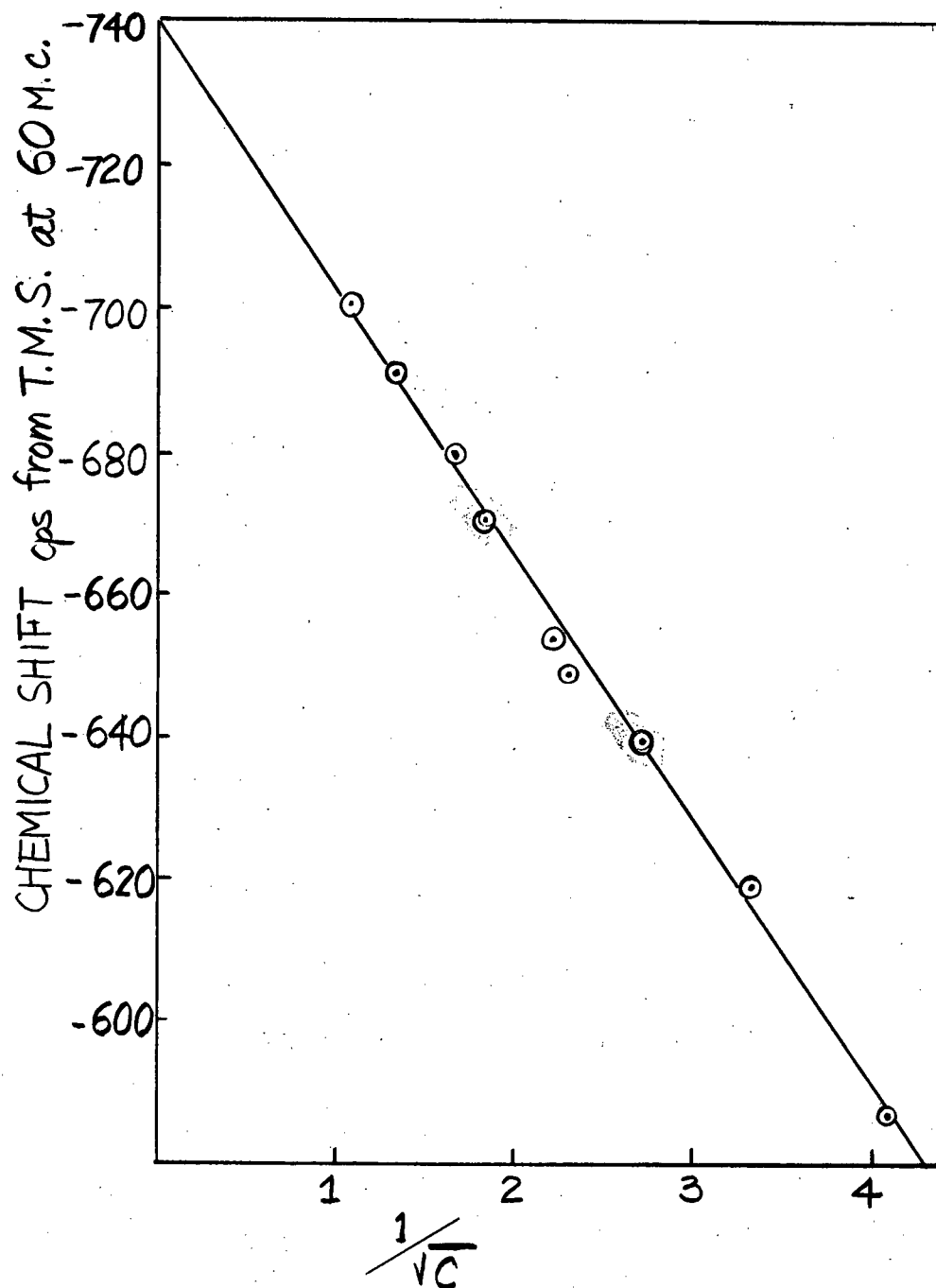


Table 3

## Cyclohexane 1,3 Dione in Chloroform at High Temperatures

0.235 mole/liter as units of dimer

<u>T(°K)</u>	<u>1/T ( x 10<sup>3</sup> )</u>	<u>R</u>	<u>K(mol/l) ( x 10<sup>-2</sup> )</u>	<u>log K</u>
302	3.31	3.30	1.88	-1.726
317	3.15	2.40	3.36	-1.474
328	3.05	1.64	6.73	-1.172
335	2.98	1.43	8.30	-1.081
348	2.87	0.87	19.7	-0.706
357	2.80	0.58	28.6	-0.544

K: overall equilibrium constant (mole/liter)

$$\Delta H \approx -RT \ln K = -\frac{RT}{2.303} \log K$$

$$\Delta H \approx 2.05 \text{ Kcal/mole}$$

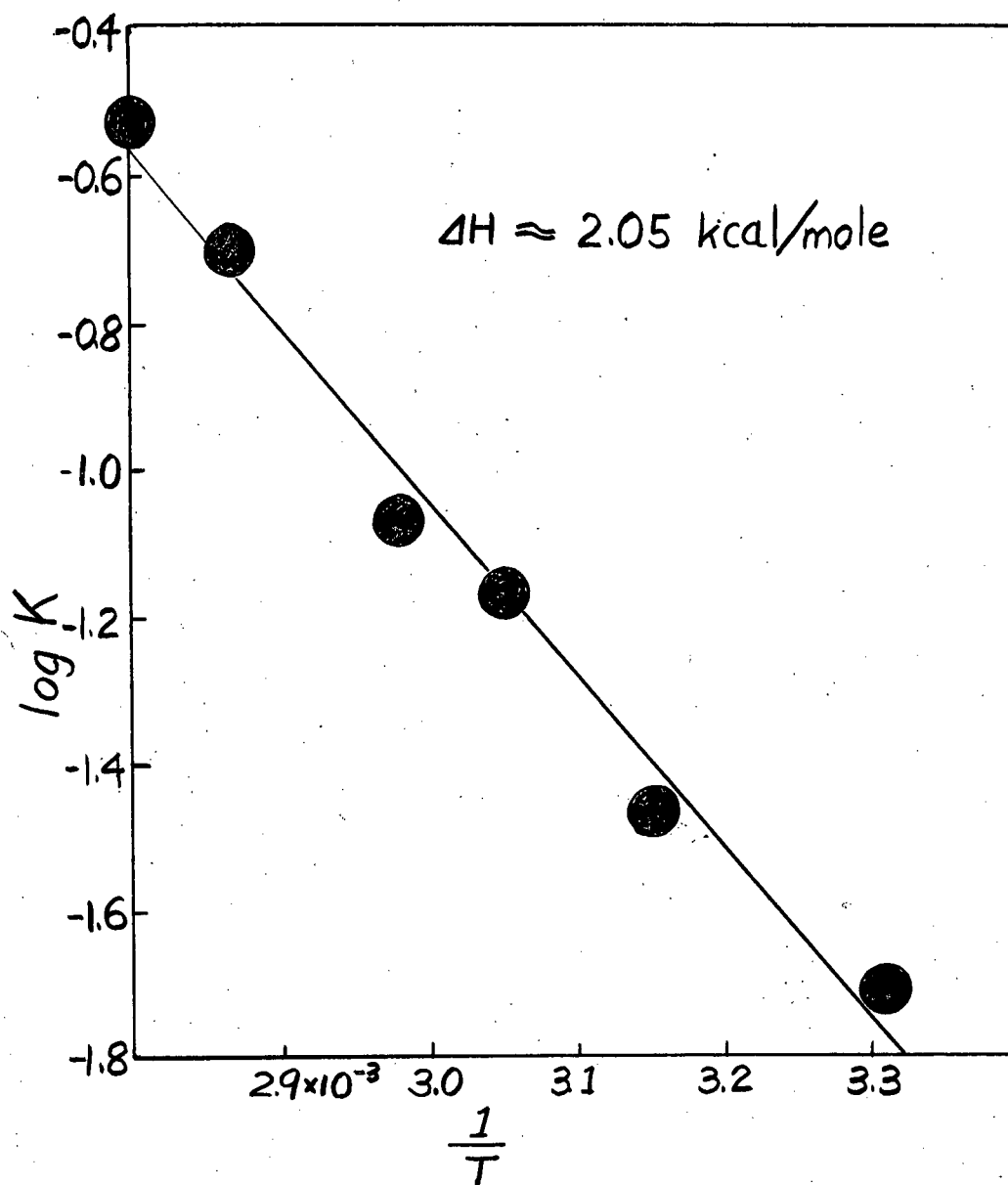
pyridine with both concentrated and dilute solutions.

The set of peaks lying between -110 and -155 cps arise from the protons at the 4,5 and 6 positions on the ring. By comparing the sets of peaks at high and low concentrations, the shaded peaks arise from the signals from the keto form. Spectra of a solution of 0.235 moles/liter dimer in chloroform were taken at temperatures between 302°K and 357°K.

All the results are shown in Table 2 and 3.

TO FOLLOW PAGE 24  
FIGURE 6

Cyclohexane 1,3 dione in  $\text{CHCl}_3$   
at various temperatures



## 2. Cyclohexane, 1,3 Dione in Acetonitrile

The acetonitrile peak overlaps the broad region of peaks at high field. However, even though the solubility limit is much less than in chloroform, the presence of the keto form was evident showing a signal at -317 cps. The position of this signal was noticeably shifted to higher field from that in chloroform, and was also concentration dependent. The keto 2-C methylene signal has a chemical shift of -201 cps compared to -205 cps in chloroform but the OH signal appeared somewhat broadened and was strongly concentration dependent. The results which were obtained from the ratio of the signals are shown in Table 4.

## 3. 5,5' Dimethyl Cyclohexane 1,3 Dione in Chloroform

This compound is less soluble than cyclohexane 1,3 dione thus placing an upper limit on the concentration dependence studies. The spectrum consisted of signals circa -60, -63, -133, -150, -198, -230 cps, and another peak, whose position varied with concentration, at lower field. The relative intensities of the signals lead to the following assignment:

keto form:	enol-form:
{ methyl      - 60 cps	{ methyl      - 63 cps
{ 4,6 ring    -150 cps	{ 4,6 ring    -133 cps
{ 2 ring      -198 cps	{ olefinic    -230 cps
	{ OH          lower field

OH peak was somewhat broad and concentration dependent. The results obtained from the ratio of keto and enol form by comparison of 4,6 ring proton peak are shown in Table 5.

Table 4

## Cyclohexane 1,3 Dione in Acetonitrile

C	R	C <sub>M</sub>	C <sub>D</sub>	K
( x 10)		( x 10)	( x 10)	( x 10)
0.62	0.568	0.29	0.33	1.02
0.95	0.699	0.38	0.57	1.01
1.37	0.951	0.47	0.90	0.988
1.56	0.944	0.54	1.02	1.14
2.11	1.062	0.68	1.43	1.28

K: overall equilibrium constant (moles/liter)

Concentrations in unit of moles/liter dimer

Table 5

## 5,5' Dimethyl Cyclohexane 1,3 Dione in Chloroform

C	R	C <sub>D</sub>	C <sub>M</sub>	K
0.57	0.222	1.7 x 10 <sup>-2</sup>	4.0 x 10 <sup>-2</sup>	9.17 x 10 <sup>-2</sup>
0.63	0.235	2.0 "	4.3 "	9.15 "
0.67	0.334	2.7 "	4.0 "	5.96 "
0.82	0.436	3.8 "	4.4 "	5.15 "
0.87	0.426	4.1 "	4.6 "	5.25 "

K: overall equilibrium constant

Concentrations in unit of moles/liter dimer

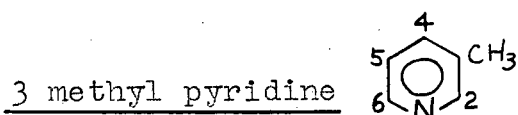


## B. Protonation on Pyridines

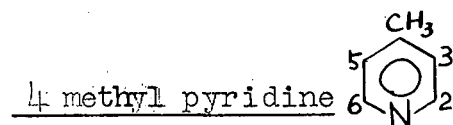
### 1. Change of Spectra on Protonation

All the chemical shifts and the coupling constants in unprotonated and protonated methyl pyridines are shown in Table 6 and 7. Almost all the signals shifted to lower field in the protonated species. The largest low-field shift occurred for the  $\gamma$ -protons, that for the  $\beta$ -protons is almost as large, while that for  $\alpha$ -protons was much smaller. This is similar to results obtained for unsubstituted pyridine.<sup>66</sup> The low-field shift of methyl protons seems independent of the position at which the methyl group is located.

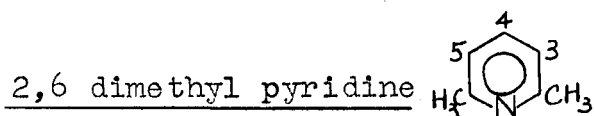
The coupling constants between ring protons obtained from first order analysis are found to increase in protonation.



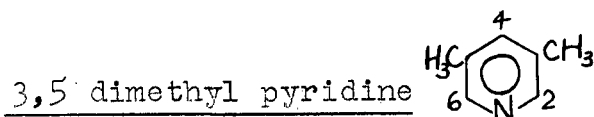
The proton resonance spectrum of 3 methyl pyridine consists of three groups of signals which correspond to the methyl, 2,6 ring, and 4,5 ring protons. The  $\gamma$ -proton signal was found to high field of the  $\alpha$ -proton signal. They were analyzed as ABXY spectrum by first order approximation. On protonation, the chemical shift between the 2,6 ring protons and 4,5 ring protons decreased. Coupling constants between the ring protons were also obtained together with the one between the  $\gamma$ -proton and the methyl protons. The largest change in coupling constant on protonation was found for that between the protons at positions 5 and 6.



The Figure 7 shows the P.M.R. spectra for 8.3 mole percent of the compound in carbontetrachloride, and 5.8 mole percent in trifluoroacetic acid. The spectra were easily analyzed and the coupling constants between the ring protons, and between the methyl protons and the  $\beta$ -proton were found. The latter constant could not be obtained for the protonated species. The chemical shift between the  $\alpha$ - and  $\beta$ -protons decreased on protonation; and the  $\alpha$ -proton signal showed further splitting by coupling from the proton bonded to the nitrogen, giving approximately a triplet, the coupling constant being almost equal to  $J_{2-3}$ .



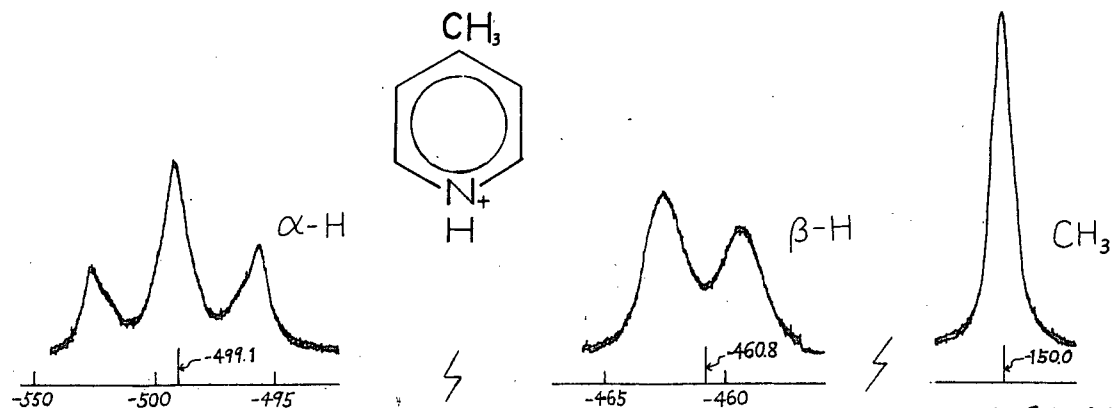
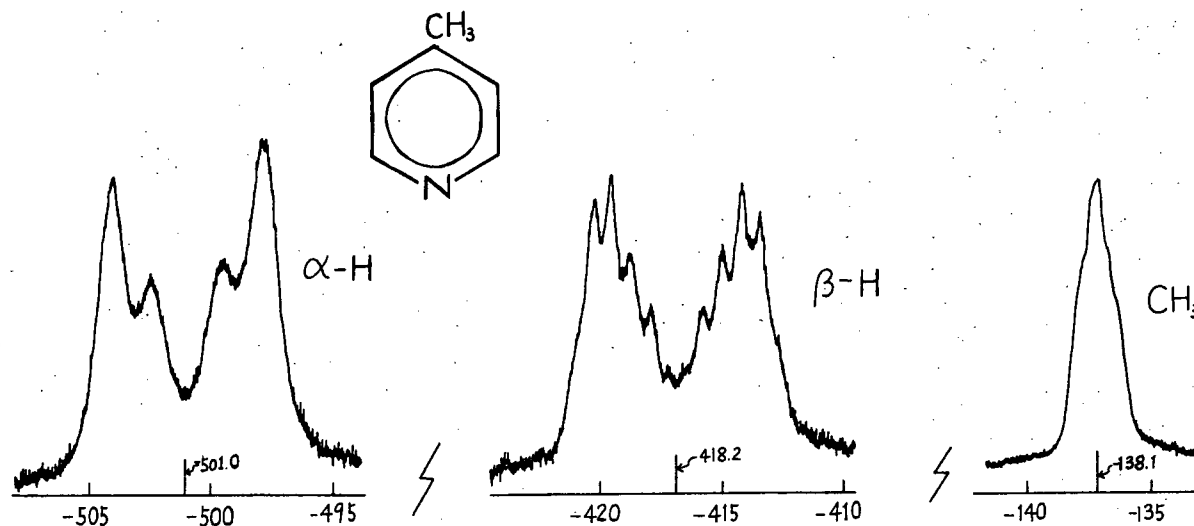
The ring protons showed a typical  $AB_2$  spectrum consisting of two groups of signals which approximately appeared as a quartet and doublet corresponding to the  $\gamma$ - and  $\beta$ -protons respectively. The spectrum was analyzed from relative spacings of the lines using the diagram of an  $AB_2$  case constructed from the available values.<sup>1</sup> All the resonance positions were shifted to low field by protonation without significant change in relative signal shape.



The ring proton signals showed two separate, slightly

# FIGURE 7

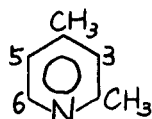
Spectra of 4 Methyl Pyridine + Its Cation



cps from T.M.S. at 60 M.C.

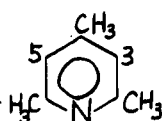
broadened signals, due to coupling from the methyl protons. As the concentration of acid was increased, the  $\alpha$ -proton signal was split into a doublet by coupling from the proton bonded to the nitrogen atom. One of the doublet peaks was completely overlapped by the  $\beta$ -proton singlet (Figure 8). The coupling constants from the methyl protons to the ring protons were found to be approximately the same for all cases ( $\sim 0.7$  cps) of unprotonated species.

2,4 dimethyl pyridine



The signal of the 3 and 5 ring protons showed almost the same chemical shift both at higher field than the one for the 6 proton. The signal of the 5 proton showed a doublet by coupling to the 6 proton. On protonation the spectrum of  $\beta$ -protons remained almost the same, while the proton signal showed further splitting by coupling from the proton bonded to nitrogen.

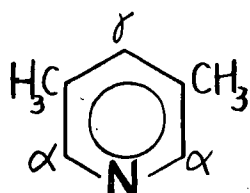
2,4,6 trimethyl pyridine



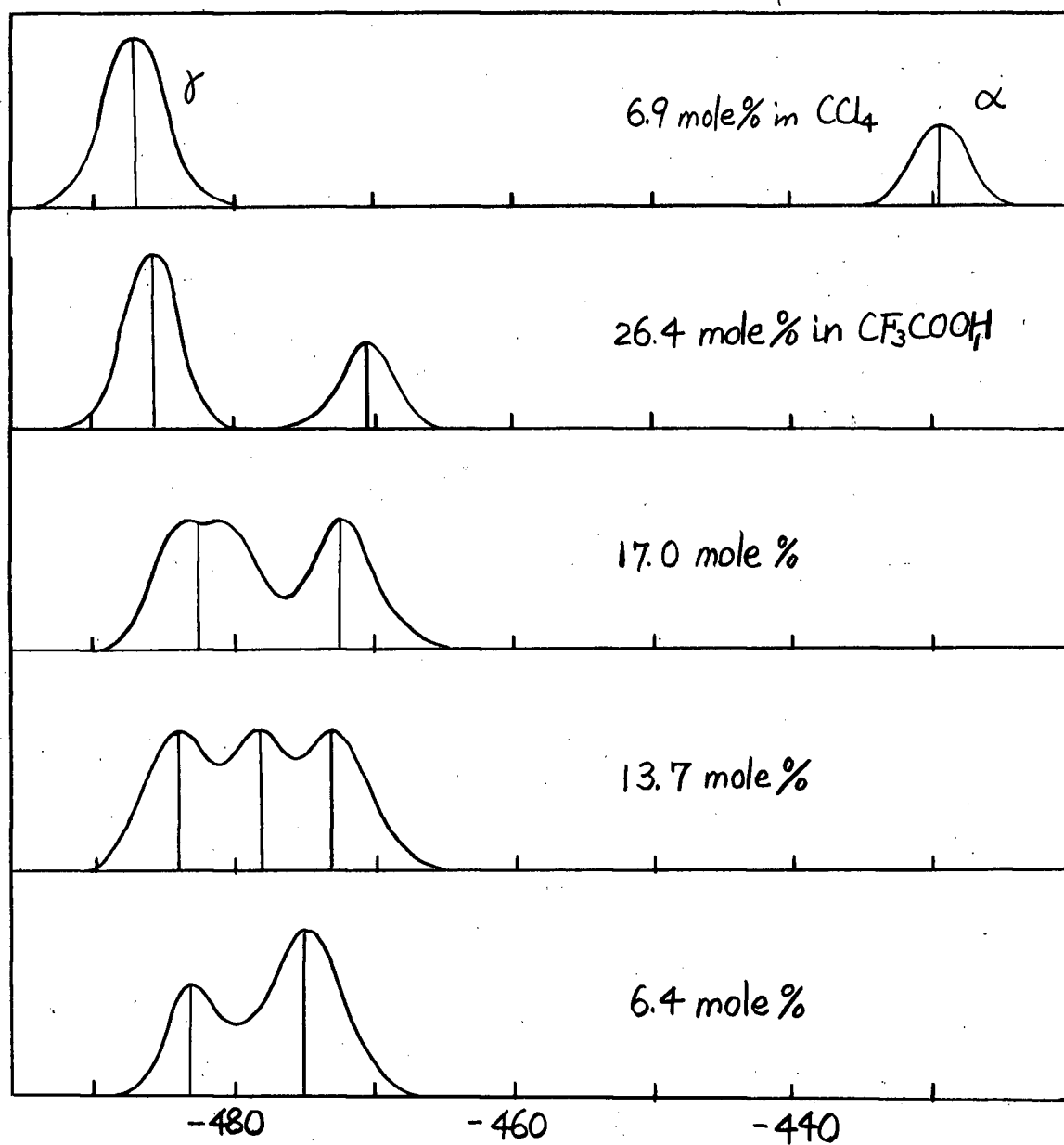
The spectrum showed three singlets corresponding to the methyl protons, at the two different position, and to the  $\beta$ -ring protons. The  $\beta$ -proton signal was broadened (half width  $\sim 4.5$  cps) because of coupling to both methyl protons. No coupling was found at all both in carbontetrachloride and in trifluoroacetic acid. The whole spectrum was chemically shifted by protonation, the individual structure remaining unchanged.

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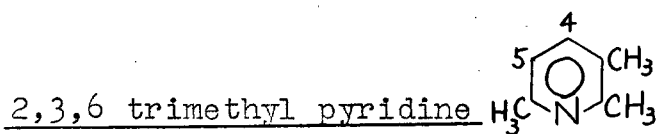
## FIGURE 8



Ring Proton Spectra of 3,5 Dimethyl Pyridine  
at Various Acid Concentrations



CHEMICAL SHIFT cps from T.M.S. at 60 M.c.



The two methyl protons at positions 2 and 6 showed the same chemical shift in carbontetrachloride about 10 cps to low field of the one at the  $\beta$ -position; although the pure compound showed two separate signals. The ring protons showed an AB spectrum consisting of two identical doublets. On protonation the  $\beta$ -proton signal was broadened to about 4 cps (half width).

## 2. Concentration Dependence of Chemical Shifts and Coupling Constants

For 4 methyl pyridine and 2,6 dimethyl pyridine the spectra at different acid concentrations were taken and the changes in chemical shift and coupling constant with varying acid concentration were obtained. Some of the compounds showed only small chemical shift and coupling constant changes at different concentrations, while the others showed appreciable dependence. The slopes of the chemical shift versus concentrations were found to almost identical for the  $\beta$ -protons in both, the  $\alpha$ -proton in the former, the  $\gamma$ -proton in the latter, and for the methyl protons at the  $\gamma$ - and  $\alpha$ -positions.

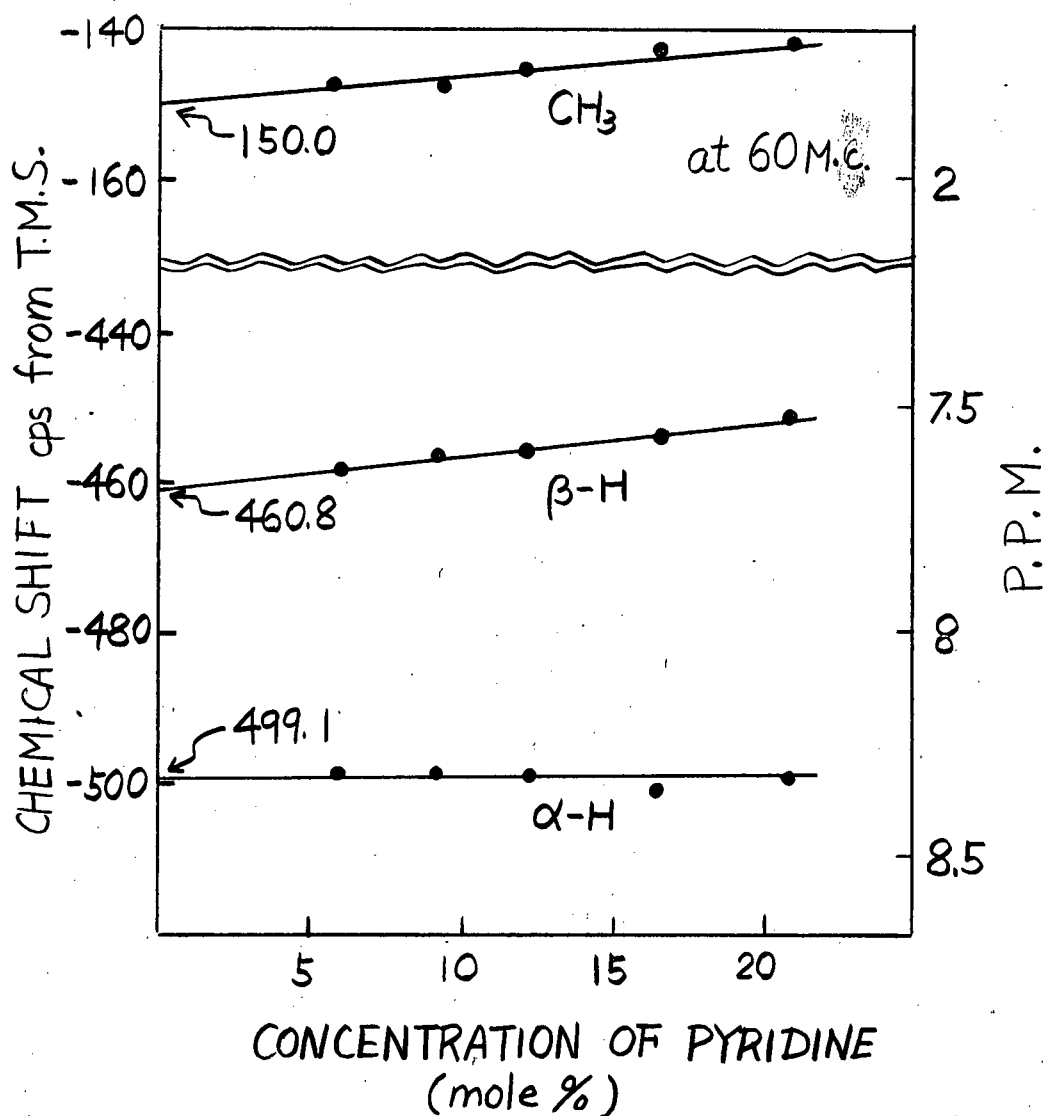
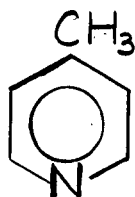
### 4 methyl pyridine

As shown in Figure 9, the  $\alpha$ -proton shift showed almost no concentration dependence, while the  $\beta$ -proton and the  $\gamma$ -methyl

TO FOLLOW PAGE 30

## FIGURE 9

Change of Chemical Shift  
with Concentration



proton signals shifted towards lower field almost linearly as the acid concentration increased giving  $\delta_{\alpha-H} = -499.1$  cps,  $\delta_{\beta-H} = -460.8$  cps,  $\delta_{CH_3} = -150.0$  cps at the infinite dilution with respect to T.M.S. The coupling constants between the  $\alpha$ - and  $\beta$ -protons and between the proton bonded to nitrogen and the  $\alpha$ -proton were found to be invariant with the concentration in the range of mole percent pyridine concentration from 5.8 to 21.4 and 5.8 to 12.3 respectively. With the higher pyridine concentration than 12.3 mole percent, the coupling constant between the  $\alpha$ -proton and the proton bonded to nitrogen was not observed.

#### 2,6 dimethyl pyridine

The chemical shift of the  $\gamma$ -proton is almost invariant, that of the  $\alpha$ -methyl proton is slightly dependent, and that of the  $\beta$ -protons showed twice as much variation as the  $\alpha$ -methyl proton. The slope of the  $\beta$ -proton was found almost the same as that in 4 methyl pyridine. The coupling constant between the  $\beta$ - and  $\gamma$ -protons was also unchanged.

#### 3,5 dimethyl pyridine

The coupling constant between the proton bonded to nitrogen and the ring protons varied as shown in Figure 10, suddenly decreasing from the pyridine concentration of 14 mole percent.

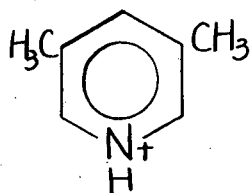
### 3. Signal of Proton Bonded to Nitrogen

As the acid concentration was increased, the broad signal

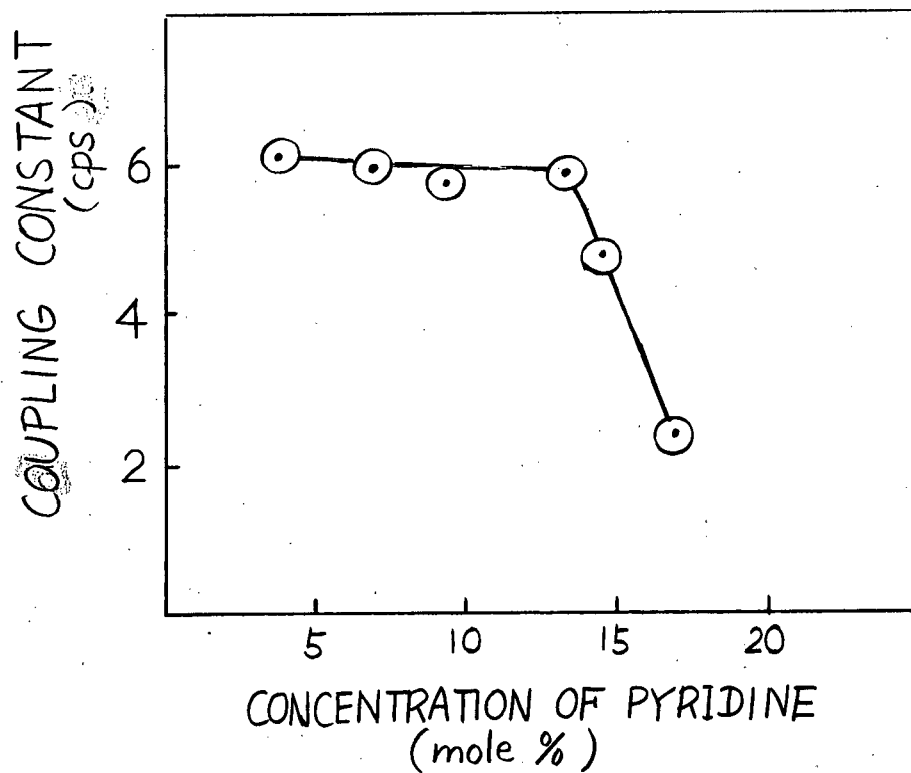


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## FIGURE 10



Change of  $J_{NH^+-\alpha-H}$  with  
Concentration



of the carboxyl group of the trifluoroacetic acid became sharper and moved toward higher field. In the presence of a large excess of acid, it has been possible, with a very high spectrum amplitude, to observe a triplet signal, characteristic of a proton bonded to nitrogen, within 100 cps to low field of the acid signal. The typical triplet is reproduced in Figure 11. This confirms the presence of the pyridinium ion. (The triplet arises from spin coupling with the  $N^{14}$  nucleus, which has a spin quantum number 1). The concentrations at which those signals were observed were about 6 ~ 8 mole percent of base. With lower acid concentrations the signals could not be observed probably because of their short lifetimes on the nitrogen atom; and with higher concentrations the signals were not observable. The high field triplet peak was not seen well because it was located at the foot of the large trifluoroacetic acid signal. The coupling constant between nitrogen  $14$  and the attached proton was found from the direct separation of the three signals to be approximately in the range 60 - 65 cps for all the pyridines. The chemical shift which was taken from the centre of the middle signal seemed to move slightly to higher field as the concentration of acid increased following the acid signal, which also moved to high field with increasing acid concentration. The observed chemical shifts are listed in Table 6.

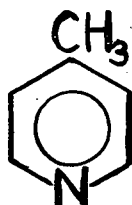
#### 4. $C^{13}$ -H<sup>1</sup> Coupling Constants in $CH_3$

The multiplets caused by coupling from  $C^{13}$  to the proton in

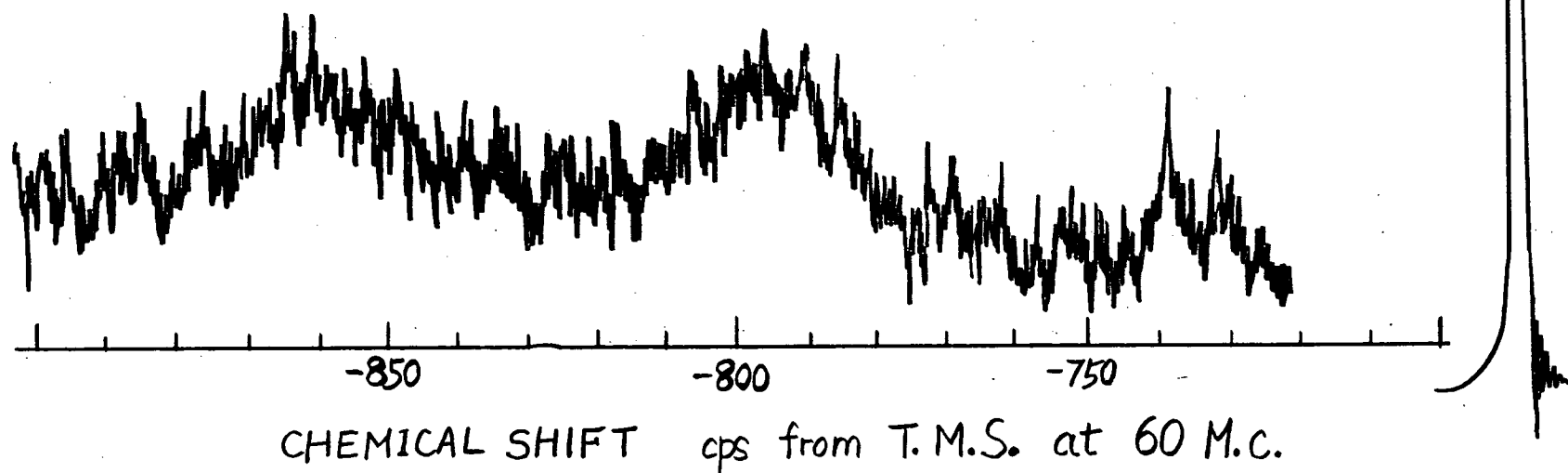
TO FOLLOW PAGE 32

# FIGURE 11

5.6 mole % in trifluoroacetic acid



$\text{CF}_3\text{COOH}$




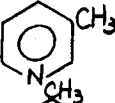

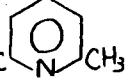
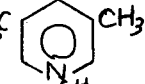
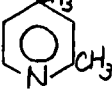
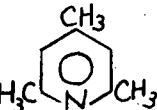
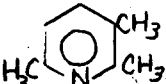
all the methyl groups were observed both for unprotonated and protonated pyridines. As shown in Table 7, the values of the coupling constants were found to be 126 - 127 cps except for the methyls at the  $\alpha$ -position in 2,3,6 trimethyl pyridine, and were independent of the position of the methyl groups. The  $C^{13}-H^1$  coupling constants in protonated pyridines were found to be increased by 3 - 5 cps in most of the cases being also independent of the position of the methyl groups. The  $C^{13}-H^1$  coupling constants in methyl groups in methyl amines are also shown in the table together with the values in trifluoroacetic acid.

Table 6

Chemical Shifts cps from T.M.S. at 60 M.c.

All measurements were made ca. 5 mole percent  
or extrapolated to infinite dilution.  
The values without bracket are in  $\text{CCl}_4$ .  
The values with bracket are in  $\text{CF}_3\text{COOH}$ .  
Volume diamagnetic susceptibility corrections  
were made for external standard.

I. Ring Protons

Compound	Chemical Shift			$\Delta\delta$		
	$\alpha$	$\beta$	$\gamma$	$\alpha$	$\beta$	$\gamma$
 *	-520 (-535)	-432 (-496)	-457 (-530)	-15	-64	-73
I 	-509 (-509)	-422.4 (-467.6)	-442.2 (-498.4)	0	-45.2	-56.1
II 	-501.0 (-499.1)	-418.2 (-460.8)	—	+1.9	-42.6	—
III 	—	-404.6 (-442.6)	-439.0 (-482.5)	—	-36.4	-44.1
IV 	-487.4 (-486.6)	—	-429.4 (-481.9)	+0.8	—	-52.5
V 	-492.6 (-500.0)	-407(3) (-442) -410(5) (-446)	—	-7.4	-35(3) -35(5)	—
VI 	—	-397.6 (-423.8)	—	—	-26.2	—
VII 	—	-404.2 (-483.5)	-427.4 (-475.5)	—	-34.3	-48.1

\* Taken from 100 and recalculated.

Table 6 continued

II. Methyl Protons and Proton on Nitrogen

Compound	$\delta$ , Chemical Shift				$\Delta\delta$		
	$\alpha$	$\beta$	$\gamma$	NH <sup>+</sup>	$\alpha$	$\beta$	$\gamma$
Pyridine	—	—	—	-830*	—	—	—
I	—	-137.7 (-147.3)	—	-796	—	-9.6	—
II	—	—	-138.1 (-150.0)	-779	—	—	-11.9
III	-146.4 (-154.0)	—	—	-762	-5.7	—	—
IV	—	-135.0 (-138.1)	—	-748	—	-3.1	—
V	-145.4 (-154.7)	—	-135.3 (-147.1)	-759	-9.3	—	-11.8
VI	-142.0 (-141.0)	—	-131.8 (-133.5)	-748	+1.0	—	-1.7
VII**	-131.0 (-150.0)	-123.4 (-139.2)	—	-730	-19.0	-10.8	—

\* Taken from 100 and recalculated.

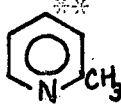
\*\* Both CH<sub>3</sub> at  $\alpha$  position have the same  $\delta$ .

Table 7

## Coupling Constants cps

The values without bracket are in  $\text{CCl}_4$ .  
The values with bracket are in  $\text{CF}_3\text{COOH}$ .

## I. Coupling Constants between Protons

	$J_{2-3}^{5-6}$	$J_{3-4}^{4-5}$	$J_{2-4}^{6-4}$	$J_{3-5}$	$J_{2-6}$	$J_{3-6}^{2-5}$	Other J's
Pyridine*	5.5	7.5	1.9	1.6	0.4	0.9	
I	4.5 (6.0)	7.8 (8.2)	1.7 (1.9)	—	<del>~0</del> (~0)	0.8 (?)	$J_{\text{CH}_3-4} = 0.7$ (0.9)
II	5.2 (6.1)	—	—	—	~0 (~0)	1.6 (?)	$J_{\text{CH}_3-3} = 0.7$ $J_{\text{NH}^+-2} = 6.9$
III	—	7.3 (8.1)	—	—	—	—	
IV	—	—	2.1 (?)	—	0 (0)	—	$J_{\text{NH}^+-2} = 6.2$ $J_{\text{CH}_3-4} = 0.7$
V	4.5 (6.4)	—	—	—	—	~0 (~0)	$J_{\text{NH}^+-6} = \sim 7.0$
VI	—	—	—	—	—	—	
VII	—	7.7 (8.3)	—	—	—	—	
***  Benzene	5.0  7~9	7.8 8.0	2.0	1.1  2~3	—	0.8  ~0	

\* Taken from the reference 100.

\*\* Taken from the reference 99.

Table 7 continued.

The values without bracket are for pure compound.  
The values with bracket are in  $\text{CF}_3\text{COOH}$ .

II. Coupling Constants between the Carbon 13 and Proton  
in Methyl Groups(cps)

Compound	$J$			$\Delta J$		
	$\alpha$	$\beta$	$\gamma$	$\alpha$	$\beta$	$\gamma$
I	—	127 (130)	—	—	+3	—
II	—	—	127 (130)	—	—	+3
III	126 (131)	—	—	+5	—	—
IV	—	127 (130)	—	—	+3	—
V	127 (131)	—	126 (129)	+4	—	+3
VI	126 (130)	—	127 (132)	+4	—	+5
VII	$\left\{ \begin{array}{l} 124 \text{ (2)} \\ 131 \text{ (6)} \\ 123 \text{ (6)} \\ 129 \text{ (6)} \end{array} \right.$	126 (131)	—	+7 (2) +6 (6)	+5	—
$\text{CH}_3\text{NH}_2$	133* (144)			+11		
$(\text{CH}_3)_2\text{NH}$	132* (143)			+11		
$(\text{CH}_3)_3\text{N}$	131* (145)			+11		
Toluene	126*					

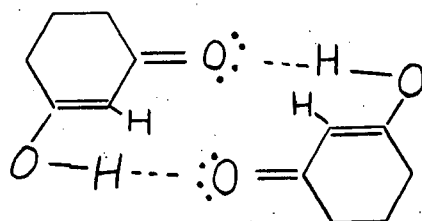
\* Taken from the reference 78.



## V. DISCUSSION

A. Keto-Enol Tautomerism of Cyclic 1,3 Diones1. Cyclohexane 1,3 Dione in Chloroform

The low field signal whose chemical shift was found to be concentration dependent indicates a strongly hydrogen bonded proton. This must arise from the enol form of the molecule and is suggestive of similar chemical shifts in intramolecular hydrogen bonded enol systems.<sup>5,6,15</sup> Enolization is also indicated from the appearance of another signal at -329 cps from T.M.S. in a region where olefinic protons are usually found. The intensities of these two resonances are the same. The formation of an intramolecular hydrogen bond in the molecule of cyclohexane 1,3 dione is sterically excluded so that intramolecular hydrogen bonding must be involved in the enol form. In agreement with previous suggestions<sup>90,91,92</sup> a dimeric unit of the structure suggested below seems likely:

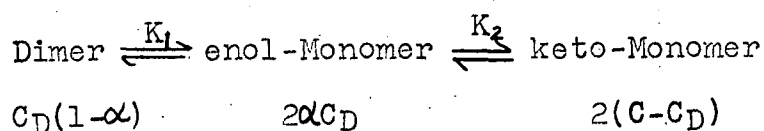


Note that the carbonyl oxygen is trigonal with respect to two non-bonding  $\sigma$  lone pair orbitals and a C-O  $\sigma$  bond. Steric repulsion of the olefinic hydrogen atoms in the dimer is avoided and linearity of the hydrogen bond is preserved by use of one of the lone pairs in the carbonyl oxygen atom.

The high field shift of hydroxyl proton by dilution also indicates the fact that the enolized molecules exist partly in non-hydrogen bonded forms; so that the observed chemical shift is the averaged chemical shift of the non-hydrogen bonded species and the hydrogen bonded ones. A linear relationship was found between the chemical shifts and  $1/\sqrt{C}$ , where  $C$  is the concentration in units of moles per liter of dimer. This is shown in Figure 5.

The chemical shift of the hydrogen bonded proton in the dimer form was obtained by extrapolation to infinite concentration. The chemical shift was -740 cps. The 4- and 6- protons of the enol form appear to be equivalent as there is only one resonance signal. This suggests that the hydroxyl function is equally probable at the 1- and 3- carbon atoms and that a rapid interconversion of these two forms occurs. Such rapid interconversion has already been noted in acetylacetone<sup>5</sup> which has an intramolecular hydrogen bond.

The system is considered to involve three species, i.e. the enol form which exists in the intermolecularly hydrogen bonded dimer, the enol form in the non-hydrogen bonded monomer, and the keto monomer. In equilibrium the system will be expressed by the following equation:



where  $C$  = initial total concentration expressed in  
units of dimer

$C_D$  = initial concentration of dimer

$\alpha$  = degree of dissociation.

Then the equilibrium constants are:

$$K_1 = \frac{4\alpha^2 C_D^2}{C_D(1-\alpha)} = \frac{4\alpha^2 C_D}{(1-\alpha)} \quad \dots \dots (1)$$

$$K_2 = \frac{2(C-C_D)}{2\alpha C_D} = \frac{(C-C_D)}{\alpha C_D} \quad \dots \dots (2)$$

The value of  $C_D$  will be obtained from the knowledge of the  
ratio of signal areas for enol to keto.

i.e.  $C_D = \frac{C}{1 + \frac{1}{2R}} \quad \dots \dots (3)$

$$R = \frac{[\text{Enol}]}{[\text{Keto}]} \quad \dots \dots (4)$$

The degree of dissociation,  $\alpha$ , will be obtained by the observed  
hydroxyl proton chemical shift.

$$\delta_{\text{obs.}} = X_D \delta_D + X_M \delta_M$$

$X_D$  = fraction of dimer OH proton

$$= \frac{2C_D(1-\alpha)}{2C_D(1-\alpha) + 2C_D\alpha} = 1 - \alpha$$

$X_M$  = fraction of monomer OH proton

$$= \frac{2C_D\alpha}{2C_D} = \alpha$$

$$\delta_{\text{obs.}} = -740(1-\alpha) + \alpha\delta_M$$

$$\alpha = \frac{740 - \delta_{\text{obs.}}}{740 - \delta_M}$$

By substituting the values obtained by equation (3) and (4) into equation (1) and (2), the equilibrium constants were obtained. The reasonable chemical shift of monomer enol hydroxyl proton which makes (1) approximately constant for all concentrations was found to be -300 cps. The results of calculation are tabulated in Table 2.

The possible factors which cause the equilibrium constants to depend on the concentrations are: 1) impurities contained in chloroform which might have hydroxyl groups. This factor increases the area of OH proton signal and gives smaller K values at lower concentrations. 2) the saturation under very high gain on the A 60 spectrometer might broaden the signals and the difficulty of finding the correct base line usually give rise to smaller areas than what one would expect. As regards factor 1), the spectrum of chloroform at the highest gain was carefully checked and it was confirmed that there existed no detectable impurity. In all cases the CH proton signal was broader than the OH proton signal. This indicates the possibility of an error in measuring areas particularly at low concentrations. Also the fact that these two kinds of protons might have slightly different relaxation times, could give incorrect ratios.

## 2. Cyclohexane 1,3 Dione in Acetonitrile

The OH enolic signal appeared somewhat broadened and strongly concentration dependent. Uncertainties in the

concentration dependence and the broadening of the signal was assigned to the presence of traces of water not removed by the anhydrous sodium sulfate treatment.<sup>104</sup> The system at equilibrium will be expressed by the same equation as for chloroform. Assuming that the presence of the monomer enol form is negligibly small, the overall equilibrium constant between the dimer enol and monomer keto forms will be:

$$K = \frac{4(C-CD)^2}{C_D}$$

where the symbols stand for the same as in the chloroform case. The results are shown in Table 4. The constancy of the equilibrium constant under this assumption supports its correctness within the concentration region studied. In this case, both of the deviation factors 1) and 2), mentioned for the chloroform case, can be thought to be important in the calculations. These two factors appear to have cancelled out each other.

For the high temperature measurements, the OH proton chemical shifts of dimer enol and monomer enol for each temperature were not available. So that the rough calculations were made for overall equilibrium constants. The Figure 6 shows the graphs of log K versus 1/T. From the slope, ( $\frac{4 \log K}{4(1/T)} = -2.38 \times 10^3$ ), the heat of conversion, from the enol dimer into the keto monomer, was found to be approximately 2.05 kcal/mol using the equation:

$$\Delta H \approx -\frac{RT}{2.303} \log K$$

This value was in the same order of magnitude as was found for acetylacetone,<sup>6</sup> which was 2.7 kcal/mol.

### 3. 5,5' Dimethyl Cyclohexane Dione in Chloroform

The same assumptions were applied to this system and the equilibrium constant was calculated. The calculation showed an increase of the values as the concentration decreased as shown in Table 5. This indicates the existence of a more than negligible amount of monomer enol form where the amount of monomer depends on the concentration. The same consideration should be made for the error sources as was made for the system of cyclohexane 1,3 dione in chloroform. However, as the signals which were compared were from approximately the same kind of protons and the number of protons involved in them were larger, the errors from the saturation or from the difference of relaxation times should be less.

The overall equilibrium constant ( $= K_1 \cdot K_2^2$ ) for the cyclohexane 1,3 dione in chloroform was found to be in the same order of magnitude as those for this system. These were roughly calculated.

## V. DISCUSSION

B. Protonation on Pyridines1. Chemical Shifts of Ring Protons\* (See Page 62)

If the nucleus is in a molecule, the electrons are not free to move in circles around the direction of the applied magnetic field. The general expression for the chemical shift in an isolated molecule was first derived by Ramsey.<sup>105</sup> The secondary field  $H'$  due to the induced currents will be;

$$H' = -\sigma H$$

where  $H$  is the applied uniform magnetic field, and  $\sigma$  is a second-rank tensor characteristic of the position of the nucleus in the molecule. However, the position of the nuclear resonance signal in liquids is determined by the mean component of  $H'$  along the direction of  $H$  averaged over many rotations.

Pople<sup>125</sup> split the screening constant for a nucleus in a molecule as follows:

$$\sigma_A = \sigma_d^{AA} + \sigma_p^{AA} + \sum_{B(\neq A)} \sigma^{AB} + \sigma_{ring}^A + \sigma_E^A$$

The interpretation of the various terms being:

- (1)  $\sigma_d^{AA}$  is the contribution to the secondary magnetic field at nucleus A due to diamagnetic currents around the nucleus A.
- (2)  $\sigma_p^{AA}$  is the contribution due to the paramagnetic-type currents on atom A which give the susceptibility term  $\chi_p^A$ . To evaluate this term, it would be necessary to have detailed knowledge of the energies and wave functions of all the excited electronic states. A rather simpler form is obtained<sup>1</sup> by replacing all the

electronic excitation energies,  $E_n - E_0$ , by an average value  $\Delta E$ , the matrix elements now being taken over the ground state only:

$$\sigma_P^{AA} = \frac{e^2 \hbar^2}{m^2 c^2 \Delta E} \langle 0 | \sum_k \frac{1}{r_k^3} \cdot \frac{\partial^2}{\partial \phi_j \partial \phi_k} | 0 \rangle \quad \dots \dots (1)$$

(3)  $\sigma^{AB}$  is the contribution to the screening of nucleus A by the atomic circulations on nucleus B. If the magnetic effects of these neighbouring currents are treated in a dipole approximation, this term involves only the local anisotropy of the local susceptibility on the atom B. An approximate relation for an axially symmetrical group of electrons, G, has been derived by McConnell:<sup>103</sup>

$$\sigma_{av}(G) = \frac{(3 \cos^2 \theta - 1) \Delta \chi}{3 r^3} \quad \dots \dots (2)$$

where  $r$  = the distance between the proton and the electrical centre of gravity of G.

$\theta$  = the acute angle which  $\chi$  makes with the symmetry axis.

$\Delta \chi$  = the difference in the transverse and longitudinal susceptibilities.

(4)  $\sigma^{A, \text{ring}}$  is the contribution to the screening due to ring currents which cannot be localized on any atom.

(5)  $\sigma_E^A$  is the contribution due to the electric polarization of the bond joining nucleus A to the molecule caused by a permanent molecular electric dipole. Buckingham<sup>107, 114</sup> made calculations on an electric field effect due to polar molecules. As suggested by Ramsey,<sup>105</sup> a chemical shift may change in an electric field because the resultant polarization of bonding electrons



causes changes in the paramagnetic correction term. The effect is estimated as:

$$\sigma_E^A = -2 \times 10^{-12} E_z - 10^{-18} E^2 \quad \dots \dots (3)$$

where  $\sigma_E^A$  = the change in the proton screening constant of an X-H bond.

$E$  = electric field

$E_z$  = the component of  $E$  in the bond direction.

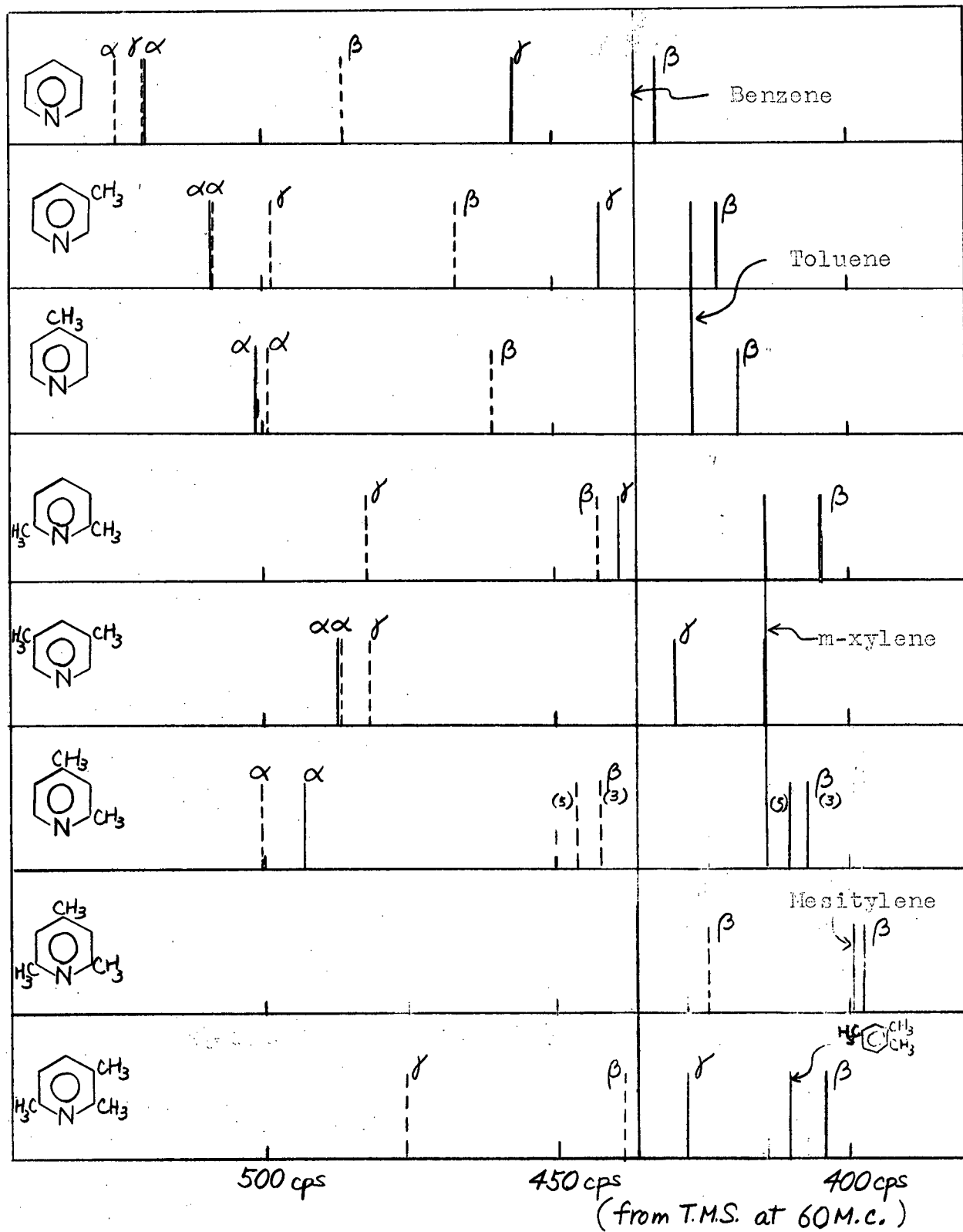
The chemical shift changes for the ring protons with benzene, methyl benzenes, pyridine, methyl pyridines, and corresponding pyridinium ions (See Figure 12) will be discussed separately.

#### a. Changes between Benzene and Methyl Benzenes

The substituent effects on the ring proton chemical shifts have been studied for pyridines.<sup>99</sup> It has been concluded that the changes in the chemical shifts arise mainly from the inductive effect of the substituent group. For example a nitro group at the  $\alpha$ -position, by withdrawing electrons from the  $\beta$ -carbon, makes the chemical shift between the  $\beta$ - and  $\gamma$ -protons smaller than in the unsubstituted pyridines. Here, the effects of a methyl group will be discussed in terms of the diamagnetic anisotropy effect,  $\sigma_{H,CH_3}$  and the inductive effect. The inductive effect is reflected in terms  $\sigma_a$  and  $\sigma_E$ , for a ring proton affected by the addition of a methyl groups. The electric dipole of a C-H bond is sufficiently different from the zero value expected in a C-C bond to cause small changes in chemical shift due to an electric field effect.<sup>107</sup>

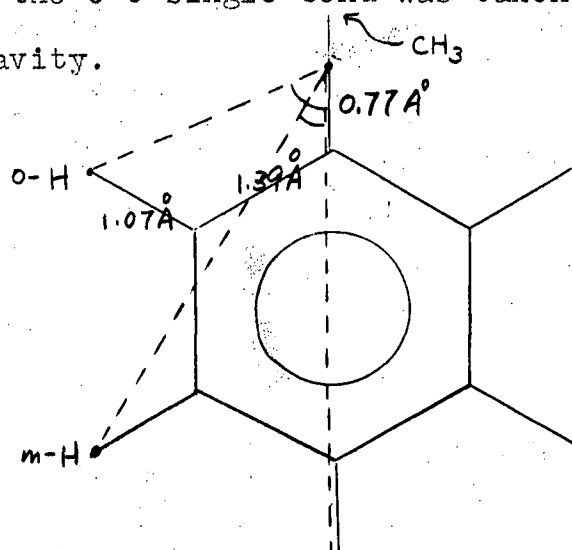
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FIGURE 12  
Position of Ring Proton Resonance  
-----after protonation



### i. Diamagnetic Anisotropy Effect of Methyl Groups

This effect arises at specific protons mostly from the anisotropy of the C-C single bond between the methyl carbon and carbon in the benzene ring. It was assumed that the diamagnetic anisotropy of the C-H bond was negligible. The diamagnetic anisotropy effects of the C-C single bond to the ortho-, meta-, and para-protons in toluene were calculated using equation (2). The centre of the C-C single bond was taken as the approximate centre of gravity.



The  $\chi$  value,  $8.3 \times 10^{-30} \text{ cm}^3/\text{molecule}$ , which Musher<sup>104</sup> suggested was used in the calculation. The chemical shift changes due to the diamagnetic anisotropy effect of a methyl group were: -11.0, +3.0, and +3.5 cps at 60 M.c. from benzene for the ortho-, meta- and para-protons respectively.

### ii. Inductive Effect of Methyl Groups

The chemical manifestations of methyl substitution are usually labeled 'inductive effect'. From the point of view of the chemical shift, these effects represent the change in the

static electron density at the nucleus in question, the change being transmitted via the sigma bonds. Presumably inductive contributions operate through both the  $\sigma_d$  and the  $\sigma_E$  terms, the first representing the total electron charge around the nucleus, and the second its distribution or polarization in the bond. For a slightly electropositive substituent such as the methyl group, it might be expected that the inductive effect results in a small high field shift for the ring protons, relative to benzene reference, the effect being the greatest at protons ortho to the substituent. The chemical shifts of the ring protons of toluene, ortho-, meta-, and para-xylenes with respect to benzene in 5 w/w % carbontetrachloride solutions were measured. The ring protons of toluene show only one signal at 10 cps to high field of the benzene proton signal at 60 M.c. This indicates that the diamagnetic anisotropy effect and the inductive effect are added together and make the chemical shift of +10 cps for all the protons at different positions relative to the methyl group.

In dimethyl benzenes it was assumed that the total effect from each methyl group was additive. Subtracting the calculated anisotropy part leaves the inductive contribution for a methyl substituent, the values being +21.0, +7.0, and +6.5 cps at 60 M.c. for the ortho-, meta-, and para-protons respectively.

#### b. Changes between Benzene, Pyridine, and Pyridinium Ion

All the above effects are operative, and in addition there

Table 8

## Calculated and Observed Chemical Shift

with respect to Benzene

(cps at 60 M.C.)

Compound	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I	-74	-73	1	+7	+14	7	+2	-6	8
II	-74	-63	11	+7	+18	11	—		
III	—			+17	+31	14	+12	-3	15
IV	-64	-51	13	—			+12	+7	5
V	-64	-57	7	+17	+26	9	—		
					+29	12			
VI	—			+27	+39	12	—		
VII	—			+27	+33	6	+22	+9	13

is a large resonance effect caused by the introduction of the hetero-atom into the ring. This results in long range  $\pi$ -electron density changes.

#### i. Resonance or Mesomeric Effects

It has long been the ambition of chemists to correlate the chemical shifts of protons attached to conjugated ring systems with the  $\pi$ -electron charge density at the ring carbon atoms. Spiesscke and Schneider<sup>121</sup> have shown that such a correlation exists at the para position in mono-substituted benzenes, where

Table 9

Calculated and Observed Chemical Shift  
with respect to Corresponding Methyl Benzene  
(cps at 60 M.C.)

Compound	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I	-84	-83	1	-3	+4	7	-8	-16	8
II	-84	-75	9	-3	+8	11	—		
III	—			-3	+9	12	-8	-25	17
IV	-84	-73	11	—			-8	-15	7
V	-84	-79	5	-3	+4	7	—		
					+7	10			
VI	—			-3	+2	5	—		
VII	—			-3	+6	9	-8	-17	9

complicating factors due to inductive, anisotropy and electric field effects are absent. The interaction between the  $\pi$ -electron cloud of the ring, and the  $\sigma$  bond joining the proton to the ring, as evidenced in the chemical shift correlation, and also in the E.S.R. hyperfine splitting correlation, is presumably through configuration interaction at the carbon atom. In terms of the previous nomenclature the mechanism of proton shielding via the  $\pi$ -electrons is through the neighbor anisotropy term  $\sigma^{CH}$ .

Theoretical calculations have been made of the  $\pi$ -electron

Table 10

Calculated and Observed Chemical Shift  
with respect to Pyridine

(cps at 60 M.C.)

Compound	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I	+10	+11	1	+10	+10	0	+10	+15	5
II	+10	+19	9	+10	+14	4	—	—	—
III	—	—	—	+20	+26	6	+20	+18	2
IV	+20	+33	13	—	—	—	+20	+28	8
V	+20	+27	7	+20	+22	2	—	—	—
					+25	5			
VI	—	—	—	+30	+35	5	—	—	—
VII	—	—	—	+30	+28	2	+30	+30	0

densities in substituted benzene<sup>108,109</sup> and in some aromatic ions.<sup>68</sup> Katritzky's<sup>102</sup> values for some heterocyclic systems are:

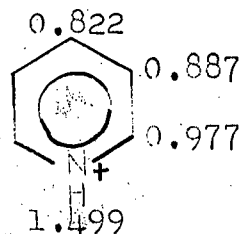
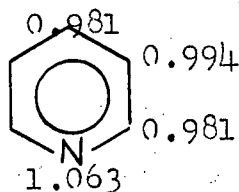
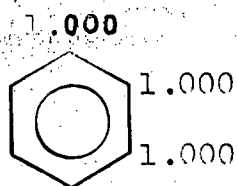


Table 11

Calculated and Observed Chemical Shift  
with respect to Benzene

Ion	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I <sup>+</sup>	-69	-73	4	-30	-31	1	-69	-62	7
II <sup>+</sup>	-69	-65	4	-30	-25	5	—		
III <sup>+</sup>	—			-10	-7	3	-39	-47	8
VI <sup>+</sup>	-49	-50	1	—			-39	-46	7
V <sup>+</sup>	-49	-64	15	-10	-6	4	—		
					-10	0			
VI <sup>+</sup>	—			+20	+11	9	—		
VII <sup>+</sup>	—			+10	-2	12	-19	-40	21

whereas for pyridine Coulson<sup>111</sup> calculated

N - 1.147       $\alpha$  - 0.962       $\beta$  - 0.987       $\gamma$  - 0.955

and Brown and Heffernan<sup>112</sup> found

N - 1.107       $\alpha$  - 0.952       $\beta$  - 1.004       $\gamma$  - 0.981

For the  $\beta$ - and  $\gamma$ -protons in pyridine, the inductive, anisotropic and polar effects should be small, and thus their chemical shifts relative to benzene should be determined mainly by the carbon  $\pi$ -electron density changes from benzene.



Table 12

Calculated and Observed Chemical Shift  
with respect to Corresponding Methyl Benzene

Ion	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I <sup>+</sup>	-79	-83	4	-40	-41	1	-69	-72	3
II <sup>+</sup>	-79	-73	6	-40	-35	5	—	—	—
III <sup>+</sup>	—	—	—	-30	-27	3	-59	-69	10
IV <sup>+</sup>	-69	-73	4	—	—	—	-59	-68	9
V <sup>+</sup>	-69	-86	17	-30	-28	2	—	—	—
					-32	2			
VI <sup>+</sup>	—	—	—	-20	-25	5	—	—	—
VII <sup>+</sup>	—	—	—	-20	-28	8	-49	-66	17

#### ii. Anisotropy Effects of the Heterocyclic Atom

There exists a large local paramagnetic contribution to the shielding at the nitrogen atom in pyridine due to the relative smallness of the  $n \rightarrow \pi^*$  transition energy,  $\Delta E$ . Protonation of the nitrogen atom in pyridine to form the pyridinium ion results in the removal of the lone pair, and increases the lowest transition energy,  $\Delta E$ , from 4.5 eV<sup>122</sup> for pyridines'  $n \rightarrow \pi^*$  process to about 10 eV for the  $\pi \rightarrow \pi^*$ ,  $\pi \rightarrow \sigma^*$  excitations in the pyridinium ion. The consequent decrease in the paramagnetic shielding causes a high field shift of 123 ppm for the N<sup>14</sup> resonance in

Table 13

Calculated and Observed Chemical Shift  
with respect to Pyridine

Ion	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I <sup>+</sup>	+18	+11	7	-27	-35	8	-50	-41	9
II <sup>+</sup>	+18	+21	3	-27	-29	2	—		
III <sup>+</sup>	—			- 7	-11	4	-30	-26	4
VI <sup>+</sup>	+38	+34	4	—			-30	-25	5
V <sup>+</sup>	+38	+20	18	- 7	-10	3	—		
					-14	7			
VI <sup>+</sup>	—			+13	+ 8	5	—		
VII <sup>+</sup>	—			+13	- 6	19	-10	-19	9

the pyridinium ion over pyridine.<sup>106</sup> This large paramagnetic contribution to the magnetic susceptibility at the N atom in pyridine implies a large anisotropy centre, affecting the neighbouring  $\alpha$ -ring protons.

### iii. Ring Current Effect

Calculations by Hall<sup>and</sup> co-workers<sup>113</sup> and the pyridine ring current using an empirical electronegativity parameter for the nitrogen atom suggest changes in the ring current of only 1% from benzene. This represents a negligible proton shift change

Table 14

Calculated and Observed Chemical Shift  
with respect to Corresponding Pyridines

Ion	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I <sup>+</sup>	+8	0	8	-37	-45	8	-60	-56	4
II <sup>+</sup>	+8	+2	6	-37	-43	6	—		
III <sup>+</sup>	—			-27	-36	9	-50	-44	6
IV <sup>+</sup>	+18	+1	17	—			-50	-53	3
V <sup>+</sup>	+18	-7	25	-27	-35	8	—		
	—				-36	9			
VI <sup>+</sup>				-17	-26	9	—		
VII <sup>+</sup>	—			-17	-34	17	-40	-48	8

due to this effect.

#### iv. Inductive and Intramolecular Polar Effects

For pyridine it may be assumed that inductive effects from the nitrogen atom are transmitted only as far as the  $\alpha$  protons. The positive charge on the pyridinium ion makes the sigma polarization much less clear. In any event, it seems that an alternating  $\pi$ -electron density in a conjugated molecule is accompanied by a polarization of the  $\sigma$ -core.<sup>123</sup>

Pyridine has a total electric dipole moment of 2.1 D<sup>124</sup>

Table 15

Calculated and Observed Chemical Shift  
with respect to Pyridinium Ion

Ion	$\alpha$			$\beta$			$\gamma$		
	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.	Cal.	Obs.	Diff.
I <sup>+</sup>	+20	+16	4	+20	+19	1	+20	+22	2
II <sup>+</sup>	+20	+26	6	+20	+25	5	—	—	—
III <sup>+</sup>	—	—	—	+40	+53	13	+40	+37	3
IV <sup>+</sup>	+40	+38	2	—	—	—	+40	+38	2
V <sup>+</sup>	+40	+25	15	+40	+40	0	—	—	—
					+44	4			
VI <sup>+</sup>	—	—	—	+60	+62	2	—	—	—
VII <sup>+</sup>	—	—	—	+60	+48	12	+60	+44	16

localized mainly at the nitrogen lone pair and this may be expected to polarize the CH bonds. An approximate dipole estimation of this  $\sigma_E$  effect shows it to result in a shift to low field of the  $\alpha$ -protons by some 0.5 ppm, with almost negligible effect at the other positions.

#### v. Solvent Effects

The effect of the solute molecular magnetic anisotropy of these disc molecules will be small at low concentrations in carbon tetrachloride or trifluoroacetic acid. The reaction field

effect back on the solute molecule by polarization of the solvent with a strongly polar solute<sup>114</sup> is small in the case of carbontetrachloride solvent with low dielectric constant, but may be expected to make small contributions to the ring proton shifts in the case of the pyridinium ion in trifluoroacetic acid.

It is concluded that the ring proton shifts at the  $\beta$ - and  $\delta$ - positions in pyridine and the pyridinium ion are affected mostly by resonance effects around the ring. Comparison of the experimental values of these shifts from benzene with the calculated  $\pi$ -electron densities yields a roughly similar correlation, the ratio  $\frac{\delta}{\rho}$  being approximately  $4.4 \times 10^2$  cps/ $\pi$ -electron. At the  $\alpha$ -position, this correlation may be used to estimate the total effect of the remaining terms (inductive, polar, anisotropy and solvent). These effects are found to total -76 cps at 60 M.c., out of the total low field shift of 84 cps at the  $\alpha$ -proton in pyridine from benzene.

$$-84 + 4.4 \times (1 - 0.981) \times 10^2 = -76 \text{ cps}$$

### c. Changes between Pyridine and Methyl Pyridine

Assuming that the ring of methyl pyridines are regular hexagons with the same bond lengths as in methyl benzenes, the diamagnetic anisotropy effect of the methyl groups will be approximately the same as in methyl benzenes. It is assumed that (1) the inductive effect of the methyl groups is the same as for the methyl benzenes, and that (2) the  $\pi$ -electron density,

the inductive anisotropy effects of the nitrogen atom and the ring current are the same as those of pyridine. With these assumptions, using the values obtained previously for these effects, the chemical shift changes of the ring protons in methyl pyridines with respect to pyridine, corresponding methyl benzenes, and benzene were calculated. Actual values for the effects in cps at 60 M.c. will be summarized:

The  $\sigma_E$ , inductive and anisotropic effects of the nitrogen atom:

$$\left\{ \begin{array}{l} -76 \text{ cps at the } \alpha\text{-proton} \\ \text{zero at the } \beta\text{- and } \gamma\text{-protons} \end{array} \right.$$

Mesomeric effect of the nitrogen atom:

$$4.4 \times 10^2 \text{ cps per } \pi\text{-electron}$$

The inductive effect of the methyl group:

$$\left\{ \begin{array}{l} +21.0 \text{ cps at the } o\text{-proton} \\ + 7.0 \text{ cps at the } m\text{-proton} \\ + 6.5 \text{ cps at the } p\text{-proton} \end{array} \right.$$

Diamagnetic anisotropy effect of the methyl groups:

$$\left\{ \begin{array}{l} -11.0 \text{ cps at the } o\text{-proton} \\ + 3.0 \text{ cps at the } m\text{-proton} \\ + 3.5 \text{ cps at the } p\text{-proton} \end{array} \right.$$

Effect of change in the ring current is negligible.

#### d. Change between Methyl Pyridines and the Methyl Pyridinium Ions

Because of the increase of the excitation energy,  $\Delta E$ , of

the protonated nitrogen atom compared to the nitrogen atom which has lone pair electrons, the paramagnetic shielding at the nitrogen and the anisotropy effect at the ring protons are decreased. The inductive effect will be increased more than the decrease of the anisotropic effect.

Comparing the ring proton chemical shifts of methyl pyridine and the protonated methyl pyridine with those of pyridine, it was found that the effect of the methyl group, including both the inductive and the diamagnetic anisotropic effect, increased by a factor of two in most cases. The total inductive and anisotropy effects of the nitrogen atom at the  $\alpha$ -position of the pyridinium ion was estimated in the same way as in the case of pyridine. The value was found to be -79 cps. The linearity between the difference of  $\pi$ -electron density and the chemical shift, and the other factors, were assumed to be the same as in the case of the pyridinium ion.

The chemical shifts of the ring protons in the methyl pyridinium ion from those of corresponding methyl pyridines, the pyridinium ion, pyridine, the corresponding methyl benzenes and benzene were calculated. The results are shown in Table 8-15 together with the observed values. A few examples of the calculation will be shown.

Example: 3methyl pyridine

$\alpha$ -proton

(1) from pyridine

$$(+21.0 - 11.0) = +10 \text{ cps}$$

(2) from toluene

$$-76 + 4.4 \times (-0.019) \times 10^2 = -84 \text{ cps}$$

(3) from benzene

$$-76 + 4.4 \times (-0.019) \times 10^2 + 21.0 - 11.0 = -74 \text{ cps.}$$

As is seen in Table 8~15, the calculated values are in good agreement with the observed values. Most of them agreed within  $\pm 5$  cps at 60 M.c. (= 0.08 ppm). Greater discrepancies were found for the  $\alpha$ -protons of the 2,4 dimethyl pyridinium ion and for the  $\beta$ - and  $\gamma$ -protons of 2,3,6 trimethyl pyridinium ion. The methyl groups at the  $\alpha$ -position seem to affect the other protons differently from those at the  $\beta$ - and  $\gamma$ -position, presumably due to non-additive effects when the hetero-atom and the substituent are ortho to one another.<sup>126</sup>

## 2. Chemical Shifts of Methyl Protons

The methyl proton chemical shifts at various positions with respect to the nitrogen atom were compared with the corresponding methyl benzenes. Those at the  $\beta$ - and  $\gamma$ -positions were only 1~2 cps shifted to high field, while those at the  $\alpha$ -position were shifted 8~10 cps to low field at 60 M.c. The inductive and diamagnetic anisotropy effects caused by the other methyl groups in di- and tri- substituted methyl pyridines and the effect of the slight change of the  $\pi$ -electron charge distribution on the ring carbon atoms as a result of replacing  $\geq\text{CH}$  by  $\geq\text{N}$ : are almost negligible on the methyl protons. The low field shift of the methyl proton at the  $\alpha$ -position indicates that the



inductive and anisotropic effects of the nitrogen atom is the only appreciable factors to influence the chemical shifts of the methyl protons at the  $\alpha$ -position.

The methyl proton chemical shifts of the protonated pyridines were also compared with the corresponding methyl benzenes. Low field shifts by amounts of  $\sim 8$  cps and  $\sim 11$  cps have been found for the  $\beta$ - and  $\gamma$ -methyl protons. The  $\alpha$ -methyl protons have also been found to be shifted further to low field by  $\sim 18$  cps. It is reasonable to assign the low field shift at the  $\beta$ - $\gamma$ -methyl protons to the greater decrease of  $\pi$ -electron density at these positions than in the neutral pyridines. The further low field shift at the  $\alpha$ -methyl protons must arise mainly from the change of the anisotropy and inductive effects of the nitrogen atom by protonation. The anisotropy effect results in a high field shift and the inductive effect in a low field shift. The sum of them is to low field.

### 3. Concentration Dependence of Chemical Shifts

Assuming that there is a rapid exchange between the neutral pyridines and the positive pyridinium ions, the observed chemical shifts must be the averaged chemical shift of the two species. At higher acid concentrations, the time the acid protons spend on the nitrogen atom should be longer than in the less concentrated solution, so that the fraction of the pyridinium ion is larger at the higher acid concentration. This explains the slight dependence of chemical shift on the acid concentration as

shown in Figure 9. The chemical shifts of the  $\beta$ - and  $\gamma$ - protons change by much larger amount than that of the  $\alpha$ -proton on protonation. This is also shown by the relative slopes of the concentration dependent chemical shift curves. The slopes of the  $\beta$ - and  $\gamma$ -proton chemical shift versus concentration curves were larger than that of the  $\alpha$ -proton, which was almost unchanged in the region of 0 to approximately 20 mole % pyridine concentration.

#### 4. Signal of the Proton Which is Bonded to the Nitrogen Atom

The significant broadening of the triplet has been attributed to a shorter  $T_1$  relaxation time of the protons which are attached to the nitrogen atom. This shorter relaxation time,  $T_1$ , is caused by the nuclear quadrupole relaxation effects of the  $N^{14}$  nucleus.<sup>66</sup> The concentration dependence of the position of this triplet is strong evidence for a hydrogen bond between the nitrogen atom and the oxygen atom in trifluoroacetic acid molecule.

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During the preparation of this thesis another paper was published.<sup>128</sup>

## 5. Coupling Constants

### a. General Considerations

Several factors affecting the coupling constants between nuclei have been considered. As mentioned in the introduction the coupling constants between  $C^{13}$  and  $H^1$  have been found to be related linearly to the s character of the carbon atomic orbitals.<sup>73,74,75,78,82</sup> The  $C^{13}$ - $H^1$  coupling constants in substituted methanes<sup>78</sup> have been found to be dependent on the electronegativity of the substituents, due to rearrangement of s character in the C orbitals. Schaefer<sup>120</sup> also found that all ethylenic H-H coupling constants decreased linearly with increasing electronegativity of the substituents. An electronegative substituent X increases the p-character of the C-X bond at the carbon atom by withdrawing  $\sigma$ -electrons, thus increasing the s character of the other carbon  $\sigma$ -bonds. This s character increase has been elegantly demonstrated by Gutowsky and Juan.<sup>127</sup> An electronegative substituent not only decreases the  $\sigma$ -electron density in the bond but also increases the polarity of the bond. Same distortion of the  $\sigma$ -bond system may also result from indirect interaction with the  $\pi$ -electron system. In previous considerations of the proton-proton coupling constants<sup>89</sup> the polarity of the  $\sigma$ -bonds and the effect of the  $\pi$ -electron distribution have been excluded. Thus McConnell<sup>116</sup> has suggested that in the aromatic system the coupling constants between protons around the ring are dominated by the  $\sigma$ -electron contributions.

## b. Benzene and Pyridine

The coupling constants between the ortho-protons in substituted benzenes are 7~9 cps, those between the meta-protons are 1~3 cps, and those between the para-protons are ~0 cps.<sup>1,116,117,118,119</sup>

In pyridine the ortho coupling constants between 2 and 3 ring protons are much less (4.5~5.5 cps) than those between 3 and 4 ring protons (7.3~7.8 cps). The latter is almost the same as in benzene. The meta coupling constants between 2,4,6 ring protons are almost negligible, while those between 3 and 5 ring protons are appreciable. At first inspection those couplings which include the  $\alpha$ -proton are much smaller than those in the benzene systems. On protonation all the coupling constants were increased.

Comparison of the  $\pi$ -electron densities and the coupling constants in the pyridine and pyridinium systems shows the latter to be independent of the  $\pi$ -electron densities at the carbon atoms to which the protons are bonded. From this, it can be concluded that the ring proton coupling constants in pyridines are mainly dependent on the  $\sigma$ -bonds and not on the  $\pi$ -bond system. Therefore one of the main factors which decreases the coupling constants must be the decrease of  $\sigma$ -electron densities in the bond through which the protons interact. When a nitrogen atom replaces  $\geq\text{CH}$ , the electronegative nitrogen atom withdraws the  $\sigma$ -electrons from the bonds. Decrease of the  $\sigma$ -electron density in the bonds causes the decrease in the coupling constants in the pyridine system relative to the benzene system. This is

what is expected from Schaefer's correlation.<sup>120</sup> The inductive effect of the nitrogen atom must be smaller in the C<sub>3</sub>-C<sub>4</sub> bond than in the C<sub>2</sub>-C<sub>3</sub> bond because the former is further separated from the nitrogen atom. Thus the ortho coupling constants between 3 and 4 ring protons in the pyridine system are less reduced than those between 2 and 3 ring protons compared to the benzene system.

All the C<sup>13</sup>-H<sup>1</sup> coupling constants in methyl groups in the pyridine system (~126 cps) are the same as that of toluene.<sup>78</sup> The s character in the carbon atomic orbital and the coupling constants increase proportionally; indicating that the nature of the C-H  $\sigma$ -bonds are not changed by the inductive effect of the nitrogen atom. It is further indicated that the C-C  $\sigma$ -bond between the ring carbon and the methyl carbon also remains unchanged. The  $\beta$ -C<sup>13</sup>-H<sup>1</sup> coupling constant in pyridine (~159cps) is also the same as that of benzene.<sup>77,119</sup> It is therefore concluded that the nitrogen atom in the ring only affects the  $\sigma$ -bonds within the ring system.

### c. Pyridinium Cation Systems

In the pyridinium ion system the H<sup>1</sup>-H<sup>1</sup> coupling constants around the ring are generally smaller than in the benzene system. However, they are larger than in the pyridine system. The electronegativity of the positively charged nitrogen atom is expected to be greater than that of the neutral nitrogen atom. Therefore the inductive effects through the  $\sigma$ -bonds cannot be the

only factor which causes variation in the  $H^1-H^1$  coupling constants. The proton-proton coupling constants decrease in the order, benzene, pyridinium ion, pyridine. Possible explanations may be sought in terms of:

(1) Isoelectronicity. The pyridinium ions are the only charged species, so that the comparison may not be fair. It may be better to compare the pyridinium ion J's with, say, those of the similarly charged anilinium ion.

(2) Inductive effects due to strong resonance perturbation of the  $\pi$ -electron charge density. There is some evidence that alternation of  $\pi$ -electron density in conjugated system polarizes the  $\sigma$ -bonds.<sup>123</sup> The relative order of  $\pi$ -electron densities at the  $\alpha$ - and  $\beta$ -carbons is altered from pyridine to the pyridinium ion. In pyridinium ions this would have the effect of reducing the inductive polarization in the  $C_2-C_3$  bond. Then if the  $\begin{array}{c} H \\ | \\ C-C \\ | \\ H \end{array}$  coupling is determined by the polarity of the C-C bond, the sequence noted in this study becomes readily understandable.

The  $C^{13}-H^1$  coupling constants are about 5 cps larger at the  $\alpha$ - and  $\gamma$ -position and 3 cps larger at the  $\beta$ -position than that of toluene. These increases indicate larger s character in the C-H bonds and confirm an increase of inductive effects on protonation. The increases are smaller here than in methyl amines because of the larger number of  $\sigma$ -bonds available for inductive effects to travel through.

Unfortunately the ring  $C^{13}-H^1$  coupling constants could not be measured owing to the small concentration of the pyridinium

ions and the spectral complication. However, they are expected to be larger than those in pyridines.

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