

The University of Manitoba

THE DETERMINATION OF ELECTRON
DENSITIES BY PROTON MAGNETIC RESONANCE

by

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A Thesis
Submitted to
the Faculty of Graduate Studies and Research
University of Manitoba
In Partial Fulfillment
of the Requirements for the Degree
MASTER OF SCIENCE

Winnipeg, Manitoba
June, 1964



TO MY PARENTS

ACKNOWLEDGEMENTS

At this, my first step into chemical research, I would very much like to thank my many teachers, who, for so many years not only taught me, but were a constant source of guidance, understanding, and inspiration.

I would like to express my sincere thanks and gratitude to Dr. T. Schaefer, who introduced me to nuclear magnetic resonance spectroscopy, for his excellent advice and encouragement during the course of the present work.

My thanks are also due to Dr. E. Bock for his kind interest in this work and for many helpful discussions.

I am indebted to my friend and colleague Frank Hruska for many valuable discussions, and help that he has given me during the course of this work.

I would like to thank Barry J. Blackburn for providing a sample of pyridine hydrobromide.

To J. M. T. M. Gieskes, my thanks are due for providing highly purified formic acid and for determining the dielectric constants of some of my solutions.

I am indebted to the National Research Council of Canada for their financial support.

ABSTRACT

Proton shifts relative to internal benzene of pyridine hydrochloride, hydrobromide and hydroiodide in methylene chloride, acetonitrile, nitromethane and formic acid are reported. A model involving a hydrogen bonded ion-pair between the pyridinium cation and the counterion is discussed. It is assumed that the counterion reduces considerably the π -electron polarization in the pyridinium ion calculated for the isolated ion by the VESCF method. If the electric fields arising from the π -electrons, the counterion, and from the positive charge in the N-H^+ sigma bond are taken into consideration, the observed order of the C-H proton shifts is predicted. The N-H^+ proton shifts are sensitive to the counterion, the solvent and traces of water. In formic acid the N-H^+ proton shifts of the hydrochloride and hydrobromide are characteristic of the solvent only. In these two cases the N-H^+ proton does not exchange rapidly and an $^{14}\text{N-H}^+$ coupling constant of 67.6 ± 0.5 c/s is found.

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Chapter I

INTRODUCTION

A - THE NUCLEAR MAGNET

Nuclear magnetic resonance is based on the fact that isotopes of the elements with non-zero spin possess a magnetic moment which is characteristic of the particular non-zero spin isotope.

A nucleus which has a magnetic moment and a spin angular momentum behaves as if it were a spinning bar magnet (1,2), a nuclear magnet. This magnetization may be said to originate from the circulation of mass and charge associated with the spinning of the nucleus about an arbitrary axis (3).

Nuclear angular momentum is given by

$$(1) \quad \underline{P} = \hbar \underline{I},$$

where \underline{P} is the nuclear angular momentum vector

$$\hbar = \frac{h}{2\pi}; \text{ and } h \text{ is Planck's constant,}$$

\underline{I} is the nuclear spin vector.

The magnetic moment vector $\underline{\mu}$ is written as

$$(2) \quad \underline{\mu} = \gamma (\hbar \underline{I}) = \gamma \underline{P}$$

where γ is the magnetogyric ratio. The vector $\underline{\mu}$ is collinear with the vector \underline{I} .

Classically, for a proton, γ was calculated to be

$$(3) \quad \gamma = \frac{e}{2Mc}$$

where e is the charge on the particle, M is the mass and c is the velocity of light. Experimentally, equation (3) was found to be incorrect, and is normally written as

$$(4) \quad \gamma = \frac{ge}{2Mc}$$

where g is called the nuclear g factor (4,5), which is dimensionless and must be determined experimentally for each nucleus. Equation (2) then becomes

$$(5) \quad \underline{\mu} = g \cdot \frac{e\hbar}{2Mc} \underline{I}.$$

According to the principles of quantum mechanics, the spin vector \underline{I} has the magnitude $[I(I+1)]^{\frac{1}{2}}$ and consequently the nuclear angular momentum vector has the magnitude

$$P = \hbar [I(I+1)]^{\frac{1}{2}}.$$

The only measureable values of the spin I are given by m , the magnetic quantum number. \underline{I} , the spin vector, is found to be in one of $(2I+1)$ states or orientations, and therefore m may take on any of the $(2I+1)$ values

$$(6) \quad m = -I, -(I-1), -(I-2), \dots, (I-1), I.$$

Finally, we may write

$$(7) \quad \begin{aligned} \underline{\mu} &= \gamma \hbar \underline{I} \\ &= g \cdot \frac{e\hbar}{2Mc} \underline{I} \\ &= g \mu_0 \underline{I} \end{aligned}$$

where μ_0 is the nuclear magneton

$$(8) \mu_o = \frac{e\hbar}{2Mc} = 5.050 \times 10^{-24} \text{ erg gauss}^{-1}.$$

The structure of the atomic nucleus assumes that the spins of the protons and neutrons in the nucleus are paired, as are the spins of the electrons in an atom. Consequently, zero magnetic moments are obtained for nuclei with an even number of both protons and neutrons, since these have a net spin of zero ($I = 0$). Nuclei whose mass number is odd have half integral spin, while those of even mass number but odd charge number have an integral spin (6). Only nuclei for which $I \neq 0$ may a nuclear magnetic resonance spectra be obtained. The proton falls into this category, but C^{12} and O^{16} do not. For this reason nuclear magnetic resonance is so valuable in the study of organic compounds, since one can study the proton spectra without interference from the latter nuclei.

B - INTERACTION OF NUCLEAR MAGNET WITH A MAGNETIC FIELD

In the absence of a magnetic field, the energy of the nuclear magnet is independent of its orientation. However, when nuclei with magnetic moments are placed in a uniform, external, magnetic field \underline{H}_0 , this degeneracy is removed. The application of the external field causes a splitting into $(2I + 1)$ energy levels, known as the Zeeman splitting, corresponding to the $(2I + 1)$ values of m .

When the magnetic moment

$$\underline{\mu} = \gamma \underline{P}$$

is placed in a strong magnetic field \underline{H}_0 , a torque, \underline{L} , is exerted on it such that

$$\underline{L} = \underline{\mu} \times \underline{H}_0.$$

The energy of the interaction is

$$(9a) \quad E = -\underline{\mu} \cdot \underline{H}_0$$

$$(9b) \quad = -\mu H_0 \cos \theta$$

where θ is the angle between the magnetic moment and the magnetic field vectors, and $\mu \cos \theta$ is the value of the component of $\underline{\mu}$ along \underline{H}_0 , and may be written as μ_H .

Therefore, equation (9b) becomes

$$(10) \quad E = -\mu_H H_0.$$

According to equation (6), the only allowed values of the spin I are given by the $(2I + 1)$ values of m , which correspond to a particular component of μ along H_0 , or to the quantization of μ along H_0 . Hence equation (7) may now be written as

$$(11) \quad \mu_H = g \mu_0 m$$

where the values of m are those given in equation (6). Hence equation (10), which gives the $(2I + 1)$ energy levels, becomes

$$(12) \quad E = - mg \mu_0 H_0.$$

Since the selection rule for transitions of nuclei between energy levels is $\Delta m = \pm 1$, (7), then the energy difference between adjacent energy levels is given by

$$(13) \quad \Delta E = g \mu_0 H_0 = \gamma \hbar H_0.$$

For such a transition to take place, absorption of energy is required, and is given by the Bohr relation

$$(14) \quad \Delta E = h \nu_0,$$

where ν_0 is the frequency of the electromagnetic radiation.

Equating equations (13) and (14), we obtain

$$(15) \quad \nu_0 = \frac{\gamma H_0}{2\pi}.$$

This is the fundamental relationship for the resonance condition in nuclear resonance.

When nuclei are placed in a magnetic field, there is a Boltzmann distribution of the nuclei among the various nuclear spin states. For a proton ($I = \frac{1}{2}$) there are two such spin states (Fig. 1 and equation 12)(8).

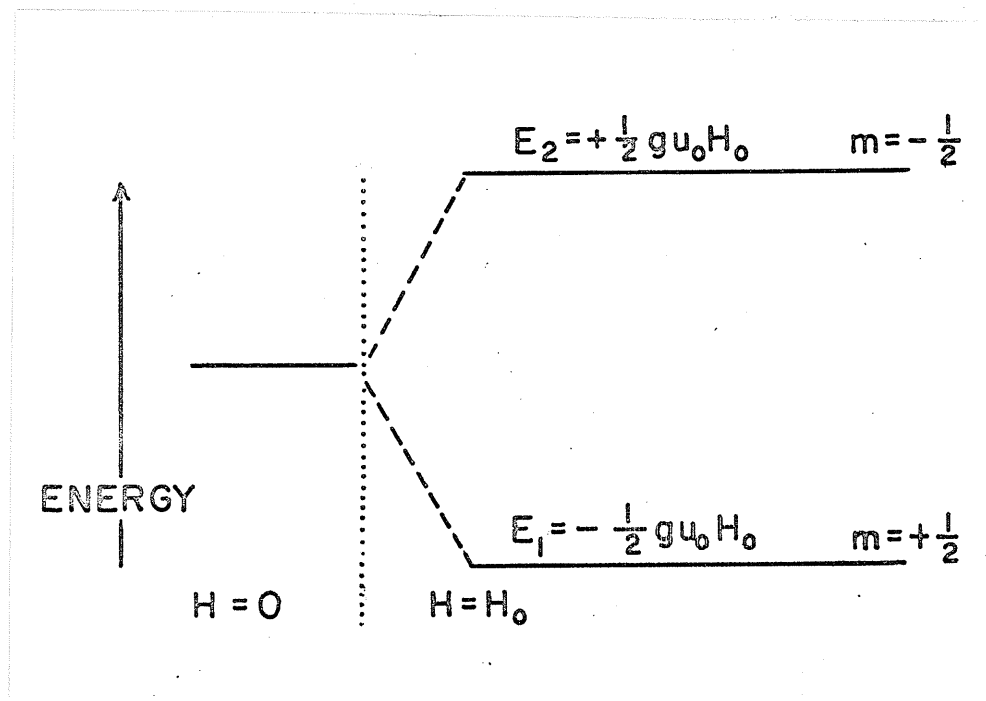


Figure 1: Energy levels for $I = \frac{1}{2}$.

When proton containing substances are placed in a magnetic field, there is a distribution of the protons between these two energy states, with a slight excess in the lower. It is due to this slight excess of nuclei in the lower state that the nuclear resonance phenomenon is observed. When radiation of the right frequency ν_0 is used to excite protons from one level to another, so as to satisfy equation (15), a net absorption of energy can occur, and the spectrum is

observed as an absorption of energy from the incident radiation.

For a bare proton, for $H_0 = 10^4$ gauss, the resonance frequency is 42.577 megacycles, which is in the radio-frequency portion of the electromagnetic spectrum.

C - MAGNETIC RESONANCE

A spinning nucleus may be treated from a classical viewpoint. If a nucleus with a magnetic moment μ is placed in a magnetic field, the field exerts a torque upon μ , tending to align it with the field. This forces the vector μ to precess about the direction of the applied field (9,10). The rate of precession is given by the Larmor precession frequency (11,12).

$$(16) \quad \omega_o = \gamma H_o,$$

where ω_o is the angular frequency of precession, and γ is the magnetogyric ratio. This equation describes the precession of a nucleus in its particular energy level, as given by equation (12).

Since

$$(17) \quad \nu_o = \frac{\omega_o}{2\pi},$$

where ν_o is the frequency of precession, equation (16) becomes

$$(18) \quad \nu_o = \frac{\gamma H_o}{2\pi}$$

and is equivalent to equation (15). Consequently, the separation of the energy levels equals the Larmor precession frequency multiplied by h ω_o .

In the nuclear magnetic resonance experiment, transitions among the energy levels are induced by a small oscillating field H_1 applied to the sample perpendicular to H_0 . This is achieved by passing radio-frequency ~~current~~ through a coil perpendicular to H_0 . At resonance, when the applied radio-frequency equals the frequency of the nuclear Larmor precession, the torque acting on the nuclear magnetic moment vector due to H_1 causes the vector μ to tip over with respect to H_0 (13). Consequently, transitions from a lower to an upper level are induced with absorption of a characteristic quantum of energy. This is the resonance condition for a single nucleus.

Resonance absorption may be observed by amplifying and rectifying the r.f. signal, since at resonance part of this radiation will be absorbed, causing a drop in the d.c. output. In actual practice, the applied radio-frequency is kept constant while the field is scanned. Descriptions of the nuclear magnetic resonance spectrometers are given in references (14) and (15).

Chapter II

THE CHEMICAL SHIFT

A - INTRODUCTION

Shortly after the discovery of the nuclear resonance phenomena, it was found that the resonance frequency for a particular nucleus may occur at a different value of the applied field, depending on the chemical environment of the particular nuclei. This effect arises because orbital electrons magnetically screen the nucleus so that the magnetic field at the nucleus differs slightly from the applied magnetic field. The difference in the resonance frequencies of a particular nucleus when it is located in different chemical environments is known as the chemical shift.

The chemical shift was first observed in metals, in 1949, when Knight (16) found discrepancies between the resonance frequencies of several metals as compared with their salts. In all cases it was found that the resonant frequencies were always higher for the metal than for the corresponding salt, for a constant value of the external, magnetic field. This shift was found to be directly proportional to the magnitude of the applied magnetic field, and was said to arise from the paramagnetic effect of the conduction electrons in the vicinity of the metal nuclei. Shortly afterwards, related effects were observed by Proctor and Yu (17) for the N^{14} nucleus. Two peaks were observed for NH_4NO_3 . The first

peak corresponds to the N^{14} nucleus in the NH_4^+ ion and the second to the N^{14} nucleus in the NO_3^- ion. Dickinson (18) soon found the same effect for the F^{19} nucleus while for protons the chemical shift was first observed by Lindstrom (19) and Thomas (20). All of these effects were observed as the precision and resolution of the available spectrometers improved.

The chemical shift may therefore be said to arise from a secondary magnetic field which is produced by the circulation of electronic charge induced by H_0 . The secondary field is proportional to, and acts in opposition to, the main magnetic field, thus decreasing the field as seen by the nucleus. Consequently, the field seen at the nucleus will be

$$(19) \quad H_e = H_0 (1 - \sigma),$$

where H_e is the "effective" field seen at the nucleus, H_0 is the external magnetic field, and σ is the shielding parameter and depends on the electronic environment in the vicinity of the nucleus.

According to equation (19), it is obvious that the separation of signals between the two nuclei will be directly proportional to the field seen by the molecule, and to the difference between the screening constants of the two nuclei. Since the difference in shielding is a function of the applied field, the chemical shift is most often expressed in terms of a dimensionless parameter δ

$$(20) \quad \delta = \left(\frac{H_S - H_r}{H_r} \right) \times 10^6 .$$

H_S is the resonant field of the nucleus being studied and H_r is the resonant field of the reference compound, often taken to be benzene, cyclohexane, water or tetramethylsilane. As defined above, δ is proportional to the shielding constants of both the reference and the sample compounds and is given in units of parts per million (ppm). When the chemical shift is defined in this manner, it is independent of the magnetic field strength and the frequency of the applied r.f. field.

B - MAGNETIC SHIELDING CONSTANT

A theoretical evaluation of the screening constant σ , introduced in equation (19), was first attempted by Lamb (21). He considered an isolated atom. When the atom is placed in a magnetic field, a diamagnetic circulation of the electrons is produced, which, in turn, produces a magnetic field at the nucleus opposing the applied field. This reduces the field seen by the nucleus, and may thus be related to the screening constant. The larger the diamagnetic currents, the larger is the shielding constant.

Ramsey (22) has calculated the shielding constant of nuclei in molecules, which have no resultant electron orbital or spin angular momentum in the absence of the external field. Unlike an atom, the electron distribution in a molecule is no longer spherically symmetrical. Ramsey found that his formula for the evaluation of the shielding constant contained two terms. The first term is similar to the Lamb formula, and corresponds to what the shielding would be if the whole electronic structure of the molecule rotated about the nucleus with the Larmor angular frequency. The second term, known as the second-order paramagnetic term, results from the lack of spherical symmetry of the electron distribution, and therefore

corrects for the hindrance to the free rotation around the nucleus. The actual numerical evaluation of the latter term is very hard, since it involves the exact wave functions of the excited, as well as the ground state of the molecule. Since these wave functions are seldom known, very few of these calculations have been carried out. For protons (23), there are no low-lying excited states, and therefore paramagnetic contributions should be small.

Further work on the evaluation of the δ constant was done by Saika and Slichter (24). After carrying out a study of fluorine resonance shifts, they were able to subdivide the components of δ into three terms. The first two terms were found to be equivalent to the two terms discussed previously. However, they added a third term which involves the contribution to the shielding constant of an atom from the rest of the electrons in the molecule. This effect is the combined effect of the diamagnetic and paramagnetic atomic currents from the other atoms in the same molecule.

A mathematical discussion of the various shielding parameters is given by McConnell (25) and Pople (26,27). The former has calculated the long-range dipolar shielding of protons, while Pople has dealt with a theoretical evaluation of the electronic currents induced in a molecule by an external, magnetic field.

Pople brings in the fourth component of the observed shielding constant σ , namely the contribution from interatomic currents. This effect is very important in aromatic molecules, since the π electrons form closed loops through which currents may flow. These in turn produce secondary magnetic fields which affect the proton screening. Ring currents will be dealt with more fully in the next section.

The observed screening constant σ may now be represented (28) as

$$(21) \quad \sigma = \sigma_d + \sigma_p + \sigma_o + \sigma_c.$$

σ_d = diamagnetic shielding of the nucleus.

σ_p = paramagnetic shielding of the nucleus.

σ_o = shielding due to the field produced by the magnetic moments induced in other atoms.

σ_c = contribution from interatomic currents.

C - CHEMICAL SHIFTS IN PROTON MAGNETIC RESONANCE

For a proton, with only a single 1s electron, the range of chemical shifts is the smallest of all nuclei (approximately 10 p.p.m.). Therefore, the electronic shielding is very small relative to the shielding of the heavier nuclei. For protons, diamagnetic shielding is important. Paramagnetic shielding, which arises from the mixing of ground and electronically excited states induced by the applied field, is very small.

The chemical shift δ will be a function of the electron density around the proton. Consequently, any changes in the electron density will be reflected by a change in the chemical shift. This has been illustrated by Meyer, Saika, and Gutowsky (29), who have determined the proton shifts of various organic compounds, with protons present in many different chemical environments.

It has also been observed that there is a rough correlation between proton acidity and the chemical shift. Very acidic protons appear at low field whereas highly shielded protons, as in methane, appear at high field. This is only a very rough correlation. Very often anomalies appear. These have to do with the low shielding of the proton, due to its lone electron. Therefore neighbouring atoms and electrons in distant parts of the molecule will have a large effect on the

proton shielding constant. An example of this is the acetylenic proton. This proton is chemically more acidic than the ethylenic proton, yet experimentally is found to be only slightly less shielded than the proton in ethane, and much more so than the proton in ethylene. Another anomaly occurs with aromatic protons, which appear to a much lower field than would be expected from their acidities. The shift of the aromatic protons may be explained by the ring current effect, while the acetylenic proton shift is explained by the magnetic anisotropy effect. These effects will now be discussed in more detail.

1. Ring Currents

When aromatic molecules are placed in a strong, external, magnetic field applied perpendicular to the plane of the molecule, the π electrons, which are free to circulate, will precess around the direction of the field. The aromatic ring then behaves as a superconducting loop of wire (30). The π electrons undergo the Larmor precession with an angular frequency ω :

$$(22) \quad \omega = \frac{eH_0}{2mc}$$

For benzene, with six π electrons, the resulting ring current i is

$$(23) \quad i = \frac{3e^2H_0}{2\pi mc},$$

where e is the charge on the electron, m is its mass and c is the velocity of light. The direction of flow is such that the magnetic field set up inside the ring is parallel to H_0 and opposed to it. Consequently, the lines of flux outside the ring at the protons are along the field, and thus give rise to a negative contribution to the screening constant of the aromatic protons. These protons then resonate at a much lower value of the applied field as compared to, for example, the protons in cyclohexane, (figure 2).

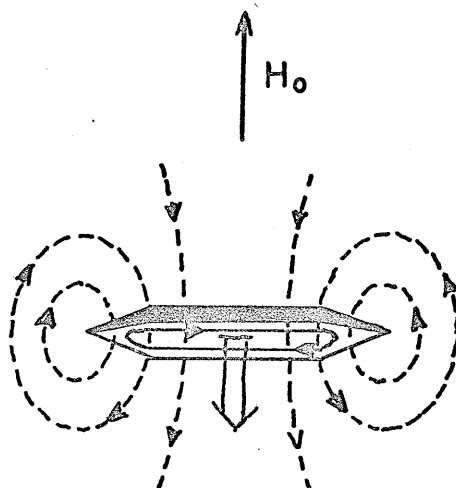


Figure 2: Ring Current Model of Benzene.

Pople (27) has made a simple estimate of the magnitude of the secondary magnetic field at the proton. He assumed that the magnetic field may be approximated by a magnetic dipole μ at the centre of the ring. He then studied the effect that this dipole has on the shielding of the ring protons. The dipole is written as

$$(24) \quad \mu = \frac{iA}{c} = \frac{3e^2 a^2 H_0}{2mc^2},$$

where A is the area of the benzene ring and a is its radius which may be approximated by the C-C distance. The dipole lies perpendicular to the ring so that its field opposes the external magnetic field. The secondary magnetic field H' at the proton due to the magnetic dipole will therefore be

$$(25) \quad H' = \frac{\mu}{(a+b)^3} = \frac{3e^2 a^2 H_0}{2mc^2 R^3},$$

where b is the C - H distance and $R = a + b$ is the distance of the proton from the centre of the ring.

If the applied field is in the plane of the molecule, the electrons are not free to circulate. Therefore averaging over all possible orientations of the molecule with respect to the external field, the ring current contribution to the screening constant becomes (dividing equation (25) by $3H_0$)

$$(26) \quad \Delta\delta = \frac{e^2 a^2}{2mc^2 R^3} \cdot$$

Pople has calculated the difference in the shift between benzene and ethylene protons to be -1.75 p.p.m. as compared to the experimental value of -1.4 p.p.m.

Waugh and Fessenden (31) recalculated the ring current effect using the free electron model. On this basis, they found that $\Delta\delta = -2.2$ p.p.m. The negative sign denotes that the ring current shift is to low field with respect to the ethylene resonance.

To check this value experimentally, Waugh and Fessenden found the difference in shift between the benzene protons and the ethylenic protons of cyclohexadiene-1,3 in carbon tetrachloride to be 1.48 p.p.m., with the benzene protons appearing at lower field. Schaefer and Schneider (32) redetermined this difference in shift, using cyclohexane as a solvent, and found it to be 1.5 p.p.m., in agreement with the value of Waugh and Fessenden. This difference in shift is the ring current shift for a single aromatic ring.

Jonathan et al (33) have studied chemical shifts and ring currents in condensed ring hydrocarbons, for which they calculated the ring current effect both theoretically and experimentally. They found the agreement between the two sets of values to be only fair. The

calculated shifts are always too large, since the calculation overestimates the ring current effect. It was also found that, for a fused ring system, one can not assume that the current intensity in each ring is the same as in benzene. For such molecules a greater portion of the electron current circulates around the periphery of the molecule and the ring current within any one ring may differ from that of benzene. Therefore, as the number of rings increases, the theoretical evaluation of the ring current becomes more difficult and less reliable.

2. Magnetic Anisotropy

Magnetic anisotropy has its origin in the field-induced diamagnetic or paramagnetic circulation of electrons on the neighbouring atom or the bond joining the neighbouring atom to the proton in question (34). If the magnetization of this neighbouring atom (or group) is highly anisotropic in character, the component of the secondary field at a neighbouring nucleus will not be averaged to zero by molecular motions. This will make a contribution to the measured chemical shift of this nucleus. For a linear diatomic molecule, for example a hydrogen halide, an external magnetic field will have a different effect on the electrons of the molecule, depending on whether the molecular axis is aligned parallel to or perpendicular to the external field. Since the C-X bond has cylindrical

symmetry, free diamagnetic circulation of electrons occurs when the bond axis is oriented parallel to the applied field. For this orientation the proton is displaced to a higher field than expected. When the applied field is directed at right angles to the C-X bond, free diamagnetic circulations are highly hindered. For this orientation, the resulting local fields are small. Therefore when an average is taken over all possible orientations of the molecule with respect to the external field, there will be a net proton resonance displacement to high field.

In the treatment of magnetic anisotropy, the currents on the neighbouring atom X are replaced by point magnetic dipoles at the centre of the atom and the effect that this dipole has on the neighbouring proton is then investigated (25,26). In the case where the X atom has cylindrical symmetry along the bond axis with the proton being studied, the magnetic susceptibilities parallel and perpendicular to the bond axis are respectively χ_{\parallel} and χ_{\perp} . The resulting contribution to the screening constant δ is then given by

$$(27) \quad \Delta\delta = \frac{\Delta\chi}{3R^3} (1 - 3 \cos^2 \theta) .$$

$\Delta\delta$ is the change in the shielding constant due to the magnetic anisotropy of the neighbouring group, and

$\Delta\chi$, the diamagnetic anisotropy, is defined as

$$(27a) \quad \Delta\chi = \chi_{//} - \chi_{\perp}.$$

R and θ define the position of the nucleus under consideration relative to the position of the point dipole. From equation (27), it is seen that $\Delta\sigma$ is zero when θ is $54^{\circ} 45'$, and will be positive (diamagnetic shielding-resonances shifted to high field) or negative (paramagnetic shielding), depending on whether θ is larger or smaller than this value.

Pople (26) has considered the diamagnetic anisotropy of acetylene, due to the magnetic anisotropy of the triple bond. If the field lies along the molecular axis, large diamagnetic currents may be induced in the molecule since the π electrons are free to precess around the magnetic field direction with the Larmor frequency. A field perpendicular to the molecular axis induces large paramagnetic currents, due to the mixing of the ground state with the $\sigma \rightarrow \pi$ excited states. Replacing the electron current at the carbon atoms by magnetic dipoles parallel to and in the direction of the applied field (paramagnetic effect) causes the lines of flux of the dipole to be opposite to the direction of the applied field at the protons. The net effect is a shielding of the protons.

The magnitude of the proton shift due to the magnetic anisotropy of substituent groups is hard to estimate accurately. However, protons close to the

anisotropic centre will be affected the most due to the $\frac{1}{R^3}$ dependence in equation (27). In nitrobenzene for example (35), the magnetic anisotropy of the nitro group has an effect on the ortho protons, but at the meta and para positions the effect is almost negligible.

D - SOLVENT EFFECTS

Large proton chemical shifts may arise from the large magnetic shielding or deshielding of a nucleus due to the medium in which the molecule is found (36). To measure the absolute value of the solvent effect on the solute proton shift, the solvent shifts should be measured as departures from the chemical shifts in the gas phase. Since the number of molecules whose spectra have been obtained in the gas phase are limited, the shift is corrected for the solvent effect by studying the solute in an inert solvent (n-hexane, cyclohexane, carbon tetrachloride), with the shift values extrapolated to infinite dilution.

Solvent effects in proton magnetic resonance have been studied theoretically and summarized by Buckingham, Schaefer and Schneider (37). They treat the observed screening constant $\bar{\sigma}$ as the sum of the screening constants for the isolated molecule ($\bar{\sigma}_{\text{gas}}$), and the screening constant due to the presence of the solvent, $\bar{\sigma}_{\text{solvent}}$. Thus

$$(28) \quad \bar{\sigma}_{\text{solvent}} = \frac{H - H_0}{H_0} ,$$

where H_0 is the applied field strength producing resonance in an isolated gaseous molecule, and H is the field required to produce resonance in the medium.

The screening constant δ_{solvent} is made up of several effects. We may write

$$(29) \quad \delta_{\text{solvent}} = \delta_b + \delta_a + \delta_w + \delta_e + \delta_c.$$

δ_b = contribution to δ due to the bulk diamagnetic susceptibility of the solvent.

δ_a = contribution to δ due to the solvent magnetic anisotropy.

δ_w = contribution to δ due to the van der Waals interaction between solute and solvent molecules.

δ_e = contribution to δ due to the reaction field of the solvent, which becomes very important for polar solute molecules and is known as the "polar effect".

δ_c = contribution to δ due to specific molecular interaction or complex formation in the solution.

1. Bulk Susceptibility Effect δ_b

When a liquid sample is placed in a magnetic field with an external reference, a correction involving the difference between the bulk diamagnetic susceptibilities of the reference and the solvent must be applied. The solvent molecules are diamagnetically polarized. This

polarization will have an effect on the solute molecules present in the solution due to the production of secondary magnetic fields. Consequently, when external references are used, the susceptibilities of the reference solution and the solution being studied are different. If the sample is contained in a spherical tube, this contribution is zero; if the sample is contained in a cylindrical tube the contribution σ_b is given by (37),

$$(30) \quad (\sigma_b)_{\text{cylinder}} = \frac{2}{3} \pi \chi_v$$

where χ_v is the volume magnetic susceptibility (38). No correction is required when internal references are used, of course.

2. Anisotropy in the Susceptibility of the Solvent 6a.

Magnetic anisotropy effects have been discussed previously for aromatic (benzene) and linear (acetylene, or carbon disulphide) molecules. When solvent effect studies are carried out in any of these solvents, the observed shifts may readily be explained by the anisotropy in the shape and the diamagnetic susceptibilities of the solvent molecules. Buckingham et al (37), classify the anisotropy in the shape into two extreme cases, namely into "rod-shaped" and "disc-shaped" solvent molecules.

With disc-shaped solvent molecules (benzene), the most favourable configuration of the solute molecules with respect to the solvent is immediately above or below the plane of the ring. In this position, the solute lies as close as possible to the solvent molecule. However, the benzene ring has large, induced magnetic moments when the ring is at right angles to the field. Since the induced moment is diamagnetic, an increase in the shielding of the solute nucleus occurs, with a resulting solute proton shift to high field.

Schneider (39) studied the chloroform proton resonance shifts in benzene and found that the chloroform proton resonance appeared nearly 1 p.p.m. to high field as compared to the chloroform proton resonance in a dilute solution of chloroform in cyclohexane (cyclohexane is taken as an inert solvent). The fact that a high field shift of the proton is observed in benzene may be explained by the presence of the anisotropy in the diamagnetism. The chloroform proton is kept above or below the plane of the benzene ring by a weak hydrogen bond between the proton and the benzene π electrons, thereby placing it in a region of increased shielding (figure 3).

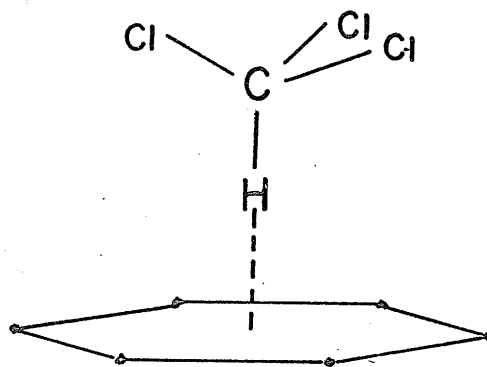


Figure 3: Formation of a weak hydrogen bond between chloroform and the benzene π electrons.

Another example involving a different type of interaction is given by Schneider (39) and is illustrated by acetonitrile when it is dissolved in benzene.

Schneider observed that in the benzene solution the acetonitrile resonance has been displaced to high field by 56.8 c/s (at 60 Mc/s) relative to the acetonitrile resonance in neopentane (assume that neopentane is an inert solvent in which there will be no specific interaction of the solvent and the acetonitrile molecules

other than the weak van der Waals interactions). This high field shift may be explained by an induced dipole interaction of the acetonitrile with benzene. Since benzene has a large polarizability in the plane of the ring, the dipole is induced as shown in figure 4. The resulting attraction will locate the methyl group over the aromatic ring in a preferred mutual orientation. Consequently, this group appears in the region of increased shielding, and the proton resonance is shifted to higher field.

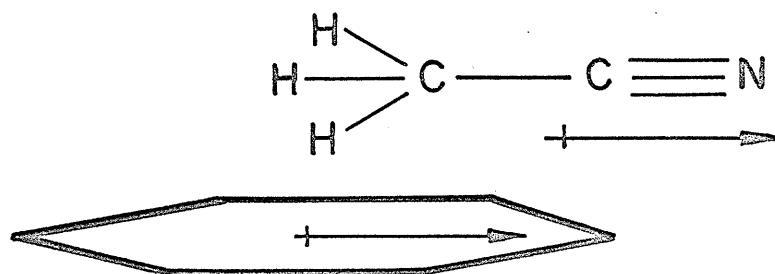


Figure 4: Interaction of acetonitrile with the benzene π electrons.

When dealing with rod-shaped solvent molecules, which have a high magnetic susceptibility along the internuclear axis, a net decrease in shielding is observed for the solute proton resonance which leads to low-field shifts. The most favourable configuration for a solute in such a solvent is either above or below the rod, rather than at either end. The solute molecule therefore lies in the region of deshielding, due to the paramagnetic effect induced in the bond when it lies perpendicular to the external field. Averaging over all possible orientations of this rod in the field, the net effect is to cause a low-field shift from the resonant field in a completely isotropic medium.

Buckingham et al (37) derived a relationship for δ_a for disc-shaped and rod-shaped solvent molecules. Using this relationship, they predict a low-field shift of -0.5 p.p.m. for methane in CS_2 , relative to methane in hexane. The observed shift is -0.42 p.p.m.

3. van der Waals Forces δ_w

In 1937, London (40) described forces of interaction between completely non-polar molecules, calling them dispersive forces. They were explained by saying that if one looks at the electronic motion around a

non-polar molecule (N_2 , O_2) over a finite length of time, no interaction is observed. However, at any one instant of time, an instantaneous attraction may be observed due to the fluctuating electric field of one molecule interacting with the instantaneously induced electric moment in a neighbouring molecule. These dispersive forces are present in both polar and non-polar molecules, but, since this interaction is very slight, in polar molecules it is outweighed by other interactions.

The attractive forces will depend on the magnitude of the induced dipole moment and hence on the polarizability of the neighbouring molecule: In intermolecular solvent effects, shifts due to δ_w are important and cause low-field shifts (37). Intermolecular dispersive forces are believed to affect the shifts in two ways.

(a) Interaction between the solvent and the solute in its equilibrium configuration causes a distortion of the electronic environment of the nucleus. This distortion causes an expansion of the electron cloud about a nucleus and hence leads to decreased nuclear magnetic shielding. A rough correlation between δ_w and the number of electrons in a solvent molecule may be expected.

(b) Molecular motion at moderate temperatures leads to a time-dependent distortion of the symmetry of the C-H bonds, and hence to a negative shift. When "side attack" of the bonds is possible, this effect may become very important. This distortion of the bond symmetry increases the paramagnetic effect, and consequently deshields the nucleus.

Marshall and Pople (41) have carried out a calculation of the nuclear magnetic screening of a hydrogen atom placed in an electric as well as a magnetic field. They found that the magnetic screening of the nucleus by the electrons is reduced in all directions by the application of a uniform electric field, the reduction being greatest when the magnetic field is perpendicular to the electric field. The decrease in the shielding constant σ due to σ_w is thus explained by the partial removal of electrons from the vicinity of the nucleus by the electric field.

The dispersion effect has been studied by Buckingham et al (37), who measured the shift of the proton resonance signal of methane dissolved in various solvents relative to the shift obtained for gaseous methane. For solvent molecules having a negligible diamagnetic anisotropy, a simple linear correlation between

the "solution-gas" methane proton shift and the van der Waals interaction energy may be expected. But the van der Waals interaction energy can not be evaluated directly. Assuming a close proportionality between solvent-solvent and solvent-solute molecular interaction, an indirect measure of molecular interaction between the solvent and methane molecules is the heat of vaporization of the solvent at its boiling point. Plotting the proton resonance shift of methane in dilute solution in various solvents against the heat of vaporization of the solvent, Buckingham et al (37) obtained a linear plot for non-polar and isotropic solvents. They observed the expected increasing shift of the methane resonance to low field with increasing interaction between the methane and solvent molecules. Aromatic and rod-shaped solvent molecules displayed the usual deviations.

Schaefer, Reynolds and Yonemoto (42) have recently suggested that intramolecular van der Waals dispersive forces may also cause low-field shifts. These forces explain the anomalous shifts of the ortho C^{13} atoms and protons in halobenzenes, the ortho methyl protons in mesitylene, the α -protons in methyl halides and the low-field shifts of the α -protons, β -protons and β - C^{13} atoms in ethyl halides. The α - C^{13} shifts in methyl and ethyl halides can be

attributed to magnetic anisotropy effects of the C-X bond.

These intramolecular van der Waals dispersive forces are probably brought about by the same two effects that cause intermolecular dispersive forces. The first effect involves an interaction in the equilibrium configuration which causes a distortion of the electronic environment of the nucleus. The second effect may arise from internal rotations and vibrations of the substituent group which may induce a time-dependent distortion of the C-H bond symmetry.

4. Polar Effect 6E

If a polar molecule is dissolved it will polarize the surrounding solvent molecules. This polarization leads to an electric field - the "reaction field" R - at the dipole. The effect of this reaction field is to cause a secondary polarization of the solute dipole to an extent depending on the polarizability of the solute molecule. If the solute molecule is sufficiently symmetrical, then the reaction field will be parallel to and proportional to μ , the permanent dipole moment of the solute molecule. Reaction field effects have been studied by Buckingham, Schaefer, and Schneider (37), Buckingham (28), and Hruska, Bock and Schaefer (43).

An estimate of the value of the reaction field can be obtained from the Onsager model (28) in which the solute molecule is represented by a sphere of radius r containing a point dipole of moment μ at its centre in a continuous medium with a uniform dielectric constant ϵ . The reaction field \underline{R} is (28)

$$(31) \quad \underline{R} = \frac{2(\epsilon - 1) \underline{m}}{(2\epsilon + 1)r^3} = \frac{2(\epsilon - 1)(n^2 - 1)}{3(2\epsilon + n^2)} \frac{\mu}{\mathcal{L}}$$

where

$$(32) \quad \underline{m} = \mu + \mathcal{L} \underline{R}.$$

n is the refractive index of the solute for sodium D light and \underline{m} represents the total dipole moment of the solute in the medium. \mathcal{L} , the polarizability of the sphere, is defined as

$$(33) \quad \mathcal{L} = \frac{(n^2 - 1) r^3}{n^2 + 2}.$$

Diehl and Freeman have carried out similar calculations for solute molecules of ellipsoidal shape (44).

The influence of an electric field on shielding parameters has been studied by Marshall and Pople (41), and Buckingham (28). Marshall and Pople found the reduction in the shielding of atomic hydrogen proportional to the square of the applied electric field E . The dependence on E^2 is required for symmetry reasons, since a reversal of the field cannot change the sign of the shielding parameter of the atom.

Buckingham (28) found that the effect of a field acting along an X-H bond will either increase or decrease the electron density at the proton, depending on the direction of E . A field perpendicular to the X-H bond destroys the axial symmetry of the bond, leading to a reduction in shielding. However, a change in the direction of the field E should not change the sign of the shielding constant. Hence, the net result is a low field shift proportional to E^2 .

Buckingham's treatment gives a calculated contribution to the shielding of a proton in an X-H bond of

$$(34) \quad \sigma_E = -aE \cos \theta - bE^2,$$

where E is the magnitude of the field, θ is the angle between the X-H bond axis and the direction of the field, and a and b are constants. For the constants, Buckingham obtains a value of $a = 2.0 \times 10^{-12}$ and $b = 1.0 \times 10^{-18}$ electrostatic units, Musher (45) quotes theoretical and experimental values ranging from 2.0 to 3.4×10^{-12} electrostatic units for a and suggests 7.38×10^{-19} electrostatic units for b , while Hruska et al (43) obtain values of $a = 1.3$ and 1.6×10^{-12} electrostatic units.

Combining equations (31) and (34) yields the contribution to the shielding of the X-H proton due to the reaction field R

$$(35) \quad \sigma_E = - a \times 10^{-12} \frac{2}{3} \frac{(\epsilon - 1)(n^2 - 1)}{(2\epsilon + n^2)} \frac{\mu}{d} \cos \phi,$$

where ϕ is the angle between μ and the X-H bond. The E^2 term is neglected since, in the most extreme case, it is only 8% of the linear term (43). Equation (35) predicts a linear variation of the proton shielding with the dielectric function of the medium

$$(36) \quad \left(\frac{\epsilon - 1}{2\epsilon + n^2} \right).$$

Since for most solutes (solid or liquid) $n^2 \sim 2.5$ (28), equation (35) becomes

$$(37) \quad \sigma_E = -2 \times 10^{-12} \frac{(\epsilon - 1)}{(2\epsilon + 2.5)} \frac{\mu}{d} \cos \phi$$

where Buckingham's value (28) for a is used.

5. Complex formation, or specific molecular interaction σ_c

Very often in solutions, strong, specific interactions between solvent and solute take place. An interaction between a proton on one molecule and a F, O, N, or Cl atom on another molecule is known as hydrogen bonding (46).

Hydrogen bonding causes a low field shift of the proton involved. The proton shift is also found to be dependent on the temperature and the degree of dilution. Increasing the temperature or decreasing the concentration tends to shift the proton resonance to high field, since the degree of association is decreased by both of these effects.

In hydrogen bonding, the proton is electrostatically attracted to the electronegative group. Three general effects must be considered which would account for the proton shift.

First of all, the formation of the electrostatic bond decreases the electron density around the proton and, at the same time, inhibits the diamagnetic circulations about the hydrogen atom. Both of these effects predict a reduction in screening and hence a shift to low field.

Secondly, the formation of a hydrogen bond will make the proton shift dependent on the electron circulations around the electronegative atom. This is an anisotropy effect, which should give rise to a high field shift (corresponding to the intramolecular neighbour-anisotropy effect). Since the hydrogen bond length is usually much greater than the intramolecular bond distances, then it is seen from equation (27) that this effect will be small. Consequently, any high field shifts, if present, are hidden by the large low field shifts arising from electrostatic effects.

The third effect that must be considered is the formation of a charge transfer complex of the type



Such a complex requires the donation of electrons from the Y molecule into the X-H bond, which leads to an increase of the electron density on the hydrogen atom. Thus the formation of such a complex would cause a high field proton shift which, if present, is completely masked by the electrostatic effect.

When charged ions are present in the solution, large electrostatic forces, similar to the ones present in hydrogen bonding, also exist in solution. This bond formation can be referred to as ion pair formation, counter ion attraction, or ion association. The existence of ion pairs in solution is seen from the deviations from ideal behaviour of conductances and activities of ionic solutions (47,48).

Regarding the theories of ion association, Bjerrum (49) found that the distance for which the probability of finding an ion at a given distance from an oppositely charged ion is a minimum is given by

$$(38) \quad q = \frac{z_i z_j e^2}{2 \epsilon_{kT}},$$

where Z_i, Z_j = valencies of the two ions.

e = unit of charge.

ϵ = dielectric constant of the solvent.

k = Boltzmann constant.

T = absolute temperature.

q = distance of separation of the charge centres.

Bjerrum proposed that ions separated by a distance smaller than q should be treated as ion pairs. All other ions are assumed to be in the free state. Consequently, if the sum of the ionic radii exceeds q , then it is assumed that the ions are completely dissociated. Therefore Bjerrum's equation gives a qualitative estimate on the possibility of ion pair formation.

Reynolds and Schaefer (48) studied proton exchange reactions of substituted anilines in trifluoroacetic acid. They found that q is approximately seven \AA for the acid molecule. Since the distance of closest approach of charge centres of the anilinium ion and trifluoroacetate ion is approximately two \AA , then anilinium trifluoroacetate can definitely exist as ion pairs. These ion pairs can only be formed between the anilinium ions and the trifluoroacetate ions if there are no directly intervening solvent molecules. The trifluoroacetic acid molecules are quite bulky and may solvate the two ions, but must not prevent the close approach of charge centres.



From equation (38) it is seen that the dielectric constant of the solvent affects ion association. The larger the dielectric constant, the more easily do the ion pairs dissociate. The solvating power of the solvent and the solvation properties of the ions must also be considered. It is known that small, highly-charged ions are easily solvated. Hence an increase in the solvation of the individual ions relative to the solvation of the ion pair will decrease the possibility of ion pair formation.

Chapter III

ELECTRON DENSITY AND THE CHEMICAL SHIFT

A - FIRST ORDER APPROXIMATION

It is known that the chemical shift of aromatic ring protons tends to reflect the π electron density on the carbon atom to which the proton is bonded. This is most readily seen by the fact that in substituted benzenes, strong electron-releasing substituents increase the shielding of the ring protons, whereas electron-withdrawing substituents decrease the shielding (35).

Fraenkel, Carter, McLachlan and Richards (50) were the first to provide evidence for a simple, empirical, linear relationship (as a first order approximation) between the proton chemical shift $\Delta\delta$ relative to benzene for an aromatic system, and the local excess charge Δe on a carbon atom adjacent to the proton in question. (On substituting equation (19) into equation (20) the relationship between the change in the screening constant $\Delta\delta$ and the proton chemical shift δ may be obtained. This relationship is of the form $\Delta\delta(\text{p.p.m.}) = \delta_r - \delta_s = \delta(1 - \delta_r)$, where δ_s is the screening constant of the proton being studied and δ_r is the screening constant of the reference proton. Since for protons δ is of the order of 10^{-5} , therefore $\Delta\delta$ and δ may be used interchangeably.) This relationship is given as

$$(39) \quad \Delta\delta = k \Delta e .$$

The chemical shift $\Delta\delta$ is given in units of parts per million from a benzene reference, and the excess π electron density Δe is given in fractions of an electron. Benzene is chosen as the basic reference both for the proton chemical shift and the excess charge density since the π electron density on the carbon atoms is unity. Therefore $\Delta e = 0$. The chemical shift is positive for proton resonances appearing to higher field from the benzene resonance, and negative for resonances at lower field. By this convention the constant k , which is determined experimentally, is positive (32).

Fraenkel et al (50) in their study found the constant k to have a value approximately 10 p.p.m. per electron. Spiesscke and Schneider (51), in their determination of the π electron densities in azulene from C^{13} and proton resonance shifts, determined k to have a value approximately 10.6 p.p.m. per electron. Schaefer and Schneider (32) studied the electron density distribution and proton magnetic resonance shifts in aromatic systems. They re-determined the value of the constant experimentally under a wide range of conditions. Error limits were also set on its value. The constant was determined by these authors to have a value of 10.7 ± 0.2 p.p.m. per electron.

The constant k may be determined in two ways:

- (a) by measuring $\Delta\delta$ for systems in which Δe is known, and
- (b) by forming positive or negative ions.

(a) The best method of evaluating the constant k is based on the proton resonance shifts of the iso-electronic series cyclopentadienyl anion ($C_5H_5^-$), benzene (C_6H_6) and the tropylium cation ($C_7H_7^+$). The excess π electron density in each case is known. The proton chemical shifts of this series have been measured originally by Leto, Cotton, and Waugh (52), Fraenkel *et al* (50) in their determination of the constant k , and by Spiesecke and Schneider (51). These shifts were confirmed by Schaefer and Schneider (32) who also investigated the possible solvent and ion association effects.

In the above series of compounds each molecule has six π electrons to contribute to the ring current. The radii of the rings are so similar that the screening constant is, in every case, almost the same. In the two ions, $C_5H_5^-$ and $C_7H_7^+$, the aromatic ring current is taken to be the same as in benzene and only small corrections are applied to allow for the effect of differing ring size. After applying these small ring current corrections, Schaefer and Schneider (32) found the shifts to be -1.98, 0, and +1.73 p.p.m. respectively for $C_7H_7^+$, C_6H_6 , and $C_5H_5^-$. The excess π electron densities Δe are -0.143, 0, and +0.20. These values for the proton chemical shifts were obtained after various salts in several solvents at various concentrations were examined, and correspond to the proton shift of tropylium bromide,

benzene, and cyclopentadienyl lithium in acetonitrile. The constant k was determined by plotting the chemical shift vs. the excess π electron density. The best straight line through these points gave a value for $k = 10.7 \pm 0.2$ ppm. per electron (32).

In this series of compounds, the question of small differences in the degree of hybridization of the carbon orbitals in the 5-, 6-, and 7- membered aromatic rings must also be considered. This will make some contribution to the measured proton shifts, but the magnitude of this effect cannot be reliably estimated (32). For this reason Schaefer and Schneider conclude that the constant k has a value of 10.7 ± 0.2 p.p.m. per electron, but a more "realistic error" may be approximately ± 1.0 p.p.m. per electron.

(b) The second method of evaluating the constant k involves measuring the proton shifts of aromatic ions relative to the proton shift of the corresponding neutral molecule. The total π electron density is altered by exactly one unit charge. Consequently, if the difference is obtained between the proton shift of the aromatic ion and the neutral molecule, the sum of these shifts over all the protons of the molecule must correspond to $\Delta e = 1$, and therefore $\sum_i \Delta \delta_i = k$.

MacLean and Mackor (53) determined the excess charges in carbonium ions, and arrived at a value for k equal to 13.4 p.p.m. per electron. However, using a proper correction for the ring current, the value of the constant k as derived in this manner becomes 11.8 p.p.m. per electron (32). This is a self-consistency check on the value of k obtained by studying the series $C_5H_5^-$, C_6H_6 , and $C_7H_7^+$.

Schaefer and Schneider applied the linear relationship to calculate the electron densities on various carbon atoms in many aromatic systems. Using the value of $k = 10.7$, they compare the electron densities derived from the proton shifts with those obtained by theoretical means. It was found that in all aromatic systems that were studied, the measured proton shifts when used in equation (30) always gave the correct sign of the excess charge $\Delta\rho$. This is strong evidence in favour of the linear relationship, at least as a first order approximation.

Among the systems studied by Schaefer and Schneider was the pentalenyl dianion which consists of two fused five-membered carbon rings. Since the two carbon atoms joining the two rings do not contain a bonded proton, their π electron densities cannot be directly determined experimentally. However, the electron

density of these two carbon atoms may be obtained from the experimental shifts indirectly. Since the electron densities on all the other carbon atoms are known from chemical shift measurements, and the total excess charge on the dianion is two, the electron density on the two carbon atoms in question may be determined by difference. The electron density determined in this manner agrees very well with the electron density obtained by molecular orbital calculations. This is further evidence as to the validity of the approximation that is made in postulating the linear relationship (equation 39), and at the same time serves as a "self-consistency" check on the value of the constant k .

Schaefer and Schneider found that in at least one case the electron densities which were determined from the proton resonance shifts did not agree with the theoretical electron densities. For the non-alternant hydrocarbon acepleiadylene, which contains four aromatic rings in a pyrene-type structure, it was found that there was a preference for the excess electron charge to reside in the 7-membered ring rather than in the 5-membered ring at the opposite end of the molecule, as is indicated by simple Huckel Molecular Orbital calculations. The reason for this is presently not known.

Further disagreement has also been observed between the experimental and theoretical electron densities for the pyridinium ion. The protonation of pyridine has been studied by proton resonance techniques by Smith and Schneider (54). The determination of electron densities of this ion and the discrepancies that have been observed will be discussed in a later section.

Various other workers have confirmed the presence of a relationship between the proton chemical shift and the excess charge densities on the adjoining carbon atoms in aromatic systems.

Zweig et al (55) have studied the proton resonance spectra of the methoxybenzenes. It was found that a plot of the aromatic proton chemical shift against the calculated charge densities at attached ring positions in nineteen methoxybenzenes gave a straight-line. These results reaffirm the underlying relationship expressed by equation (39) and the proportionality constant of ~ 10 p.p.m. per electron for aromatic ring protons.

Waack and Doran (56) have applied the linear relationship in their determination of electron densities of aromatic organolithium compounds. Their values are in reasonable agreement with SCF values. Sandel and Freedman (57) found good agreement for the π electron densities of

arylmethyl carbanions as calculated from the proton chemical shifts with those from molecular orbital calculations.

Schaefer and Yonemoto (58) have recently applied the linear relationship for the first time to an aliphatic system in their study of the gas phase proton shifts of substituted ethylenes. Using values for the excess charge Δe obtained from theoretical calculations, they obtained the contribution to the chemical shift due to this excess charge using equation (39). This contribution was added to the shift due to the electric dipole originating from the substituents, as well as to the contribution arising from the magnetic fields from a point dipole representing the magnetic anisotropy of the substituents. The sum of these three effects yields values for the chemical shifts which were found to be in reasonable agreement with the experimental shifts.

B - PERTURBING EFFECTS

Four perturbing effects must be considered before equation (39) may be applied to the evaluation of local π electron densities. These effects contribute to the experimental proton shifts in addition to those caused by the altered electron density. Large contributions arising from any one of these effects seriously limit the reliability with which the electron density can be evaluated. Corrections may often be applied to the measured chemical shifts. If not, the perturbing effect can often be lessened, or altogether removed by the proper choice of experimental conditions. Schaefer and Schneider (32) summarize these four effects, which are:

- (a) the magnetic anisotropy of substituents or of hetero atoms in the aromatic ring,
- (b) ring current effects of neighbour rings in polycyclic aromatic compounds,
- (c) ion association effects of aromatic ions,
- and (d) solvent effects.

(a) Magnetic anisotropy, which has been discussed in Section II C 2, is the most difficult to correct for. The contribution to the screening constant $\Delta\delta$ due to magnetic anisotropy is given by equation (27).

The magnetic anisotropy due to the effect of substituent groups on an aromatic ring cannot be estimated very accurately. As seen from equation (27), a substituent group will affect mainly those protons in the aromatic ring that are close to the anisotropic centre. In nitrobenzene, for example, the magnetic anisotropy of the nitro group has a large effect on the ortho proton shift, but at the meta and para positions the effect is almost negligible.

Hetero atoms in aromatic rings also complicate the derivation of electron densities from proton chemical shifts. Baldeschwieler and Randall (59,60) found that the magnetic anisotropy of the nitrogen atom in pyridine gives rise to a slight unshielding contribution to the resonance shift of the ortho protons. It was observed that on protonation there is a large low field shift of the meta and para protons, while the ortho proton resonance is little affected when a comparison is made between the proton shifts in pyridine and the pyridinium ion. This was also observed by Smith and Schneider (54). Baldeschwieler and Randall have suggested that the signals from the ortho protons of pyridine are affected

by a large paramagnetic contribution to the magnetic susceptibility due to the low-lying $n \rightarrow \pi^*$ transition. Therefore, on protonation, the addition of a positive charge to the pyridine molecule leads to a displacement of the meta and para proton signals to low field by 1.07 p.p.m. and 1.22 p.p.m. respectively, whereas the ortho proton signal is shifted to low field by only 0.25 p.p.m. (54). The paramagnetic contribution to the magnetic susceptibility of the nitrogen atom may also explain the high field shift of the N^{14} resonance signal on protonating pyridine. The actual value of the shift is 123 ± 11 p.p.m. (59, 60).

Gil and Murrell (61) have attempted a quantitative estimate of the contributions to the proton and nitrogen chemical shifts in pyridine and the pyridinium cation. They are able to show that the high field shift of the nitrogen signal on protonating pyridine can indeed be accounted for by the large paramagnetic contribution to the susceptibility of the nitrogen atom. They calculated the change in the paramagnetic contribution on the nitrogen chemical shift on protonation to be 97 p.p.m., a value which fortuitously agrees, since many approximations have to be made, with the experimental shift of 123 ± 11 p.p.m.

Gil and Murrell also considered the changes in the proton chemical shifts in pyridine due to the differences between the magnetic susceptibility of the

carbon and nitrogen atoms, as well as due to the substitution of a $\text{C}=\text{H}$ dipole by a nitrogen dipole arising from the lone pair electrons. They calculated that the ortho proton signal in pyridine will be shifted to low field by 0.33 p.p.m. and the para proton signal to high field by 0.03 p.p.m. relative to benzene due to the difference in the magnetic anisotropy of N and $\text{C}=\text{H}$. The meta protons are shifted to low field by 0.01 p.p.m. relative to benzene. As a result, the ortho proton signal in pyridine is expected to lie about 0.36 p.p.m. to low field of the para proton signal. Evaluating the change in the proton shielding from an electric field at the protons on replacing a $\text{C}=\text{H}$ dipole by a dipole associated with the nitrogen lone pair electrons, it was found that the contributions to the chemical shifts were -0.52, -0.19, and -0.14 p.p.m. respectively for the ortho, meta, and para protons. The predicted difference in the shift between these protons ($\sigma_p - \sigma_o$) is thus 0.74 p.p.m., as compared with the experimental value of 0.93 p.p.m.

It is thus seen that the low shielding of the ortho protons in pyridine, relative to the meta and para protons, is appreciably influenced by both the magnetic anisotropy of the nitrogen atom and by the local dipole moment associated with the nitrogen lone pair electrons. After correcting the observed pyridine proton resonance shifts for the above effects, and assuming that the

remaining part of the shifts can be correlated with the π electron density at the attached carbon atom, Gil and Murrell derive π electron densities for the pyridine molecule using the value of $k = 10$ p.p.m. per electron. This π electron distribution is found to be in good agreement with the theoretical π electron densities calculated by Brown and Heffernan (62). In their calculations, however, the contribution to the proton chemical shift arising from the π electron densities on the ring carbon atoms other than the attached carbon atom, or that arising from the change in the reaction field due to the polarization of the medium has not been taken into account (61).

Gil and Murrell have also calculated the changes in the proton screening constant when $\text{C} - \text{H}$ is replaced by $(\text{N} - \text{H})^+$. Their results indicate an almost complete absence of paramagnetic effects in the pyridinium ion, which have such a large influence on the ortho protons in pyridine. This in part explains the small shift of the ortho proton signal of pyridine on protonation relative to that of the meta and para protons.

(b) Ring current effects can be corrected for much more easily than other magnetic anisotropy effects. Ring currents have already been discussed in full detail in section II C 1. Several important points must be mentioned here however.

Since benzene has been chosen as the basic reference, no ring current corrections are required for monocyclic systems. For five or seven membered rings, the corrections are small and introduce little error. However, for a polycyclic ring system, the resonance shift of a particular ring proton must be corrected for the ring current of neighbour rings to bring the shift in line with the benzene reference. Schaefer and Schneider (32) found that the correction δ_c for a particular proton due to the ring current in a neighboring ring may be expressed as

$$(40) \quad \delta_c = 12.0 \left(\frac{a^2}{R^3} \right),$$

where a (in \AA units) is the radius of the neighbouring ring, and R (in \AA units) is the distance of the proton being considered from the centre of the neighbouring ring. The contribution to the shift due to the ring current δ_c is expressed in p.p.m. For bicyclic systems this correction is accurate to within 0.1 p.p.m. For larger molecules, however, the number of corrections increase and hence the errors begin to mount.

(c) Before electron densities may be determined for aromatic positive or negative ions, from proton magnetic resonance shifts, ion association effects must be considered. These effects have already been mentioned in section II D 5. The counterion will cause a shift of the proton resonance of the aromatic ion being studied. This effect is most important with small aromatic ions, and in ions where the charge is largely concentrated on one atom in a molecule (anilinium ion). With larger ions, in which the charge is displaced over the whole molecule, counterion association effects are much smaller. Ion association effects may be minimized by a high degree of dilution of the ionic species with a solvent of high dielectric constant.

(d) Solvent effects will also influence the chemical shift, and hence the determined electron densities (section II D).

C - SECOND ORDER APPROXIMATION

When a comparison is made between the experimentally derived charge distributions for an aromatic system with that calculated from simple Huckel molecular orbital calculations, it is seen that the latter calculations tend to overemphasize the charge differences at various carbon atoms in a molecule. The experimental electron densities indicate that the excess charge tends to be more uniformly distributed over the molecule (32). This may be explained in terms of a π - σ interaction.

Since the proton resonance responds to an altered π electron density on a carbon atom due to an essentially electrostatic polarization of the C - H σ bond, it is also possible that the σ bonds to neighbouring carbon atoms will similarly be polarized, thus contributing to the resonance shift of their bonded protons. Therefore the densities derived from proton resonance shifts give a measure of the combined local density alteration in both the σ - and π - electron systems, whereas the densities calculated by simple molecular orbital theory yield an "idealized" local density for the π electron system only.

For neutral molecules this basic difference is not very pronounced. However, for aromatic ions, where the excess charges are greater, the difference in the resulting density distributions is increased. Consequently, for aromatic ions, as well as for heterocyclic aromatic

molecules, or molecules containing highly polar substituents which would create strong electric fields at the protons due to bond dipoles (hydroxy-benzenes), the simple linear relationship between the excess charge Δe on the carbon atom and the chemical shift $\Delta\delta$ of the bonded proton from benzene is considered to be a poor approximation (45, 61, 63, 64).

In order to bring the electron densities as derived from the proton chemical shifts into better agreement with theoretical electron densities, the simple linear relationship (first order approximation) has to be modified. Two corrective factors may be brought in (second order approximation).

First of all, a term proportional to the square of the field arising from the excess charges should be taken into account. The complete expression for the change in the proton screening due to a perturbing field E is given by Buckingham (28), equation (34). This relationship includes terms that are first and second order with respect to E . Marshall and Pople (41) note that the second order term can be accounted for by the distortion of the hydrogen 1s orbital by the electrostatic field arising from the excess charge, whereas the linear term originates from bond polarization.

Musher (45) has included a term proportional to E^2 in the linear relationship (equation 39) in calculating the proton shift measurements of $C_5H_5^-$ and $C_7H_7^+$, which were determined by Fraenkel et al (50). He was also able to calculate the effect of an E^2 term on the carbonium ion proton shifts as studied by MacLean and Mackor (53). The results indicate that the square term is fairly important when dealing with aromatic ions, due to the very large fields involved.

The second effect which must be considered is the field at a proton arising from the π electron densities on all the other atoms in the molecule, as well as from the charge on the carbon atom to which the proton is bonded. Schug and Deck (63), in their study of the proton chemical shifts and the π electron distribution in the hydroxy-benzenes, indicate that a more general expression to replace equation (39) should be of the form

$$(41) \quad \Delta\delta_i = \sum_i k_i (\Delta\rho_i),$$

where $\Delta\delta_i$ is the chemical shift of the i^{th} proton, and the sum is over all atoms that contain π electrons.

At present, the most sophisticated treatment of estimating the value of the chemical shift due to an uneven distribution of π electrons in an aromatic system is the one adopted by Schweizer et al (64), who

considered the effect of charge densities on proton resonance shifts in terms of a field effect. Not only is the excess π charge at the carbon atom to which the proton is directly bonded taken into account, but the polarization of the C - H bonds due to the excess charge densities on all the other atoms in the molecule is also included (63). A term in the square of the field arising from the excess charges (45) is also considered.

Schweizer et al considered Buckingham's equation for field effect calculations

$$(34) \quad \Delta\delta = -aE_Z - bE^2,$$

where $\Delta\delta$ is the shift relative to benzene for the proton in question, E_Z is the electric field along the C - H bond direction, and E is the field at the proton in question. Rewriting equation (34) in terms of the excess charge density $\Delta\rho$, and interatomic distances, Schweizer et al obtain the expression

$$(42) \quad \Delta\delta = 12.5 \times 10^{-6} \sum_i \frac{\Delta\rho_i}{R_i^2} \cos \theta_i - 17.0 \times 10^{-6} \left(\sum_i \frac{\Delta\rho_i}{R_i^2} \right)^2$$

where $\Delta\rho_i$ is the excess π electron density at the i^{th} atom, R_i is the distance (\AA) from that atom to the proton in question, and θ_i is the angle between the C - H bond and the electric field direction. The value of the constant a , which is used in equation (34) is 2.60×10^{-12} electrostatic units, which is close to the value of

2.0×10^{-12} obtained by Buckingham (28) and 2.9×10^{-12} obtained by Musher (45). Musher's value for b (7.38×10^{-19} electrostatic units), which was obtained from Marshall and Pople's (41) calculation, was used.

D ~ PYRIDINIUM CATION ELECTRON DENSITIES

Smith and Schneider (54) studied the protonation of pyridine in trifluoroacetic acid using proton resonance techniques. They observed, in addition to the ring protons, a triplet signal characteristic of a proton bonded to a nitrogen atom. The triplet splitting arises from spin coupling of the N - H proton with the N^{14} nucleus having spin $S = 1$. The spin coupling constant was found to have a value of 70 cycles/sec.

Smith and Schneider determined the low field displacement for the ring protons of pyridine on protonation, which arise from the decrease in electron charge density at the individual carbon nuclei as a result of adding the positively charged proton at the nitrogen atom. Applying equation (39), with the constant k equal to 9.5 p.p.m. per electron, the excess charge Δe , by which the local charge density of pyridine is altered on forming the pyridinium cation, was calculated. The value of the π electron density on the nitrogen atom was obtained by normalization, since the total charge on the ion (+1) as well as the excess π electron density on each carbon atom is known. This value was compared with the electron density obtained by comparing the N - H proton shift in conjunction with that in pyrrole as a reference state. Using the same value of k as for aromatic C - H

bonds, Smith and Schneider derived an electron density for the nitrogen atom which was in fair agreement with the value obtained by normalization.

This latter procedure is very rough, since pyrrole is not an aromatic molecule, and consequently is not a good reference. The N - H proton shift in pyrrole must be corrected for the ring current effect which would be present if pyrrole were an aromatic system. There is a large uncertainty in the magnitude of this correction. Also, the constant k is expected to have a different value for an N - H bond as compared with the value for an aromatic C - H bond (65).

The agreement between the electron densities for the pyridinium cation as obtained from proton resonance shifts (32, 54) with those calculated theoretically by Brown and Heffernan (62) is poor. It is observed experimentally that the ortho protons resonate at lowest field, followed by the para protons while the meta protons appear at highest field (Table IV). Molecular orbital calculations indicate on the other hand that the para protons are the least shielded, followed by the meta protons, while the ortho protons are most highly shielded (Table IV)(62).

For the pyridinium cation, due to the presence of a net positive charge, Gil and Murrell note that a poor approximation is made by assuming that the proton chemical shift is influenced only by the π electron density at the

attached carbon atom. The electron densities on all the other ring atoms must also be taken into account. However, taking into consideration the field arising from the localized charges on all carbon atoms results in poor agreement of the theoretical electron densities with the experimental shifts. It was therefore postulated that the counterion, present in the solution being measured, must have a very large effect on the experimental proton shifts.

Chapter IV

NATURE OF THE PROBLEM

The object of this research is to present experimental evidence illustrating the fact that the counterion may play a large part in determining the proton resonance shifts of the pyridinium cation.

Proton shifts relative to internal benzene of pyridine hydrochloride, hydrobromide and hydroiodide are studied in various solvents. Calculations based on various models involving the counterion are carried out, which suggest that the counterion is very important in determining the measured proton shifts. By means of these models, an attempt is made to explain why the shifts predicted by the theoretical calculations for the isolated pyridinium cation (62) do not agree with the experimental proton shifts (32, 54).

Chapter V

EXPERIMENTAL METHODS

A - PREPARATION OF SALTS AND SOLVENTS1. Salts

Pure pyridine hydrochloride, which is extremely hygroscopic, was prepared by passing dry hydrogen chloride gas into a solution of pyridine in anhydrous ether (one part by volume of pyridine to three parts of ether). The ethereal solution was cooled in an ice bath to prevent the large heat of reaction from boiling the mixture. The salt was filtered off after precipitation was complete. Hydrogen chloride gas was obtained by the action of sulphuric acid on dry sodium chloride, and was dried by being passed through sulphuric acid before coming in contact with the reaction mixture (66, 67).

Pyridine hydrobromide was prepared as the crystalline salt by neutralizing aqueous hydrogen bromide (48%) with pyridine (68). The excess water was then evaporated under vacuum on a water bath. The salt was moderately hygroscopic, but not to the same degree as pyridine hydrochloride.

Pyridine hydroiodide was prepared by extracting a solution of pyridine in ether with 47% hydriodic acid in several operations. The aqueous solution was then evaporated under vacuum on a water bath (66, 69). Pyridine hydroiodide was not visibly hygroscopic.

All of the above salts were washed with anhydrous ether, then dissolved in absolute alcohol and recrystallized several times by the slow addition of anhydrous ether. The salts were completely dried by pumping the salt in vacuo in a vacuum desiccator, in which they were kept all the time.

2. Solvents

The solvents used were spectroquality methylene chloride and acetonitrile from Matheson, Coleman and Bell, and spectroquality nitromethane from Eastman Kodak. They were not purified further.

Formic acid was further purified however (70). Eastman Kodak practical formic acid (97⁺%) was dried first of all with anhydrous copper sulphate, and was finally purified by means of fractional freezing. The observed freezing point was 8.1°C as compared with the literature value of 8.4°C (70). The dielectric constant of the purified acid was experimentally determined to be 65, as compared with the dielectric constant of ~ 80 for the unpurified, practical grade reagent which contains water. Experimentally however, the proton spectra, including the N - H proton spectrum, did not differ noticeably in the two cases.

The dielectric constants for the other solvents were obtained from reference 71 for 25°C.

B - MEASUREMENT OF THE SPECTRA

All measurements of the proton chemical shifts were carried out at 25°C, using a Varian DP60 spectrometer operating at 60 Mc/sec. Chemical shifts, using the standard audio sideband technique, were measured with a Hewlett-Packard audio oscillator and an electronic counter. The calibrations were carried out relative to internal benzene. Samples were contained in glass sample tubes of 4 mm inner diameter and 5 mm outer diameter. Results are the average of between six to ten runs.

The solubility of the three salts in nonpolar solvents is very low. The proton magnetic resonance spectra were taken on 3 mole % solutions, whenever possible, in the solvents methylene chloride, acetonitrile, nitromethane and formic acid. When the solubility was less than 3 mole %, saturated solutions were used.

Chapter VI

EXPERIMENTAL RESULTS

A - DETERMINATION OF THE CHEMICAL SHIFT

The ring proton shifts were obtained by determining the centres of gravity of the multiplets arising from the three types of ring protons. These shifts are listed in Table I. The multiplets corresponding to the ortho, meta and para protons were assigned on the basis of the observed splittings. The assignment was in agreement with the one proposed by Smith and Schneider (54). A proper analysis of the proton spectra implies an A_2B_2C approach. However, from Table I it is seen that the shift between protons ortho to each other is not less than 0.5 p.p.m. Also, since the coupling constant for protons ortho to each other is approximately 8 c/s, while the meta and para coupling constants are still smaller, the spectra were therefore treated as first order (72, 73). In this way the error in the shift is approximately one, or perhaps two c/s, and is certainly less than 0.03 p.p.m.

A typical ring proton spectrum is shown in Figure 5 for pyridine hydrochloride in methylene chloride. The vertical lines indicate the estimated shifts of the C - H protons. In several of the other solvents, however, part of the meta peak multiplet was covered by the solvent peak. But the meta proton shift could still be determined, except in the case of pyridine in formic acid. In this case the meta proton multiplet could not

be observed at all, since it was completely covered by the solvent C - H peak. In several of the solvents, only six peaks, and not nine, were observed for the para proton multiplet. The small low-field triplet was hidden under the ortho proton peaks. The shift could still be determined accurately, however.

From Table I it is seen that the C - H proton shifts are always in the order $\Delta\delta_{\text{ortho}} < \Delta\delta_{\text{para}} < \Delta\delta_{\text{meta}}$. This same order is observed for the C - H proton shifts of the pyridine protons (73). Averaging over all salts and all solvents, the C - H proton shift is $\Delta\delta_{\text{ortho}} = -1.53 \pm 0.12$, $\Delta\delta_{\text{meta}} = -0.78 \pm 0.13$ and $\Delta\delta_{\text{para}} = -1.30 \pm 0.14$ (in p.p.m.) to low field of benzene. The error limits indicate the maximum observed deviation for any salt in any solvent. From Table I it is seen that for the C - H proton shifts there is no rational trend in shift with respect to salt, solvent, or the dielectric constant.

N - H⁺ proton shifts were determined by estimating the centre of gravity of the peak and calibrating this position with respect to internal benzene. Since these peaks are fairly broad, there was some uncertainty in determining the exact position of the centre. The standard deviation was found to be under one cycle.

For NH⁺ protons in solvents other than formic acid, only broad single peaks were obtained. This indicates that an exchange process is going on, probably with traces of water present in the solution. The N - H⁺ proton shift was found to depend strongly on the counterion

FIGURE 5

The proton resonance spectrum of a saturated solution (< 3 mole %) of pyridine hydrochloride in methylene chloride. The relative peak intensity in arbitrary units is plotted as a function of the external magnetic field H , which increases linearly from left to right across the spectrum. The calibration is in p.p.m. to low field of internal benzene. The vertical lines indicate the estimated shifts of the C - H protons.

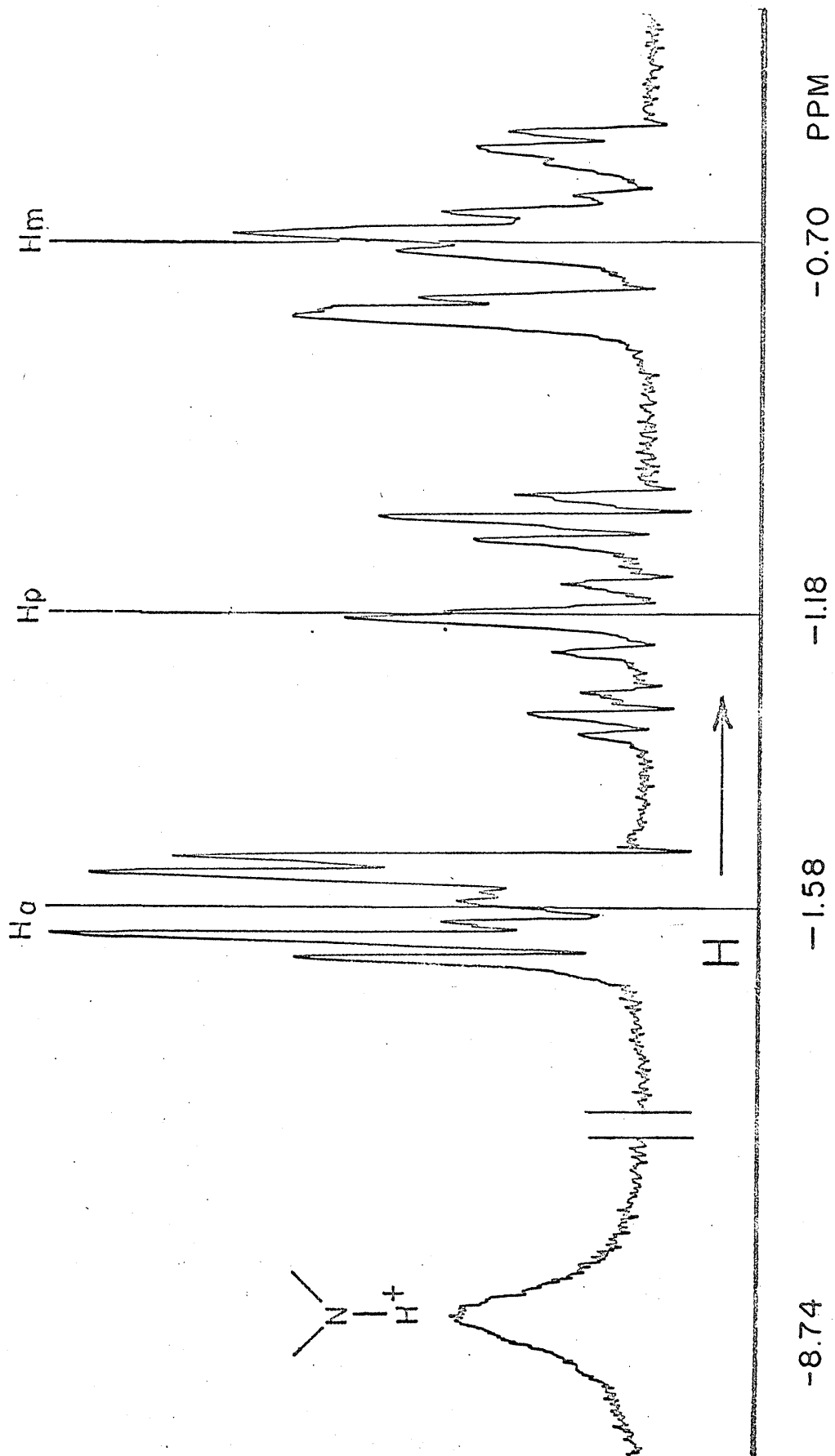


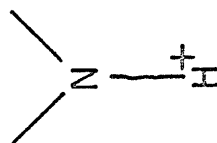
FIGURE 6

The proton resonance spectra of a 3 mole % solution of pyridine hydrobromide in formic acid (purified). The relative peak intensity in arbitrary units is plotted as a function of the external magnetic field H , which increases linearly from left to right across the spectrum. The $N - H^+$ protons are calibrated in p.p.m. to low field of internal benzene.

PyH^+ indicates the pyridinium cation proton resonance position.

C¹³C₆H₆PyH⁺-CHC¹³

-OH



H

0 PPM

-5.62

-6.74

-7.87

present in the solution as well as on the particular solvent (Table I). The proton shifts are lowest for the hydrochloride and highest for the hydroiodide.

In formic acid, a triplet is obtained for the $N - H^+$ proton for both pyridine hydrochloride and pyridine hydrobromide. In these two cases the $N - H^+$ protons do not exchange. From the observed triplets the $N^{14} - H$ coupling constant was determined to be 67.6 ± 0.5 c/s. In Figure 6 a typical spectrum of pyridine hydrobromide in formic acid (purified), clearly illustrates the observed triplet. All the peaks are labelled. Of special interest are the C^{13} sidebands from the $C - H$ proton peak of the solvent. These C^{13} sidebands were used in further calibrations, which will be described in the next section. No $N - H^+$ proton peaks were observed for pyridine hydroiodide or for pyridine in formic acid. The hydroiodide was also studied in trifluoroacetic acid with the same negative result.

The choice of benzene as an internal standard reference in determining both the $N - H^+$ and the $C - H^+$ proton shifts has been justified. The position of the benzene proton resonance was determined in all four solvents with respect to internal cyclohexane. Cyclohexane was chosen since it is an inert solvent and not subject to a ring current effect. The difference in shift between the benzene proton and the cyclohexane proton resonance remained constant in all four solvents.

B - EFFECT OF WATER IN SOLVENTS

As the experimental proton shifts were determined, it was observed that traces of water in solvents other than formic acid had a large effect on the proton shifts. Consequently, experiments were carried out to determine the effect of water on the proton spectrum of pyridine hydrochloride in methylene chloride. The results are tabulated in Table II. A plot of the N - H⁺ proton shift in p.p.m. relative to internal benzene as a function of water concentration is given in Figure 7. The results indicate that the C - H proton shifts were not much affected whereas the N - H⁺ proton shifts were strongly shifted with the addition of very small amounts of water to the solution. This large shift is doubtlessly due to the rapid exchange of the N - H⁺ proton with the water protons.

This was not the case with formic acid solutions. When pyridine hydrobromide was studied in both highly purified and reagent grade formic acid (which contains some water), the N - H⁺ proton shift was the same in both cases. C - H proton shifts also remained unchanged.

The experimental results indicate that there is a large uncertainty in determining the water concentration (Table II, Figure 7). In solutions which are not saturated with respect to water (< 0.6 mole %), this error arises from the experimental procedure (weighing out the solutions).

The solubility of water in methylene chloride, however, was determined to be approximately 0.6 mole % by comparing the C^{13} sideband intensity from the solvent with that of the water peak. Since the natural abundance (1.108%) of C^{13} is known (74), the total number of water protons and hence the solubility is also known.

Several problems arise in this determination. First of all, the field has to be scanned rapidly to minimize saturation. Secondly, the solubility of water in methylene chloride is not necessarily the same when a salt is also present in the solution. This became evident when a saturated solution of sodium chloride and water in methylene chloride was prepared and the experiment of comparing peak intensities carried out. It was found that the ratio of the intensity of the water peak to the C^{13} peak was much smaller when salt was present in the solution as compared to the case when salt was absent.

The experiments determining the effect of water on the proton shifts were carried out on 3 mole % solutions of the hydrochloride. The solubility of pyridine hydrochloride in methylene chloride is under 3 mole % when an anhydrous solvent is used. However, when traces of water are added to the solution, the solubility of the salt increases to an extent of at least 3 mole %. (The experimental proton shifts were determined with respect to internal cyclohexane. To these shift values, the difference in the shift between a benzene and a cyclohexane

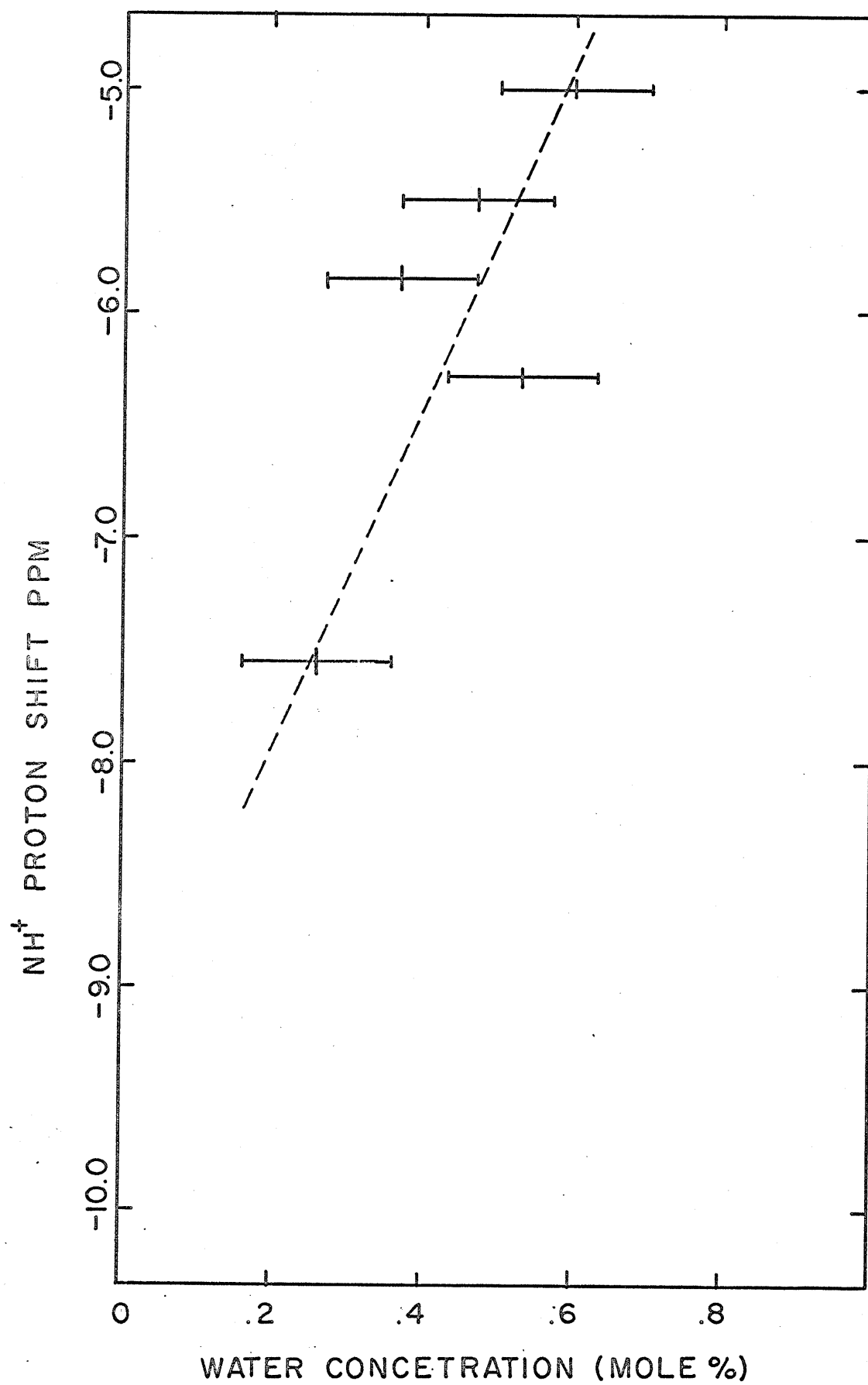
TABLE II

N - H⁺ PROTON SHIFTS OF PYRIDINE HYDROCHLORIDE IN METHYLENE CHLORIDE IN PPM TO LOW FIELD FROM INTERNAL BENZENE AS A FUNCTION OF WATER CONCENTRATION

Water Concentration (mole %)	$\Delta\delta_{N-H^+}$
0.26 \pm 0.10	7.56
0.37 \pm 0.10	5.84
0.47 \pm 0.10	5.51
0.53 \pm 0.10	6.28
0.60* \pm 0.10	4.98
* Solubility of water in CH ₂ Cl ₂	

FIGURE 7

A plot of the N - H⁺ proton shift in p.p.m. relative to internal benzene of pyridine hydrochloride in methylene chloride as a function of water concentration. The uncertainty in the water concentration is estimated at ± 0.1 mole %.



reference in methylene chloride was added. Consequently, the proton shifts as given in Table II and Figure 7 are with respect to benzene).

Several attempts were made to determine a good value for the $N - H^+$ proton shift in the absence of water. First of all, the straight line in Figure 7 was extrapolated to the ordinate. The point of intersection corresponds to the $N - H^+$ proton shift in a completely dry media. This however did not give a reliable value of the proton shift due to the large uncertainty in determining the water concentration.

The second approach that was attempted was one involving chemical exchange studies. When water is present in a solvent, proton exchange between the pyridinium cation and the water molecules is so rapid that separate $O - H$ and $N - H^+$ resonances are not obtained. For this reason, in all solvents except formic acid single peaks were observed for the $N - H^+$ proton resonance. This result may be compared with the work of Ogg (75) who studied the proton resonance of aqueous ammonia and super dry ammonia. He found that anhydrous ammonia gave a triplet resonance pattern, corresponding to the three spin states of the N^{14} nucleus. However in the presence of water, exchange of protons between the ammonia and water molecules was so rapid that the spin-spin splitting is washed out and a single peak was obtained.

From exchange studies, the N - H⁺ proton shift in a dry solvent may be determined using the relationship (76)

$$(43) \quad \bar{\delta}_m = p_{\text{H}_2\text{O}} \bar{\delta}_{\text{H}_2\text{O}} + p_{\text{N-H}^+} \bar{\delta}_{\text{N-H}^+},$$

where

$$(43a) \quad p_{\text{H}_2\text{O}} + p_{\text{N-H}^+} = 1.$$

$\bar{\delta}_m$ is the mean chemical shift of the N - H⁺ proton in a solution saturated with water, $\bar{\delta}_{\text{H}_2\text{O}}$ and $\bar{\delta}_{\text{N-H}^+}$ are the chemical shifts of the water and the N-H⁺ protons respectively when these substances are present in the solvent by themselves, and $p_{\text{H}_2\text{O}}$ and $p_{\text{N-H}^+}$ represent the number of protons in the water and salt solutions capable of undergoing exchange.

Therefore, this procedure was tried. The shift of the water protons in methylene chloride was determined and the solubility of the water was known from C¹³ measurements. The N - H⁺ proton shift of a 3 mole % solution of pyridine hydrochloride in methylene chloride saturated with water was also determined. Consequently all the variables are known, except $\bar{\delta}_{\text{N-H}^+}$ which may thus be calculated using equation (43). This procedure was unfortunately not very reliable due to the large uncertainty in determining the water concentration in a solution containing both salt and water.

The problem of determining the N - H⁺ proton shift in the absence of water may be solved, however. Salts and solvents should be dried as well as possible, and should only be handled in a dry box. But N - H⁺ proton shifts also depend strongly on the counterion due to ion pair formation, and on the solvent, as well as on traces of water in the solution. Since electron density determinations are obtained from the C - H proton shifts, which are not sensitive to small amounts of water, this aspect of the problem was not pursued any further.

Chapter VII

DISCUSSION OF RESULTS

A - DIRECT DETERMINATION OF ELECTRON
DENSITIES FROM THE CHEMICAL SHIFTS

Electron densities at the various carbon atoms and at the nitrogen atom of the pyridinium cation have been determined directly from the proton chemical shifts (Table III) using the simple linear relationship (equation 39). They have been calculated by averaging the proton shifts: by solvent over all salts (Table IIIa), by salt over all solvents (Table IIIb) and over all salts and all solvents (Table IIIc). Error limits have been calculated and correspond to the maximum deviation in the electron density in each case.

From Table III a, b, c, it is seen that the smallest deviations in the electron densities occur in case a, where ring proton shifts are averaged by solvent over all salts, since these shifts are nearly independent of the counterion present in the solution. However, ring proton shifts are strongly dependent on the solvent. Therefore a much larger deviation in the electron densities is obtained when proton shifts are averaged by salt over all solvents (case b). Finally, electron densities determined by applying the linear relationship to an average value of the shift over all salts and solvents exhibit the maximum deviation (case c). However electron densities in case c are the preferred experimental values since solvent effects and effects arising from the presence of the counterion are taken into consideration and averaged out.

The observed electron densities as given in Table IIIc are in good agreement with those obtained by studying the proton shift of pyridine in formic acid (Table IIIId). The electron density on the meta proton (and hence on the nitrogen atom) could not be determined since the meta peaks were completely covered by the solvent C-H proton peak. In Table IIIe the experimental electron densities are compared with the electron densities determined from the proton shift of pyridine in trifluoroacetic acid (54). The agreement is within experimental error for the ortho and meta carbon atoms, but for the para carbon the deviation is slightly larger.

In all the above cases the electron density on the nitrogen atom was determined by normalization, since the linear relationship (equation 39) was derived for protons bonded to a carbon atom in the sp^2 state. Consequently, the maximum observed deviation in the electron density is the largest for the nitrogen atom.

All of the experimental electron densities (Table III a-e) may be compared with electron densities calculated by theoretical means (Table IIIf). These values correspond to an average value of the four sets of π electron densities calculated by Brown and Heffernan (62) for an isolated pyridinium cation. The agreement between the two sets of values is very poor. Consequently, to

bring the shifts predicted by the π densities (62) into at least the same order as the experimental proton shifts, further effects on the proton shifts must be considered.

Table III

Electron Densities for the Pyridinium Cation Determined
from the Proton Chemical Shifts¹ listed in Table I and
Compared with Literature Values.

(a) <u>PROTON SHIFTS AVERAGED BY SOLVENT</u>				
Solvent	e_{Ortho}	e_{Meta}	e_{Para}	e_{N}^2
CH ₂ Cl ₂	0.851±0.001	0.934±0.001	0.889±0.001	(1.54±0.01)
CH ₃ CN	0.866±0.002	0.936±0.003	0.885±0.004	(1.51±0.01)
CH ₃ NO ₂	0.861±0.005	0.926±0.004	0.876±0.005	(1.55±0.02)
H ₂ CO ₂	0.848±0.002	0.917±0.002	0.866±0.001	(1.60±0.01)
(b) <u>PROTON SHIFTS AVERAGED BY SALT</u>				
Salt				
Py.HCl	0.859±0.009	0.930±0.012	0.882±0.014	(1.54±0.06)
Py.HBr	0.855±0.010	0.927±0.010	0.878±0.012	(1.56±0.05)
Py.HI	0.858±0.009	0.924±0.010	0.874±0.009	(1.56±0.05)
(c) <u>PROTON SHIFTS AVERAGED BY SALT AND SOLVENT</u>				
	0.857±0.011	0.927±0.012	0.879±0.013	(1.55±0.06)
(d) <u>PROTON SHIFTS OF Py IN H₂CO₂</u>				
	0.850	--	0.866	--

Table continued,

Table III - continued,

(e) <u>PROTON SHIFTS OF Py IN CF₃COOH³</u>				
	ρ_{Ortho}	ρ_{Meta}	ρ_{Para}	ρ_{N}
	0.854	0.915	0.862	(1.60)
(f) <u>CALCULATED⁴ ELECTRON DENSITIES (VESCF)</u>				
	0.949	0.903	0.824	1.473

NOTE:

The error limits for the electron densities correspond to the maximum deviation.

Abbreviations: Py, pyridine; Py.HCl, pyridine hydrochloride; Py.HBr, pyridine hydrobromide; Py.HI, pyridine hydriodide; VESCF, variable electronegativity self-consistent field molecular orbitals.

1. Electron densities obtained by applying equation (39).
The value of k employed is 10.7 p.p.m. per electron.
2. Electron densities for the nitrogen atom are determined by normalization, except in case f.
3. References 32, 54.
4. Average of the four sets of π electron densities given in reference (62).

B - SECONDARY CONTRIBUTIONS TO THE CHEMICAL SHIFT

Several effects may influence the proton chemical shift besides the excess π electron density on the carbon atom to which the proton is bonded (Chapter III).

The first effect that must be considered is the magnetic anisotropy of the nitrogen atom. Since we measure our proton shifts for the pyridinium cation relative to benzene, the replacement of a C-H by the N-H⁺ entity introduces a magnetic anisotropy contribution to the chemical shifts. Gil and Murrell (61) have calculated that this amounts to not more than 0.03 p.p.m. at the ortho proton and is smaller for the meta and para protons. This is small enough to be within the experimental error.

Protonation of pyridine changes the paramagnetic contribution of the nitrogen electrons. Pyridine has a low-lying state which is associated with an electronic transition from the lone pair orbital to the lowest vacant π antibonding orbital (the $n \rightarrow \pi^*$ state)(61). This low-energy transition lies at about 4.5 ev (61, 77). It is no longer present in the pyridinium cation, and the proton can be considered to have increased the ionization potential of the nitrogen lone pair of electrons. This supports the assumption that the N-H⁺ bond in the pyridinium cation is essentially a covalent bond. Consequently, any contribution from this source will be ignored since the new $\sigma \rightarrow \pi^*$ transition will be close to that for benzene (reference) and is unlikely to be below 8 ev (61).

The ring current effect need not be considered for the pyridinium cation, since it has six π electrons. The effect due to a slightly different ring size from that of benzene is very small and will affect the ring current only very slightly (32).

The proton shifts in Table I show no clear trend with the dielectric constant of the solvent. Thus acetonitrile and nitromethane have the same dielectric constant and according to the reaction field theory as described by Buckingham (28) the shifts should be the same in the two solvents (at least for the same salt). A plot of the ortho, meta or para proton shift, with respect to benzene, versus the dielectric function given in equation (36) shows no correlation between these two variables. This relationship could not be fully tested however since experiments were carried out in only four solvents with high dielectric constants. Consequently the range of values of the dielectric function was very small. A solvent of very low dielectric constant could not be used for reasons of solubility.

The reaction field shifts can be discussed as follows. For the pyridine molecule the π electrons are localized to a large extent on the nitrogen atom. A π electron dipole will therefore arise with its negative end centred on the nitrogen atom and the positive end on the ring. For the pyridinium cation a net positive charge is

added to the system, causing a π electron shift. This results in an increase of the π electron density on the nitrogen atom and a decrease at the carbon atom (62). Therefore in the pyridinium cation the π electron dipole still has the same sense as in pyridine. For this reason the order of appearance of the ring protons in both systems is the same, namely $\delta_o < \delta_p < \delta_m$ (54).

From the chemical shifts given in Table I it is seen that the reaction field of the solvent (28) does have an effect, though small, on the proton shift arising from the polarization of the solvent molecules by the dipole moment of the pyridinium cation. This dipole will polarize the surrounding medium and this polarization leads to an electric field, the reaction field, at the solute (28). The reaction field tends to shift the meta and para signals to low field (the meta being influenced less than the para) and the ortho proton signal to high field. This proton displacement is expected to increase as the dielectric constant of the solvent increases.

The ortho-para difference in shift is expected to decrease on changing from a solvent of low dielectric constant to one with a higher dielectric constant. The ortho-meta difference in shift should also decrease. However, the rate of change of the ortho-meta difference in shift should be less than the rate of change of the ortho-para difference, since the para protons are affected to a

larger extent by a change in the dielectric constant than the meta protons. The meta-para difference in proton shift is expected to increase with an increase in the dielectric constant of the solvent.

Therefore the proton shifts listed in Table I were averaged over all salts for any one solvent. The differences between the average values of the ortho, meta and para proton shifts were then determined for each solvent. These values are listed in Table IV. The dielectric constant of the solvent increases from left to right across Table IV (CH_3CN and CH_3NO_2 have the same constant).

There is a decrease in the ortho-para proton shift difference (Table IVa) in going from a solvent of low to one of high dielectric constant. This is also observed for the ortho-meta difference in proton shift (Table IVb). A comparison of these shifts shows that the rate of change of the ortho-meta difference is smaller than the ortho-para difference, as expected from reaction field theory.

The meta-para difference in shift (Table IVc) is not very pronounced.

From these results it is seen that the reaction field does have a slight effect on the proton shifts but it is not larger than about 10% of the observed shifts.

It therefore appears that the main function of the solvent is as a solvating agent for the counterion. If it forms a bulky solvated complex either with the counterion or with the pyridinium cation, thus removing the counterion sufficiently far from the cation, the effect on the proton shifts will be much larger than any reaction field shifts. Consequently ion pair formation affects the electron densities at the various positions of the pyridinium cation, and hence the proton chemical shifts, to the largest extent. Ion pair formation masks the expected correlation between the proton shifts and the dielectric function (equation 36). This effect will be discussed in the following sections.

Table IV

Differences in the Ring Proton Shifts in P.P.M. for Pyridine Hydrohalides in Four Solvents. The Shifts Which Are Used Are the Average Values Over All Salts in any One Solvent.

(a) <u>ORTHO-PARA DIFFERENCE</u>			
CH_2Cl_2	CH_3CN	CH_3NO_2	H_2CO_2
0.41	0.20	0.16	0.20
(b) <u>ORTHO-META DIFFERENCE</u>			
0.89	0.74	0.69	0.73
(c) <u>META-PARA DIFFERENCE</u>			
0.48	0.54	0.53	0.54

C - ION-PAIR FORMATION: EVIDENCE FROM OTHER WORK1. Infrared Spectroscopy

Lord and Merrifield (78) studied strong hydrogen bonds in crystals. They found that the infrared absorption spectra of tertiary amine hydrochlorides show features which indicate the presence of strong $N^+ - H \dots X^-$ bonds in these salts. A large shift of many hundreds of cm^{-1} in the N-H stretching frequency of solid pyridinium chloride was observed. This shift was also found to persist in solutions of the salt. These results indicate that the strong hydrogen bond interaction, perhaps even of a covalent character, of the $N-H^+$ entity with the counterion is also present in the solution, indicating ion-pair formation.

Chenon and Sandorfy (66) and Brissette and Sandorfy (79) made an intensive study of the infrared spectra of amine hydrohalides, including those of pyridine. For the solid state and in nonaqueous solvents they found that the observed broad band corresponding to the N-H stretching frequency occurred in the neighbourhood of $2700-2400\text{ cm}^{-1}$ rather than between $3300-3100\text{ cm}^{-1}$, the N-H stretching frequency in substituted ammonium salts where there is no hydrogen bonding. They also found that the observed broad band shifts towards higher frequencies (hypsochromic shift) by about 200 cm^{-1} going from hydrochloride to hydrobromide to hydroiodide.

The broadness of the bands diminishes in the same order. These results indicate that the type of counterion present in solution is very important.

The above results indicate that in the solid state as well as in solution hydrogen bonds exist and are of the $N^+ - H \cdots X^-$ type (In water they are of the $N^+ - H \cdots O$ type). Sandorfy et al conclude that the energy of these hydrogen bonds comes mainly from electrostatic forces but that delocalization of the positive charge also makes a significant contribution to the hydrogen bond energy. Spinner (80) in his study of the vibration spectra of some monosubstituted pyridines and pyridinium ions reached similar conclusions.

Many other pyridinium salts with various counterions have been prepared and their solid state infrared spectra determined. Nuttall, Sharp and Waddington (81) observed that the strong band below 3000 cm^{-1} (characteristic of $N^+ - H \cdots X^-$ hydrogen bonding) is present for the pyridinium halides, nitrate, bifluoride and metasulphonate but for many other salts this cation-anion interaction is not observed. Kynaston, Larcombe and Turner (82) studied solid pyridinium tetrachloroborate and also found strong hydrogen bonding for this salt. Gill, Nuttall, Scaife and Sharp (83), Evans and Kynaston (84) and Cook (85) obtained similar

results for various other salts. Evans and Kynaston also determined the effect of ortho substituents on the N-H stretching frequency.

All of these infrared studies, especially of the hydrohalides, indicate a strong interaction between the N-H^+ proton and the halide anion. The magnitude of this interaction depends on the counterion and for the hydrohalides it is somewhat less for the hydroiodide than for the hydrochloride but still very strong compared to the free state (85).

2. X-ray Crystallography

The crystal structure of pyridine hydrochloride has been determined by Rérat (86) from electron-density studies. The atomic coordinates have been refined by a least squares treatment. The results indicate that the pyridinium cation exists as a slightly distorted hexagon. The N-Cl distance is 2.95 \AA , considerably less than the sum of the van der Waals radii of 3.3 \AA . The chloride ion lies 0.14 \AA out of the plane of the ring along the N-H^+ bond direction.

Together with the infrared data, indications are that the pyridinium cation may exist in solution as an ion pair with the counterion situated on an average in the plane of the ring along the N-H^+ bond direction.

3. Proton Magnetic Resonance

Fraenkel (87) has studied the formation of ion pairs of anilinium salts in solution by NMR techniques. Proton resonance measurements of the salts of aniline, p-toluidine, p-chloroaniline and their N-methyl derivatives were determined in various solvents and the ring proton line shapes were found to be strongly dependent on the accompanying anion. These results strongly suggest ion pair formation with, however, rapid exchange of counterions between pairs. Since the time taken for transfer is very small on an NMR time scale (88, 89), then the evidence for the existence of the pyridinium cation in solution as an ion pair is still valid.

Reynolds and Schaefer (48, 90) studied the ring proton chemical shifts and proton exchange reactions of substituted anilines in trifluoroacetic acid. They found that an ion pair model predicted shifts of the ring protons which were in reasonable agreement with experimental values. It was also found that an ion pair model may be brought into reaction rate studies. The exchange rates of protonated N,N-dimethylaniline in trifluoroacetic acid indicate that the formation of ion pairs followed by an internal transfer of protons explained the proton exchange reaction mechanism.

4. Electron Spin Resonance

Further evidence for the existence of ion pairs in solution has been obtained from ESR studies. Reddoch (91) has studied the proton hyperfine coupling constants of the azulene anion in dimethoxyethane with lithium ions. Their experimental results could only be explained in terms of a rapid association-dissociation equilibrium between azulene and lithium ions.

Bolton and Fraenkel (92) have recently studied the ESR spectra of the positive and negative ions of anthracene. They also found that the anion forms ion pairs with the alkali metal cations. The results showed that small cations like Li^+ or Na^+ are highly solvated and therefore affect the anion less strongly than the more weakly solvated cation like K^+ . This does not apply to radical anions with functional groups that can form relatively tight complexes with the counterions. Radicals such as the nitrobenzene negative ion have been studied by Ward (93) and appear to form strong complexes with the alkali metal cations at the site of the functional group that compete with the solvation process.

5. Conductivity Data

Aten, Dieleman and Hoijsink (94) studied the conductivity and uv spectra of solutions of aromatic-hydrocarbon negative ions. Their results indicate that one-to-one ion pair complexes are formed between negative ion radicals and alkali-metal cations in ether solvents. They also found that ionic association increases with an increase in the radius of the counterion, with a decrease in the dielectric constant of the solvent and with an increase in the temperature.

All of the above data support the assumption of ion pair formation at the site of the $N-H^+$ group in solutions of the pyridinium cation.

D - THE COUNTERION MODELS1. Electric Field Calculations

As has been discussed before, the experimental proton shifts for the pyridinium cation do not fall in the same order as the shifts predicted from the π electron densities calculated for the isolated cation. In an attempt to explain the experimental proton shifts, we consider various models of the state of the pyridinium cation in solution. In all the models it is assumed that the cation exists in solution as an ion pair with the counterion situated in the plane of the ring along the N-H^+ bond direction.

The effect of the fields arising from the various charges on all the atoms, including the counterion, on the shift of a particular C-H proton have been determined by an application of equation (42)

$$(42) \quad \Delta\delta = 12.5 \times 10^{-6} \sum_i \frac{\Delta\rho_i}{R_i^2} \cos\theta_i - 17.0 \times 10^{-6} \left(\sum_i \frac{\Delta\rho_i}{R_i^2} \right)^2.$$

This equation was used by Schweizer (64) and has been discussed before. The contribution to the chemical shift ($\Delta\delta$), arising from the charges present, is given in p.p.m. if the excess π electron density on atom i ($\Delta\rho_i$) is given in fractions of an electron. The distance

(R_i) of the atom from the proton in question is given in \AA . The effect on the proton shift on increasing the distance between the counterion and the ring is taken into account as well as the effect of the fields arising from a positive charge placed on the N-H^+ proton and at various positions along the N-H^+ bond.

The pyridinium cation was drawn to a large scale. The distances from each proton to every carbon atom, to the nitrogen atom and to the various positions of the counterion were measured. Distances were also determined from the position of the single positive charge to each C-H proton. The angles between the C-H bond directions and the direction of the field vectors at all the ring protons were also determined from the diagram.

The geometry of the pyridinium cation was taken as a regular hexagon with C-C bond lengths of 1.39 \AA and a C-H bond length of 1.08 \AA (95). The N-H^+ bond length was taken as 1.03 \AA , the same as in the ammonium ion. This latter value has been determined by several workers. Gutowsky et al (96) studied the proton magnetic resonance absorption of ammonium halide crystal powders and determined the N-H^+ distance to be $1.035 \pm 0.01 \text{ \AA}$. Bersohn and Gutowsky (97) have examined ammonium chloride in monocrystalline form and found this distance to be $1.032 \pm 0.005 \text{ \AA}$. A neutron diffraction

study of the crystal structure of ammonium chloride by Levy and Peterson (98) gave a value of $1.03 \pm 0.02 \text{ \AA}^0$ for the N-H^+ bond length, in agreement with the above values.

The crystal structure data for pyridinium chloride, as determined by Rerat (86), indicates that the cation in the solid state exists as a slightly distorted hexagon, but the use of these data would result in relatively small changes in the calculated shifts, well within the approximation inherent in our models.

2. The Various Models

The models that have been considered for the pyridinium cation in solution will now be discussed. The results of these calculations are given in Table V.

1) This model uses the average of the four sets of π electron densities as calculated by the VESCF method (62). The excess π electron densities are $\Delta\rho_o = -0.051$, $\Delta\rho_m = -0.097$, $\Delta\rho_p = -0.176$, and $\Delta\rho_N = +0.473$. The effect of the polar N-H^+ sigma bond is ignored. The counterion, approximated by a point charge of $\Delta\rho = +1.00$ electron units, is placed at various distances from the N-H^+ proton along the N-H^+ direction in the plane of the ring.

2) This model differs from the first only in that it takes the N-H^+ bond into account by considering the additional contribution from a single positive charge of one electron unit ($\Delta e = -1.00$) placed

(a) at the N-H^+ proton and

(b) 0.34 \AA^0 along this bond from the proton.

3) This model assumes that the π electron density is unity on all the ring atoms. Otherwise it is the same as the second model but the positive charge is placed

(a) at the N-H^+ proton and

(b) 0.515 \AA^0 (half-way) along the N-H^+ bond.

4) Here much smaller charges on the ring carbons arising from the polarization of the π electrons are assumed. These charges are $\Delta e_o = -0.01$, $\Delta e_m = -0.02$, $\Delta e_p = -0.05$, and $\Delta e_N = +0.11$. These values run in the same order as those calculated for the isolated cation (62). It is very probable that the counterion will affect a reduction in polarization. The positive charge is placed

(a) at the N-H^+ proton and

(b) 0.515 \AA^0 along the N-H^+ bond.

The convention followed in all of the above calculations was that an excess of π electron charge is denoted with a positive sign while a deficiency is denoted with a negative sign.

Table V

Average Observed Shifts (in ppm. to Low Field from Internal Benzene) and Calculated Shifts for the C-H Proton in Solutions of Pyridine Hydrohalides.

Counterion Distance, Å ^o	$\Delta\delta(\text{exp})$			$\Delta\delta(1)^*$		
	ortho	meta	para	ortho	meta	para
2.0	1.53	0.78	1.30	0.06	1.04	2.15
2.5	± 0.12	± 0.13	± 0.14	0.09	1.09	2.20
3.0				0.10	1.14	2.24
4.0				0.10	1.20	2.30
∞				0.01	1.39	2.53
	$\Delta\delta(2a)$			$\Delta\delta(2b)$		
	ortho	meta	para	ortho	meta	para
2.0	1.16	1.84	2.91	1.64	1.99	3.03
2.5	1.27	1.90	2.96	1.75	2.06	3.09
3.0	1.33	1.95	3.01	1.82	2.10	3.13
4.0	1.41	2.02	3.07	1.91	2.18	3.20
∞	1.51	2.24	3.32	2.03	2.41	3.44
	$\Delta\delta(3a)$			$\Delta\delta(3b)$		
	ortho	meta	para	ortho	meta	para
2.0	1.19	0.35	0.27	1.93	0.54	0.41
2.5	1.30	0.39	0.30	2.05	0.59	0.44
3.0	1.37	0.43	0.33	2.13	0.63	0.47
4.0	1.45	0.49	0.38	2.23	0.69	0.52
∞	1.56	0.66	0.55	2.37	0.86	0.70
	$\Delta\delta(4a)$			$\Delta\delta(4b)$		
	ortho	meta	para	ortho	meta	para
2.0	1.16	0.64	0.89	1.89	0.85	1.05
2.5	1.26	0.70	0.93	2.01	0.90	1.09
3.0	1.33	0.73	0.96	2.09	0.94	1.12
4.0	1.41	0.79	1.01	2.19	1.00	1.17
∞	1.52	0.97	1.21	2.33	1.19	1.37

* The shifts are calculated for the different models described in the text.

From Table V it is seen that the value of the calculated low-field shift increases as the distance between the counterion and the N-H^+ proton increases. This is due to the fact that the shielding of the protons by the fields arising from the charge on the counterion is largest when the counterion is nearest the ring (highest field shift). This field effect quickly falls off since it is proportional to the square of the distance between the counterion and the proton (equation 42).

An exception is the ortho proton in model 1 where the magnitude of the calculated low field shift first increases as expected, but then decreases. This is explained by the fact that the angle θ between the C-H bond direction and the electric field vector at the proton increases from 86° to 97.5° as the distance between the counterion and the ring increases from 2\AA to 4\AA . In all the other models this angle is always less than 90° for all protons. From equation (42) it is seen that when angle θ is 90° , the linear term arising from the field effect is zero. When angle θ is less than 90° , the electric field tends to deshield the proton causing the observed increase in the low field shift. However when the angle is greater than 90° , the field acts in the opposite direction (shielding). Since the contribution to the proton shift from the second term in equation (42) (which is not dependent on the angle) is much smaller than that

from the first term, the net effect of the counterion on the calculated ortho proton shift in model 1 is determined mainly by the magnitude of angle θ .

This is also observed experimentally. From an analysis of the proton shifts in Table I, it is seen that for any one solvent the ring proton shifts move to lower field as the size of the counterion increases, since the centre of negative charge is located further from the ring.

3. Comparison of Observed and Calculated Shifts.

It may be expected that the interaction of the halide ion with the cation will vary from ion to ion and from solvent to solvent. However the simple models that have been considered can not take this variation into account, except as a variation of the $N - H^+ \dots X^-$ distance. Therefore to a first approximation the average of the observed shifts over all salts and all solvents is considered. These observed shifts together with the calculated shifts are given in Table V.

From Table V it is seen that no model which assumes the VESCF π electron densities of the free cation reproduces correctly the order of the observed shifts for the ortho, meta and para protons (models 1, 2a, 2b). This is true also for the models (3a, 3b) which assume unit π electron densities on all the ring atoms. The models (4a, 4b), in which much smaller charges on the ring carbons

arising from the polarization of the π electrons are assumed, do reproduce the observed order of the shifts. Only a slight adjustment of the assumed π electron densities, of the order of 0.01 units, together with a small shift of the positive charge along the N-H^+ bond would produce complete agreement between the calculated and observed proton chemical shifts for any counterion distance.

The agreement between the observed and calculated chemical shifts is seen to depend to a large extent on the positive charge in the N-H^+ sigma bond. Our models take it into account in a naive sort of way. In the calculations it was assumed that all of the positive charge is located either on the N-H^+ proton or along the N-H^+ bond. In actual practice the positive charge is probably delocalized to a certain extent over the whole ring.

From models 4a and 4b it is seen that the observed order of the proton shift is also predicted in the absence of the counterion. This may suggest that the formation of ion pairs is not a necessary requirement in explaining the observed proton shifts. However, if the counterion was not present, it would be hard to account for the reduced polarization of the π electrons. Therefore these results, together with the other evidence which has been discussed previously, present a reasonable case for ion pair formation in our solutions.

E - N-H⁺ PROTON SHIFTS

From Table I it is seen that the N-H⁺ proton shift in any one solvent except formic acid is displaced to high field by several p.p.m. as the size of the counterion increases. This shift, which is a function of the solvent, is also affected by traces of water present in the solution.

No definite statement can be made about the isolated N-H⁺ proton shift. Equation (42) can be modified to apply to an N-H⁺ bond in calculating this shift. For this bond the constant a in Buckingham's equation (equation 34) is approximately 6 to 6.2×10^{-12} electrostatic units while the value of the constant b remains the same as for a C-H bond (65). Therefore in applying equation (42) to calculate the N-H⁺ proton shift, the coefficient of the linear term becomes 28.8 to 29.8×10^{-6} units. However the inclusion of a point positive charge very close to the N-H⁺ proton in our models make them useless in calculating this shift.

In these solvents the order of the shifts (Table I) can be rationalized if incipient bond formation is assumed between the proton and the halide ion. It has been found (99) that the proton chemical shifts of HCl,

HBr and HI in the vapour phase appear to the high-field side of methane gas due to the neighbour-anisotropy effect. HI has the highest proton shielding and appears to highest field. For this reason the highest N-H^+ proton shift in any solvent is observed for pyridine hydroiodide. If the shift had been completely determined by exchange with traces of water, the highest field shift would have been observed for the hydrochloride since this salt is the most hygroscopic of all salts that were studied.

A triplet was obtained for the N-H^+ proton of pyridine hydrochloride and hydrobromide in formic acid. The chemical shift for this proton was found to be the same for both salts, indicating that the counterion has very little effect in determining this shift. It therefore appears that the shift is characteristic of the solvent due to the formation of $\text{N-H}^+ \dots \text{O}$ instead of $\text{N-H}^+ \dots \text{X}^-$ bonds (X^- is the halide ion). Similar conclusions were reached by Chenon and Sandorfy (66) from their infrared studies of these salts in water. The very similar shifts of the C-H protons for the three salts and pyridine in formic acid support this suggestion.

When pyridine hydroiodide and pyridine were studied in formic acid, an N-H^+ proton signal was not observed. This may be explained by a fast exchange process between the N-H^+ protons and the solvent or water

protons. But no proton exchange occurs for the hydrochloride or the hydrobromide in formic acid. Exchange may therefore be explained by an interaction between the proton and the counterion. Since the electronegativity of the atoms decreases from chlorine to iodine, the interaction between the proton and the chloride or the bromide ion will be stronger than between the proton and the iodide ion. This interaction may be strong enough to prevent exchange in the former but not in the latter case. Proton exchange of the $N - H^+$ proton for pyridine in formic acid may also be explained by a weak interaction between the proton and the formate ion.

Chapter VIII

SUMMARY AND CONCLUSIONS

Pyridine hydrochloride, hydrobromide and hydroiodide were studied in methylene chloride, acetonitrile, nitromethane and formic acid. The electron densities on all the ring carbon atoms of the pyridinium cation were determined by applying the simple linear relationship (equation 39) between the excess charge Δe on the carbon atom and the shift $\Delta\delta$ relative to benzene of the bonded proton. The value of the constant k that was used in equation (39) was 10.7 p.p.m. per electron. The electron density on the nitrogen atom was determined by normalization.

The observed ring proton chemical shifts were in poor agreement with the proton shifts obtained from the calculated π electron densities. This lack of agreement may be explained by the existence of hydrogen bonded ion pairs in solution between the pyridinium cation and the counterion.

Various models involving the counterion were therefore postulated which show that the presence of the counterion is very important in determining the measured proton shifts. The presence of the counterion considerably reduces the π electron polarization calculated for the isolated pyridinium cation by the VESCF method. It was found that models which take into account the positive

charge in the N-H^+ sigma bond, the π electron densities on the ring atoms, as well as the counterion, account for the observed order of the C-H proton shifts. The π electron densities on the ring atoms were assumed to be smaller than those for the isolated cation due to the polarization of the π electrons. The ring proton shifts were calculated using equation (42).

N-H^+ proton shifts are very sensitive to the solvent, counterion and traces of water in the solution. The inclusion of a point positive charge very close to this proton in our models makes these models useless in calculating the N-H^+ proton shift.

In solvents other than formic acid, in which only single N-H^+ proton peaks were observed, the order of these shifts can be rationalized if incipient bond formation between the proton and the halide ion is assumed. Due to the magnetic anisotropy effect, the N-H^+ proton shift of pyridine hydroiodide appears to highest field and for pyridine hydrochloride it appears at lowest field.

In formic acid the N-H^+ proton shifts of the hydrochloride and hydrobromide are characteristic of a complex involving the solvent rather than the halide ion, i.e. $\text{N-H}^+ \dots \text{O}$ instead of the $\text{N-H}^+ \dots \text{X}^-$, where X^-

is a halide ion. In these two cases the N-H^+ proton does not exchange rapidly and an $\text{N}^{14} - \text{H}^+$ coupling constant of $67.6 \pm 0.5 \text{ c/s}$ is found.

No N-H^+ proton signal was obtained for pyridine hydroiodide or pyridine in formic acid. This may be explained by a fast exchange process between the N-H^+ protons and the solvent or water protons.

Chapter IX

RECOMMENDATIONS FOR FUTURE RESEARCH

The limiting value of the N-H^+ proton shift in the complete absence of water may be determined by studying solutions of pyridine hydrohalides prepared from carefully dried salts and solvents. All preparations would have to be carried out in the dry box.

Various other pyridinium salts besides the halides have been prepared and their infrared spectra, mostly in the solid state, have been determined. This work has been done by Cook (85) as well as other workers mentioned in Chapter VII. It would therefore be interesting to study the N-H^+ proton shifts of many of these salts. Ion pair formation and hydrogen bonding can be studied in solutions of these salts and the results compared with infrared data. The degree of hydrogen bonding in these salts can also be studied by determining the effect various ortho substituents on the pyridine ring have on the N-H^+ proton shift.

Some of the pyridinium salts that have been studied include the ZnCl_4^- , SnBr_6^- , SnCl_6^- , ClO_4^- , BF_4^- , SbCl_6^- as well as the halide anions.

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