

HYDROGEN BONDING AND PROTON EXCHANGE IN
TRIFLUOROACETIC ACID-QUINOLINE AND METHANOL-ORTHOCHLOROPHENOL
MIXTURES

BY NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

by

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A B S T R A C T

High resolution nuclear magnetic resonance is used to investigate proton exchange in two hydrogen bonded systems.

The change of the chemical shift of the acid proton with concentration in mixtures of trifluoroacetic acid and quinoline have been used to indicate the formation of a strongly hydrogen bonded ion pair in the pure acid-base system and in acetonitrile as solvent.

Spectra at -18°C show resolved peaks for the >NH^+ and -COOH protons confirming the nature of the exchange process. The kinetic processes involved in the exchange are discussed but the experimental difficulty in carrying out a low temperature (0 to -60°C) study of an equimolar mixture of the two components prevents any detailed investigation of the rate processes.

The chemical shifts measured for the acid and hetero-ring protons are averages for the various environments so that charge density changes on protonation of a basic species are not proportional to the observed chemical shift changes.

Intermolecular hydrogen bonding and proton transfer rates between methanol and orthochlorophenol have been experimentally investigated in the slow exchange approximation for the modified Bloch Equations (0°C to -41.1°C). Interpolations of the results to the fast exchange limit are consistent with experimental line widths in this region. The activation energy obtained for the first order kinetics is 4.58 Kcal mole $^{-1}$. It is considered that the intramolecular hydrogen bond

in orthochlorophenol does not impede the proton exchange process in the two component system.

Variations in the line width of the exchange averaged -OH resonance signal are used to indicate the effect of small quantities of water added to the methanol-orthochlorophenol mixtures.

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INTRODUCTION

CHAPTER I

A) Magnetic Properties of Nuclei

Many nuclei have magnetic dipole moments which are directed along the axis of spin of the nucleus (1). If each nucleus has a spin vector \underline{I} , then its angular momentum is $\hbar \underline{I}$ and its nuclear magnetic moment is $\gamma \hbar \underline{I}$, γ being the magnetogyric ratio.

Each nucleus with spin $I = \frac{1}{2}$ has two independent states whose degeneracy is removed by the application of a magnetic field, H_0 . If H_0 is acting in the negative z direction, then the energy of the nucleus in this field is $\gamma H_0 I_z / 2\pi$. The Hamiltonian describing the Zeeman energy for a set of nuclei acted upon by fields, H_i is:

$$\mathcal{H}^{(0)} = \frac{1}{2\pi} \sum_i \gamma_i H_i I_{z(i)} \quad (1)$$

and $\omega_i = \gamma_i H_i \quad (2)$

where $H_i = H_0(1 - \sigma_i) \quad (3)$

ω_i is the nuclear precession frequency and σ_i is the screening constant (2)(3). The screening constant, which is a second rank tensor, $\underline{\sigma}$, describes the relation between the secondary magnetic field due to the induced currents and the applied field, H_0 . It is characteristic of the position of the nucleus in the molecule. The two fields will be in the same direction only if the applied field is directed along one of the principle axes of this tensor. However, in a

liquid, where the molecule passes very rapidly from one state to another, only an average over the states is observable so that the tensor, $\underline{\delta}$, can be replaced by the scalar σ in describing the Zeeman energy of the nucleus.

Spectral line splitting in nuclear magnetic resonance occurs as a result of two or more non-equivalent nuclei in a spin system experiencing electron coupled spin-spin interaction (4)(5). This interaction is described in terms of the bonding electrons and as such is an inherent property of the spin system. The indirect spin coupling may be represented by a Hamiltonian involving the scalar products of the spin vectors of all pairs of magnetic nuclei.

$$\mathcal{H}^{(1)} = \sum_{i < j} J_{ij} \underline{I}_i \cdot \underline{I}_j \quad (4)$$

J_{ij} is the coupling constant in cycles per second.

In liquids where the rate of rotation of the molecules is rapid enough for dipole-dipole interaction to be neglected, the complete Hamiltonian is given by:

$$\mathcal{H} = \mathcal{H}^{(0)} + \mathcal{H}^{(1)} \quad (5)$$

Therefore

$$\mathcal{H} = \frac{1}{2\pi} \sum_i \gamma_i H_i I_{Z(i)} + \sum_{i < j} J_{ij} \underline{I}_i \cdot \underline{I}_j \quad (6)$$

B) Proton Exchange

A proton exchanging between different sites * in a chemical system constitutes a time dependent process which influences the shape and width of the resonance signal (1)(6)(7). If the exchange rate is slow, the proton spends a sufficient time in a site to be detected there. In the case of rapid exchange, the n. m. r. signal is a time average of the rate processes under investigation.

The Bloch equations (8), which describe the appearance of a resonance signal, have been modified by Gutowsky (9) who obtained a quantitative relation between the line shape and the rapid exchange rate for a number of chemical systems. Gutowsky and Saika (10) solved the Bloch equations (8) in a similar manner (9) in their investigation of the dissociation properties of acids and bases. The collapse of spin multiplets (1)(4) as the exchange rate is increased has been used to study the rates and mechanisms of fast protolysis reactions of the methylammonium ion in water (11). The Bloch equations (8) have also been used to describe electron-transfer reactions (12). McConnell (13) has generalized the modified (9) Bloch equations (8) in a more convenient manner and at the same time investigated the case where the exchanging nucleus has different relaxation (1)(7)(14) properties in the separate environments. This work (13) will now be briefly described.

* A proton exchanging between two or more chemically distinct environments will precess with a different Larmor frequency in each of these sites.

Consider a nucleus X, transferring between two environments A and B. The lifetimes of X in A and B are T_A and T_B . The solutions of the Bloch equations (4) give the variation of the macroscopic nuclear moment M per unit volume. In the reference frame rotating with the R.F. field H_1 , u and v are the transverse components of M along and perpendicular to the rotating field H_1 . v, the out-of-phase component, is proportional to the absorption intensity. If M_z is the component of X nuclear magnetization in the direction of H_0 , then

$$u = u_A + u_B \quad (7)$$

$$v = v_A + v_B \quad (8)$$

$$M_z = M_z^A + M_z^B \quad (9)$$

Assuming that any magnetic environments of X are only associated with sites A and B, (i.e. a possible transition state is very short-lived) and defining $-\mu_A/\gamma_A$ as the rate at which u_A decreases due to the chemical transfer of u magnetization out of site A, then with a similar definition for $-\mu_B/\gamma_B$ the modified Bloch equations (1)(8)(13) are:

$$\dot{u}_A + \Delta\omega_A v_A = -\mu_A/\gamma_A + \mu_B/\gamma_B \quad (10)$$

$$\dot{u}_B + \Delta\omega_B v_B = -\mu_B/\gamma_B + \mu_A/\gamma_A \quad (11)$$

$$\dot{v}_A - \Delta\omega_A u_A = -v_A/T_{2A}' + v_B/\gamma_B - \omega_1 M_z^A \quad (12)$$

$$\dot{v}_B - \Delta\omega_B u_B = -v_B/T_{2B}' + v_A/\gamma_A - \omega_1 M_z^B \quad (13)$$

$$\dot{M}_z^A - \omega_1 v_A = M_0^A/T_{1A}' - M_z^A/T_{1A}' + M_z^B/\gamma_B \quad (14)$$

$$\dot{M}_z^B - \omega_1 v_B = M_0^B/T_{1B}' - M_z^B/T_{1B}' + M_z^A/\gamma_A \quad (15)$$

M_0 is the equilibrium z magnetization of the X nuclei and $\omega_1 = \gamma H_1$.

Nuclear relaxation times are defined by T_1 and T_2 (1)(2)(7)(14). Relaxation processes constitute radiationless transitions caused by nuclei exchanging energy with their environment. Spin-lattice relaxation (T_1) describes the relaxation of a nucleus in an upper spin state to a lower state, the energy being dissipated to the lattice where the lattice refers to the entire molecular system. T_1 relaxation establishes the Boltzmann excess of nuclei in the lower spin states. Thus a nuclear ensemble is perturbed when the resonance condition is established. T_1 is then the time constant required for this system to reach equilibrium. This is essentially the time required for M_z to decay back to M_0 so that

$$M_z = M_0(1 - 2e^{-t/T_1}) \quad (16)$$

where t is the time in which M_z is sampled. Spin-lattice relaxation times are measured by steady-state rapid passage methods (3) or the spin-echo technique (7)(15).

Spin-spin relaxation (T_2) defines the exchange of energy among nuclei in slightly different environments in the spin system. Whereas T_1 describes the rate of decay of M_z to M_0 , T_2 relaxation considers the rapid decay of the transverse components of the X magnetization, namely M_x and M_y . This describes the effects of local fields on neighbouring nuclei (1). In a given spin system, nuclei precess at angular frequencies of $\gamma(\delta H)$ where δH describes the range of local fields. These nuclei will then get out of phase in a time $1/\gamma(\delta H)$

and the decay of M_x and M_y is then described by $T_2 \approx 1/\gamma(\delta H)$. Hence the spin-spin relaxation can result in a broadening of the resonance line resulting from a time-average of the nuclei in different spin states.

If $\gamma_A, \gamma_B \gg (\omega_A - \omega_B)^{-1}$, where $(\omega_A - \omega_B)$ is the frequency separation between the two sites A and B, then the n. m. r. spectrum will consist of two signals near ω_A and ω_B (1). The Bloch equations are then modified for the case of slow exchange. If the frequency H_1 (the R. F. field) is close to ω_A , then the out-of-phase component is:

$$V = -\gamma H_1 M_0 \frac{p_A T_{2A}'}{1 + (T_{2A}')^2 (\omega_A - \omega_B)^2} \quad (17)$$

and the width of the broadened signal is given by

$$\frac{1}{T_{2A}'} = \frac{1}{T_{2A}} + \frac{1}{T_A} \quad (18)$$

where T_{2A}' is the relaxation time including the exchange effects.

T_{2A} is the "natural" relaxation time.

It is concluded then that chemical exchange results in a broadened signal centered at ω_A .

If the exchange is rapid, a time-averaged signal over the exchange process is obtained. In this region of rapid exchange, a corresponding expression for the line width parameter is given by: (1)

$$\frac{1}{T_2'} = \frac{p_A}{T_{2A}} + \frac{p_B}{T_{2B}} + p_A^2 p_B^2 (\omega_A - \omega_B)^2 (\gamma_A + \gamma_B) \quad (19)$$

where p_A and p_B are the populations of sites A and B.

The exchange modified Bloch equations (8) have been used to investigate potential barriers to hindered rotation in alkyl nitrites (16). A more recent investigation of this system using the spin-echo (15) technique, has been reported (17). An interesting account of proton exchange in water has been given by Meiboom (18). He has found that the proton relaxation rate is pH dependent and accounts for this in terms of the coupling of the proton resonance with O^{17} ($I = 5/2$) being only partially averaged out by proton exchange. He has calculated the coupling constant between H^1 and O^{17} to be 92 ± 15 c.s. and develops theoretical equations relating relaxation rates and exchange. The Bloch equations modified for a nuclear species exchanging between two environments having a different relaxation time have been solved for n. m. r. pulse experiments (15)(19). The spin-echo technique (15) allows for the investigation of relaxation mechanisms in the absence of the applied H_1 field. This fact may be used in a more accurate study of chemical systems in which nuclear exchange occurs (17).

C) The Hydrogen Bond

Hydrogen bond formation is the result of an interaction between a donor molecule X-H and an acceptor group Y providing that the charge distribution of the X-H bond orbital is such that the proton is sufficiently unscreened. Under these conditions, a stable hydrogen bond X-H---Y is formed.

The proton magnetic resonance (1) method may be usefully applied to hydrogen bonded systems (20) since the chemical shift difference between a proton in its non-associated and hydrogen-bonded states is generally quite large. This hydrogen bond shift is a result of the magnetic field experienced by the proton being modified when a hydrogen bond X-H---Y is formed.

The variations in chemical shift may be interpreted in terms of an electrostatic field along the hydrogen bond. In this respect, when a donor group X-H and an acceptor molecule Y are in a position to form a hydrogen bond, a change in the chemical shift of H is attributed to Y introducing an added electric field in the vicinity of the proton. The effect of this field is to draw the proton away from its bonding electrons and reduce the electron density around it. The electric field would also tend to inhibit diamagnetic circulations within the hydrogen atom so that the combined effect results in a low field chemical shift, the magnitude of which reflects the strength of the hydrogen bond (21).

Liddel and Ramsey (22) first recognized the possibility of applying nuclear magnetic resonance to hydrogen bond studies from the temperature dependence of the -OH chemical shift in ethanol. The same shift is observed in dilution studies of ethanol in an inert solvent (23)(24).

An interesting account of the use of n. m. r. in measuring the strength of a hydrogen bond has been given by Korinek and Schneider (25). The proton shift of the acceptor molecule chloroform has been measured in a variety of different donor liquids. Dilution of chloroform in an inert solvent results in a high field shift indicative of intermolecular hydrogen bonding. In triethylamine, however, which is a strong donor molecule, a low field shift results. At infinite dilution, this shift is characteristic of chloroform in a hydrogen bonded state. A comparison of the infinite dilution shift in an inert solvent and in triethylamine gives the association shift and some measure of the strength of the hydrogen bond. Similar n. m. r. dilution studies have been carried out on a large number of chemical systems having hydrogen bonded structures (26)(27)(28).

The hydrogen bond may be used as a path for a proton to exchange between two magnetically inequivalent sites (29). An infra-red study of proton exchange in hydrogen bonded systems has been given by Bellamy and Rogasch (30) and Reeves and co-workers have studied a number of related systems using n. m. r. (29)(31)(32).

Freedman (33) has examined a number of compounds containing similar O-H---O and O-H---N bonds and has indicated that the strength of the O-H---N bond had been previously underestimated and is in fact stronger

than the O-H---O bond. A recent comparison of infrared and n. m. r. data on substituted phenols has been carried out by Allan and Reeves (34). Equilibrium constants for the cis-trans conversion in orthohalophenols are determined and heats of formation of the O-H---X bonds are evaluated.

D) Aqueous Electrolytes

(i) Magnetic Resonance of Strong Acids:

An interesting application of nuclear magnetic resonance involves the study of dissociation equilibria in solutions of aqueous electrolytes which yield hydrogen-containing ions (1). Gutowsky and Saika (10) were the first to apply n. m. r. in this way by investigating dissociation and chemical exchange in hydrochloric, nitric and perchloric acids. Room temperature spectra of all these acids show a single proton resonance peak whose chemical shift is an average for all species in solution. The equilibrium in aqueous solutions of these acids may be written as:



Defining x_1 and x_2 as the fraction of protons in H_3O^+ and H_2O respectively the observed chemical shift is given by:

$$\delta = x_1 \delta_{H_3O^+} + x_2 \delta_{H_2O} \quad (21)$$

and the concentration dependence of the chemical shift reflects the dissociation of the acid. In one of the earlier papers (35) in a series by Hood and co-workers, based on studies carried out by Gutowsky (10), a linear relation exists in dilute acid solutions between the chemical shift and the fraction of protons present as H_3O^+ assuming complete conversion of the acid proton to H_3O^+ . The slope of the line has been used in evaluating the dissociation constants for nitric and perchloric acid to be 22 and 38 respectively. In more concentrated acid solutions, there is evidence that little ionization into H_3O^+ and A^- exists. An

investigation of these three acids studying the magnetic resonance of nuclei other than the proton have been reported by Masuda and Kanda (1) (36)(37).

The investigations of nitric and perchloric acid have been extended to trifluoroacetic acid as an example of a moderately strong acid (38). The dissociation constant for the acid was estimated to be 1.8 and both fluorine and proton resonance of the acid in different water concentrations showed the influence of electrolytic dissociation in dilute acid solutions and of hydration above 50 mole % acid.

Early investigations of aqueous electrolytes have been focussed on the properties of the acid in dilute solutions. In an interesting account, Happe and Whittaker (39) have considered proton resonance shifts for the concentrated region of the nitric acid-water and nitric acid-KNO₃ systems. They have demonstrated that ionization into H₃O⁺ and NO₃⁻ is only slight in this region and have used the chemical shift data of the nitric acid-water system to interpret the association of nitric acid in terms of hydrogen bonding and also to investigate the ionization equilibria in the anhydrous acid. The temperature dependence of the chemical shift in the nitric acid-water system is reported in the region of the anhydrous acid.

Hood and Reilly (40) have extended their investigations on the ionization of strong electrolytes to considering the temperature coefficient of dissociation of nitric and perchloric acids. In concentrated solutions of nitric acid, the proton shift for a given solution shows no variation with temperature. This is consistent with the fact that in high acid

concentrations, the solution contains undissociated monomers and polymers. However perchloric acid does dissociate even in concentrated solutions and a temperature dependence of the chemical shift is observed.

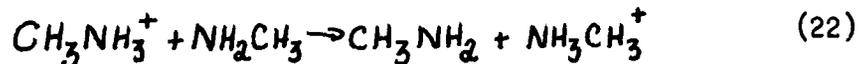
(ii) Diamagnetic Salt Solutions:

A study of the effect of diamagnetic salts on the proton resonance of water has been examined by Shoolery and Alder (1)(21). Low and high field shifts from water of several salts are interpreted in terms of water molecules strongly bonded to ions. A high field proton shift is attributed to the ion breaking up the hydrogen bonded structure of water. In general the smaller the ion and the higher its charge, the greater is the proton shift to low field. A recent study by Hindman (41) briefly reviews the work of Shoolery and Alder (9) and attempts to quantitatively measure the contributions of hydration, structure and polarization to the ion shift data.

(iii) Rate Studies of Protolysis:

The adaptability of the n. m. r. method to studies of chemical exchange provides an interesting approach to rate studies of protolysis. Grunwald, Loewenstein and Meiboom (11) have carefully studied the rates and mechanisms of protolysis of the methylammonium ion in aqueous solution. Rate constants (1) obtained from the CH_3 and NH_3^+ n. m. r. lines have been used in formulating reaction mechanisms and the exchange broadening of the water signal measured the mean time that a proton spends on a water molecule before returning to the nitrogen. It is therefore possible to estimate the fraction of protolysis that proceeds by transfer of a proton

to a water molecule compared to the direct proton transfer between methylammonium groups, i. e.



A parallel investigation of the di- and trimethylammonium ions was carried out by Loewenstein and Meiboom (42). The results complement those on the methylammonium ion (11) so that a complete comparison of the kinetics of the three methylammonium ions has been made available. Related n. m. r. studies of the ammonium ion have also been carried out (43)(44)(45).

An n. m. r. study of the hydrogen exchange kinetics in methanol and ethanol have been carried out by Luz, Gill and Meiboom (46). The exchange is catalyzed by acid or base and the kinetics have been interpreted in terms of proton exchange between the neutral alcohol and an alcoxonium ion in an acidic medium and between the alcohol and an alcoxide ion in a basic medium. The influence of water on the exchange mechanism has also been determined for several alcohol-water mixtures.

E) The Assignment of Charge Densities

Nuclear magnetic resonance and the chemical shift parameter (1) may be used in the assignment of electron charge densities about protons in chemical systems (47). Corio and Dailey (48) were the first to use n. m. r. in this way by investigating several substituted benzenes. They concluded that polarization effects were the important factors in determining the directive influences of substituents. Therefore the position of the substituent is related to the value of the electron density at the ortho, meta and para positions and, assuming no changes in bond hybridization, the chemical shift will reflect an approximate measure of the charge density. Most of the mono-substituted benzenes are AB_2C_2 (or AB_2X_2) (1) cases and analysis of their spectra is tedious. In this respect, the work of Corio and Dailey (48), in using an H_0 field of 30 M.c.s., was more or less qualitative. Bothner-By (49) considered solvent effects in correcting some of Corio's (48) chemical shift data and Taft (50) derived an equation which gave good agreement between chemical shift data and Hammett's σ constants. Some related theoretical work on monosubstituted benzenes has been done by Buckingham (51) whose charge density assignments to the ring protons of nitrobenzene are in good agreement with the results of Corio and Dailey (48). In a careful study, Fraser (52) investigated a number of substituted xylenes. His findings bear out the fact that the chemical shifts at the meta and para positions are determined by both inductive and resonance effects of the substituents but there is no agreement with Buckingham's theory (51).

Several papers (53)(54) have dealt with the complete spectral line assignments of substituted benzenes and established accurately chemical shift and spin-spin coupling constant data. Together with the work done by Fraser (52), this information has been very useful in establishing peak positions for substituted benzenes prior to charge density assignments.

Following a parallel course of development, magnetic resonance studies of C^{13} in natural abundance ($\sim 1.1\%$) have proven to be beneficial in the assignment of charge densities to aromatic systems. Lauterbur (55) has investigated C^{13} resonances in a large variety of compounds observing the resonance at a fixed frequency of 8.5 M.c.s. in magnetic fields of about 7940 gauss. The dependence of the C^{13} -H spin coupling constant on the s character of the bond has been studied by Shoolery (56). In a more recent study, Muller (57) has concluded that J_{C-H} is independent of the polarity of the C-H bond, but uses this parameter as an indication of the hybridization of the carbon atomic orbital.

A detailed investigation of C^{13} nuclear magnetic resonance in aromatic hydrocarbons has been carried out by Lauterbur (58)(59). In the first paper of this series (58), C^{13} assignments are given for a large number of substituted benzenes. Using deuteration and methyl substitution, the spectra have been simplified and the analysis indicates that C^{13} shifts are influenced directly by the π electron density distribution in the molecule.

In ferrocene, the value of J_{C-H} is larger than in the other six membered rings studied and following the arguments of Shoolery (56) and Muller (57), this may be attributed to the increased s character

of the C-H bond expected for a carbon in a five-membered ring. In a continuation of these studies Lauterbur (59) investigated the C^{13} resonance of phenols and related compounds providing evidence for a relation between C^{13} chemical shifts and the π electron distribution in these organic systems. Spiesscke and Schneider (60) have carried out a complete C^{13} and H^1 resonance investigation of monosubstituted benzenes (aryl-x) finding large resonance shifts for the carbon directly bonded to x. A detailed account of the effects of the substituent on the ortho, meta and para positions in terms of inductive and magnetic anisotropic effects suggest that both C^{13} and H^1 resonance data are important in establishing π density distributions.

Along with several other workers (61) Spiesscke and Schneider (62) have been instrumental in assigning charge densities to ionic systems. The π electron density ρ , in the series $C_5H_5^-$, C_6H_6 , $C_7H_7^+$, $C_8H_8^{++}$ had been established using proton magnetic resonance (16). The C^{13} shifts which are very much larger show a parallel behaviour so that both C^{13} and H^1 nuclei can be used in local π electron density assignments.

A room temperature proton magnetic resonance study has been carried out on a number of azulenes and their conjugate acids (63)(64). Using trifluoroacetic acid, indications are that protonation will occur at the carbon atom with the largest excess of electron charge density and the change in chemical shift on protonation may be interpreted in terms of ρ changes in the π electron density at the carbon atom. Macleod and Mackor (65) have investigated the distribution of charge in methylated naphthalenes and have discussed variations in the chemical shift of the

ring protons in terms of the inductive effect of the methyl group. These same authors (66) have studied proton exchange in carbonium ions of methylated benzenes. In an interesting account, a study of mesitylene dissolved in anhydrous HF (saturated with BF_3) at -75°C reveals that proton exchange does not proceed via the acid but that the captured proton remains on the ion as it moves around the ring. Charge density assignments to the ring protons are also given. A recent study by Dailey (67) and co-workers reinvestigates a number of substituted benzenes and a series of nitrogen heterocyclics attempting to establish a linear relation between the chemical shift and charge densities. An attempt has been made to review the important contributions to the chemical shift. This has led them to the conclusion that a lack of an empirical relation in most cases between the chemical shift and electron density indicates that not all factors have been determined (68).

E X P E R I M E N T A L

CHAPTER II

A) Trifluoroacetic acid - Quinoline

Trifluoroacetic acid was purified by fractional distillation and a middle cut selected for immediate use. A few drops of trifluoroacetic anhydride were added to the remainder of the distillate which was stored in the absence of light at 0°C. Quinoline is more difficult to purify due to its hygroscopic nature and the rapid rate at which it is oxidized. Three successive fractional distillations were required to obtain a colourless sample from the brown colour that quinoline acquires when left standing for a prolonged period. The purity of the sample was checked spectroscopically using a Varian A-60 n. m. r. spectrometer. Most of the quinoline was used immediately and the remainder was stored over $\text{CaSO}_4 \cdot 1/2\text{H}_2\text{O}$ ("Drierite") in a dry nitrogen atmosphere at 0°C.

Solutions of the acid and base at different relative concentrations were prepared by weighing out each of the components in small vials. In all cases, the vials became warm when the acid and the base were mixed (32). A small amount (~2%) of tetramethylsilane was used as an internal reference (1) and the mole fraction of the acid was computed on the basis of the total number of moles of acid, base and standard.

A careful study of this system was only possible on a limited

number of solutions due to the formation of a white crystalline salt between 20-60 mole % acid. However in one experiment the trifluoroacetic acid-quinoline solution was dissolved in 50 mole% acetonitrile which had been previously distilled. Since the salt was soluble in this polar solvent, investigation of the system over the entire concentration range was possible.

Three solutions between 80-100 mole % acid were dissolved in methylene chloride and studied at -18°C . However attempts to prepare a 50-50 acid-base mixture for a low temperature study were unsuccessful in that no suitable solvent could be found to completely dissolve the salt between 0°C and -60°C .

Samples were prepared for n. m. r. analysis in 5 mm. O. D. tubes which had been rounded off at one end. The tube was attached to a high vacuum system and the sample was thoroughly degassed by freezing with liquid nitrogen and allowing it to warm to room temperature under vacuum. This freeze-pump-thaw process was repeated several times and the tube finally sealed off.

Most of the concentration studies were done on a Varian A-60 n. m. r. spectrometer. Since this instrument is normally used for organic qualitative analysis, accurate chemical shifts were obtained by externally connecting to the A-60, a Hewlett-Packard Wide Range Audio oscillator and a model 522 B Electronic frequency counter. In this manner, preselected side bands (1) could be placed on any part of the spectrum as the main field H_0 , was swept through

resonance. This technique proved to be successful in obtaining chemical shifts accurate to within 0.5 c.s. and producing very symmetrical traces for line width determinations over a narrow frequency range. * Further room temperature experiments and the single low temperature run on this system were performed on a Varian Model V-4300 high resolution spectrometer operating at 40 and 60 M.c.s. Maximum field homogeneity was obtained with the aid of field homogeneity controls and a V-K3506 Super Stabilizer. In most of the experiments, ethanol slightly acidified with hydrochloric acid was used as a standard in setting up an optimum field. Observation of the second order splitting of the methylene quartet indicated a field capable of detecting peak separations of less than 0.5 c.s. All chemical shifts were obtained using the sideband technique (1) which involved modulating the main field so that the reference peak was superimposed on the signal under study. Permanent spectra were recorded on a Varian Model G-10 recorder and calibrated in a similar manner as outline for the A-60.

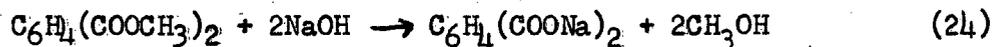
* I wish to thank Mrs. C. Brion whose careful maintenance of the A-60 unit and co-operation in allowing me to use the spectrometer after hours simplified the task of obtaining well resolved n. m. r. spectra.

B) Methanol-Orthochlorophenol

Methanol is very difficult to purify due to its exceedingly hygroscopic nature. In this investigation two methods were used to obtain a relatively water-free sample. The first method, as outlined in Vogel (69) suggests that sodium cannot be used for the complete removal of water in methanol due to the following equilibrium:



If however the sodium hydroxide is removed by allowing it to react with a high boiling ester, such as methyl phthalate (B.P. 282°C) then dry methyl alcohol may be obtained. The reaction is given as:



and methanol is removed from the ester by distillation when required for immediate use.

A good test of the purity of methanol is the detection of the $\text{I}\cdot\text{I}$ interaction between the hydroxyl proton and three equivalent methyl protons (70). Therefore the n. m. r. spectrum of pure methanol should consist of a quartet (-OH resonance) and a doublet to high field (-CH₃ resonance). Methanol prepared in the above manner did not show this splitting. This is not necessarily due to the presence of water but perhaps because of a trace of sodium methoxide or some other impurity capable of rapidly exchanging with the alcohol resulting in a collapse of the spin multiplet. Nevertheless this methanol was used to investigate the effect that water had

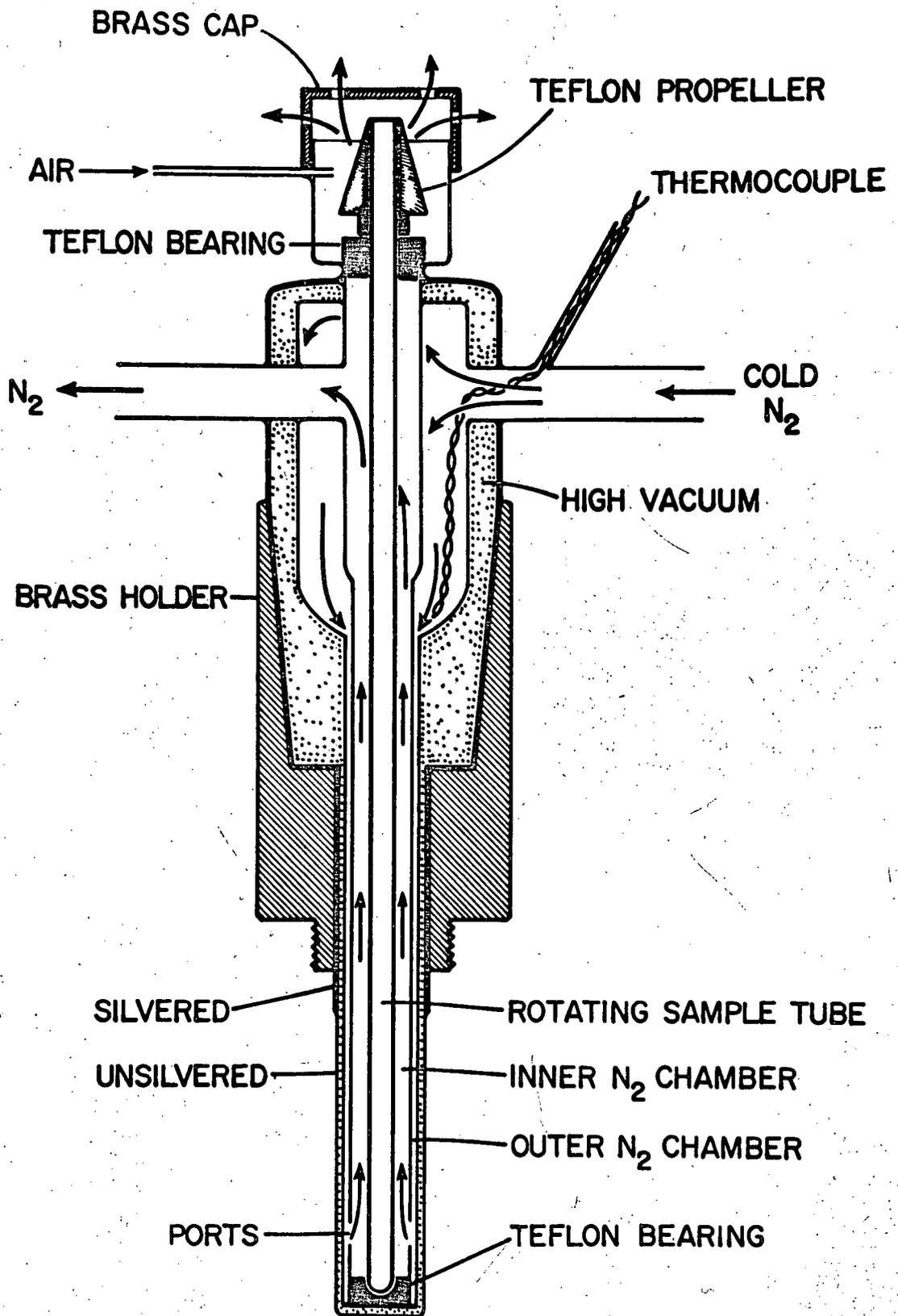
on several solutions of the alcohol mixed with orthochlorophenol.

The second method, described by Moore (71) involves the vacuum distillation of methanol onto a suitable drying agent. Reagent Grade Methanol was distilled into a specially designed Quickfit container which could be attached immediately to a high vacuum system. The alcohol was frozen with liquid nitrogen and the flask evacuated. It was then allowed to distill into another bulb containing $\text{CaSO}_4 \cdot 1/2\text{H}_2\text{O}$ ("Drierite") which had been baked out under vacuum for twenty-four hours. The methanol was left in contact with the drying agent overnight and then a small amount of it distilled into an n. m. r. sample tube (5mm. O.D.) previously attached to the vacuum line. The tube was then sealed off and methanol prepared in this manner was resolved into the quartet and doublet.

Orthochlorophenol was purified by two successive fractional distillations selecting a middle cut each time and used immediately. Progress of its purification between distillations was checked on the A-60.

Moore's (71) method of purifying methanol was used in preparing an approximately 50-50 solution of methanol-orthochlorophenol in order to carry out a low temperature investigation of the system. This experiment was performed using a recently designed "Spinning Dewar" ** (Fig. I). The Dewar is fitted into the Varian probe and the entire

** Thanks are accorded to Mr. W. Janzen whose talent in designing this apparatus has aided the high resolution n. m. r. group of this laboratory in carrying out successful variable temperature runs.



'SPINNING SAMPLE' DEWAR INSERT

apparatus centralized in the magnetic field. A Dewared connector leads to a 25 l. tank of liquid nitrogen fitted with a heating device. In this way cool N_2 gas is circulated around the sample. The temperature of the sample, measured with a copper-constantin thermocouple, is controlled by the rate of flow of the N_2 gas. A powerstat connected to the heater controls the flow rate to the sample. This arrangement is very satisfactory in that samples may be investigated between $-120^{\circ}C$ and $+200^{\circ}C$ and at any given temperature, samples may be interchanged. An hour is normally required for the sample to equilibrate with its surroundings. There is also the added advantage that sample spinning, required for high resolution, is accomplished with the use of a separate air lead and is independent of the stream of nitrogen gas.

R E S U L T S

CHAPTER III

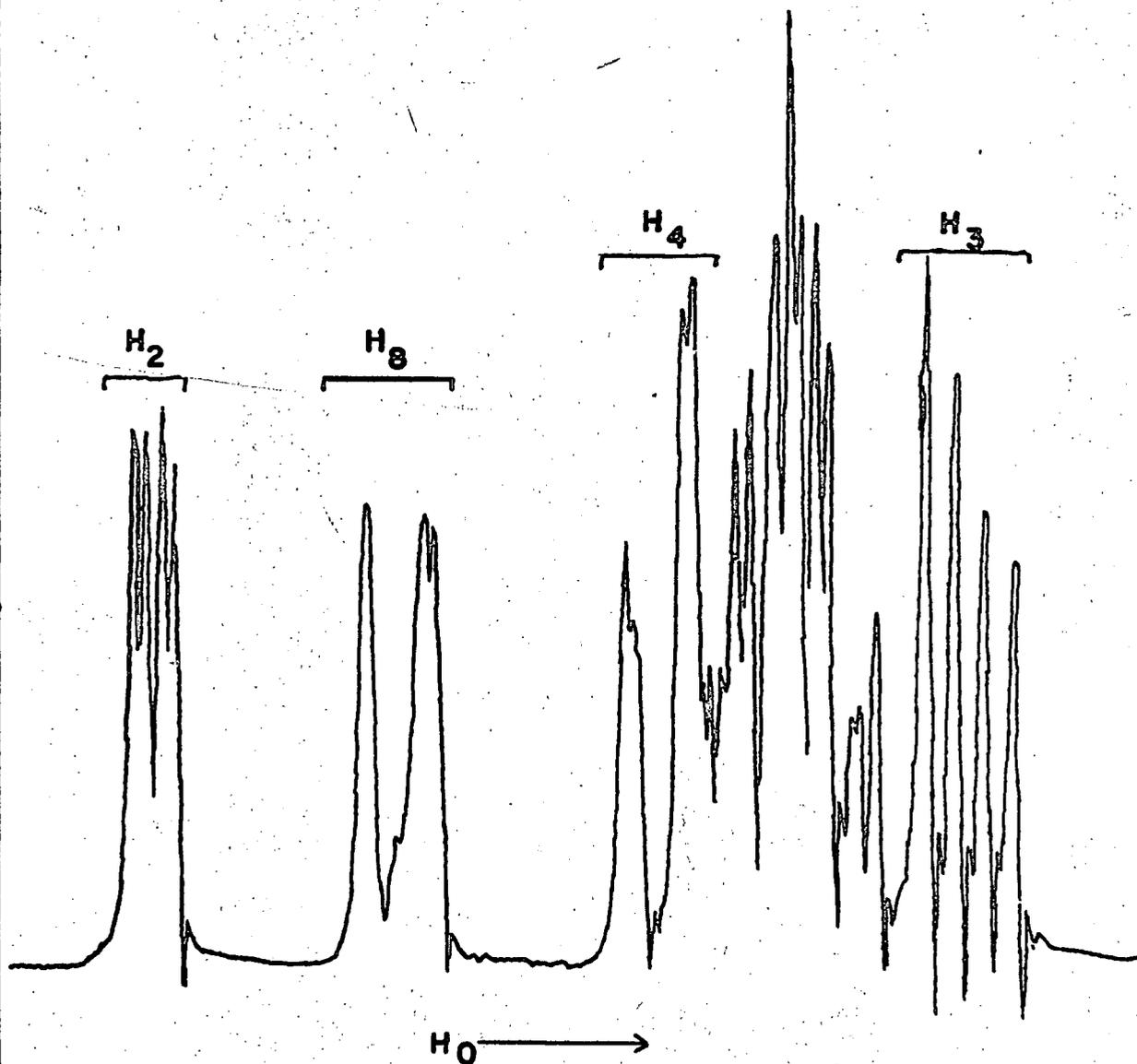
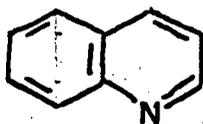
A) Trifluoroacetic acid - Quinoline

The proton resonance spectrum of quinoline (Fig. II) is resolved into a series of peaks resulting from sets of three and four spins on the two aromatic nuclei. The three protons on the hetero-ring make up an ABX system (1) and the assignment of each resonance signal, together with the coupling constants is given in Pople, Schneider and Bernstein (1). Peak assignments are verified by observing the n. m. r. spectra of several methyl quinolines. The quartets at lowest and highest field (Fig. II) are identified as the α (H_2) and β (H_3) protons respectively and the more poorly resolved signal of the γ proton (H_4) appears to the immediate high field side of H_3 in the aromatic ring. There is also some cross coupling of the nuclear spin energies between the aromatic and hetero-ring systems involving protons at the four and eight positions (72). On the basis of the discussion by Pople et al (1) and more recent investigations of 8-hydroxy- and 8-methylquinoline carried out by Reeves and Strømme (73), the spin-spin coupling constants between the protons in the hetero-ring are given as: $|J_{\beta\gamma}| = 8.3$ c.s., $|J_{\alpha\beta}| = 4.4$ c.s. and $|J_{\alpha\gamma}| = 1.7$ c.s. Anet (72) has evaluated the cross-coupling between H_4 and H_8 to be 0.8 c.s. The proton resonance spectrum of trifluoroacetic acid consists of a single sharp peak chemically shifted 445 c.s. (at 40 M.c.s.) to the low field side of tetramethylsilane.

TO FOLLOW PAGE 25

FIGURE II

N.M.R. SPECTRUM OF QUINOLINE



The room temperature spectra of the two component system consists of two sets of peaks. The high field series of peaks are identified as the quinoline protons although the appearance of the line shapes is modified quite considerably from the spectrum of pure quinoline. The low field single peak time averaged because of rapid proton transfer represents contributions from trifluoroacetic acid and the protonated quinoline. When the relative acid-base concentration is varied, the low field signal broadens and the quinoline peaks, as well as being broadened, are modified considerably. At no concentration however are separate peaks resolved for the QH^+ species and the trifluoroacetic acid proton. Smith and Schneider (74) studied the n. m. r. spectrum of pyridine in trifluoroacetic acid and in addition to the -OH carboxyl proton and the α , β and δ protons of pyridine they observed a triplet signal characteristic of a proton bonded to a nitrogen atom ($I = 1$). The absence of this peak in the quinoline system is attributed to the reduced basicity of quinoline.

The concentration dependence of the exchange averaged peak in mixtures of the pure acid and base is shown in Fig. III. The chemical shifts are measured relative to an internal reference of tetramethylsilane. All chemical shift data were checked on a Varian A-60 spectrometer and the results, reduced to 40 M.c.s., were in good agreement to those shown in Fig. III. The acid-base mixture forms a salt in the region 20-60 mole % acid accounting for the discontinuity in the curve. Fig. IV shows a similar set of results but the mixtures of acid and base were dissolved in 50 mole % acetonitrile.

FIGURE III

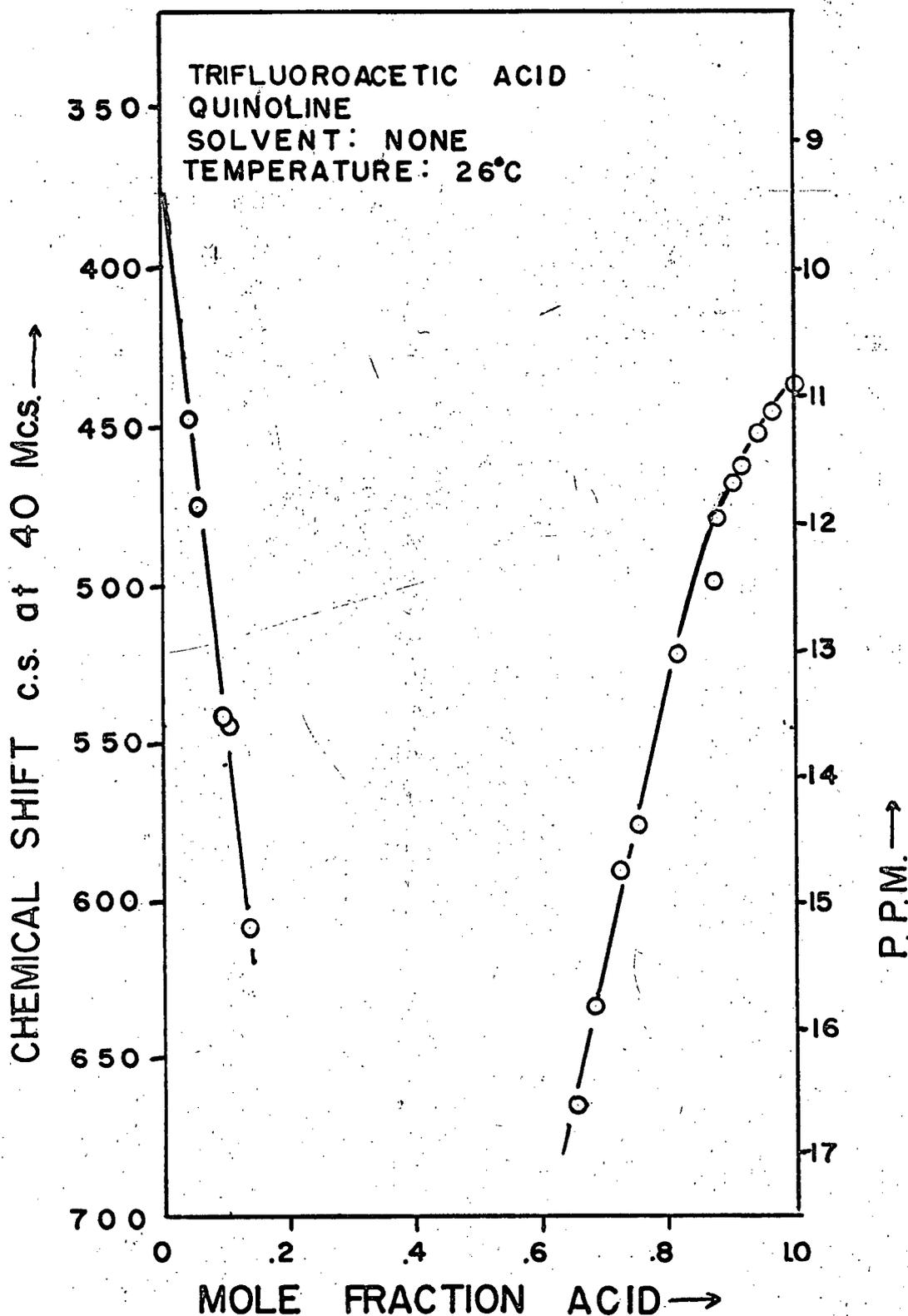
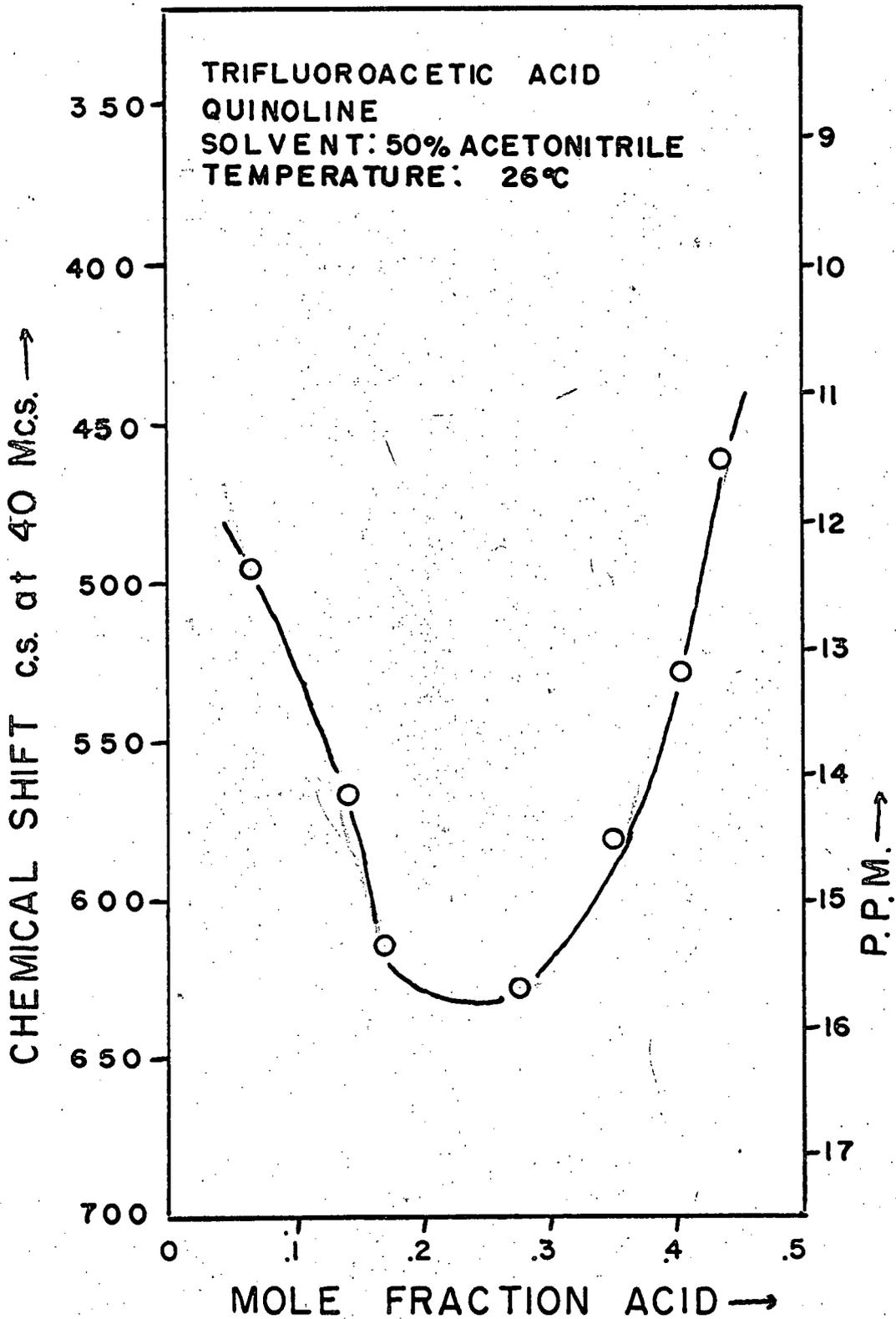


FIGURE IV



The salt formed in the pure system is readily taken up at room temperature in acetonitrile so that chemical shift measurements could be carried out over the entire concentration range. Both of these curves undergo a considerable concentration dependent shift to low field and although the minimum of the line in Fig. III could not be obtained, it appears that in both cases, the maximum displacement to low field occurs in a 50:50 mole ratio acid-base mixture. Comparison of Figs. III and IV show a decrease in the low field shift after mixtures of the acid and base have been dissolved in acetonitrile.

A low temperature investigation of three solutions dissolved in dichloromethane was carried out using ~2 mole % of cyclohexane as an internal standard and the results are shown in Fig. V. At -18°C , the exchange rate is sufficiently reduced to observe distinct signals for the QH^+ species and $\text{CF}_3\text{CO}_2\text{H}$. Both signals are still exchange broadened at this temperature and the $\gg\text{NH}^+$ peak to low field undergoes additional quadrupolar broadening due to the proton being coupled to N^{14} ($I = 1$) but shows no resolution into a triplet structure. Fig. V shows the concentration dependence of the individual proton resonances along with the low field concentration dependence of the exchange averaged $\gg\text{NH}^+-\text{CF}_3\text{CO}_2\text{H}$ resonance signal at $+24^{\circ}\text{C}$. At -18°C both the $\gg\text{NH}^+$ and $-\text{OH}$ signals show a parallel displacement to low field as more quinoline is added.

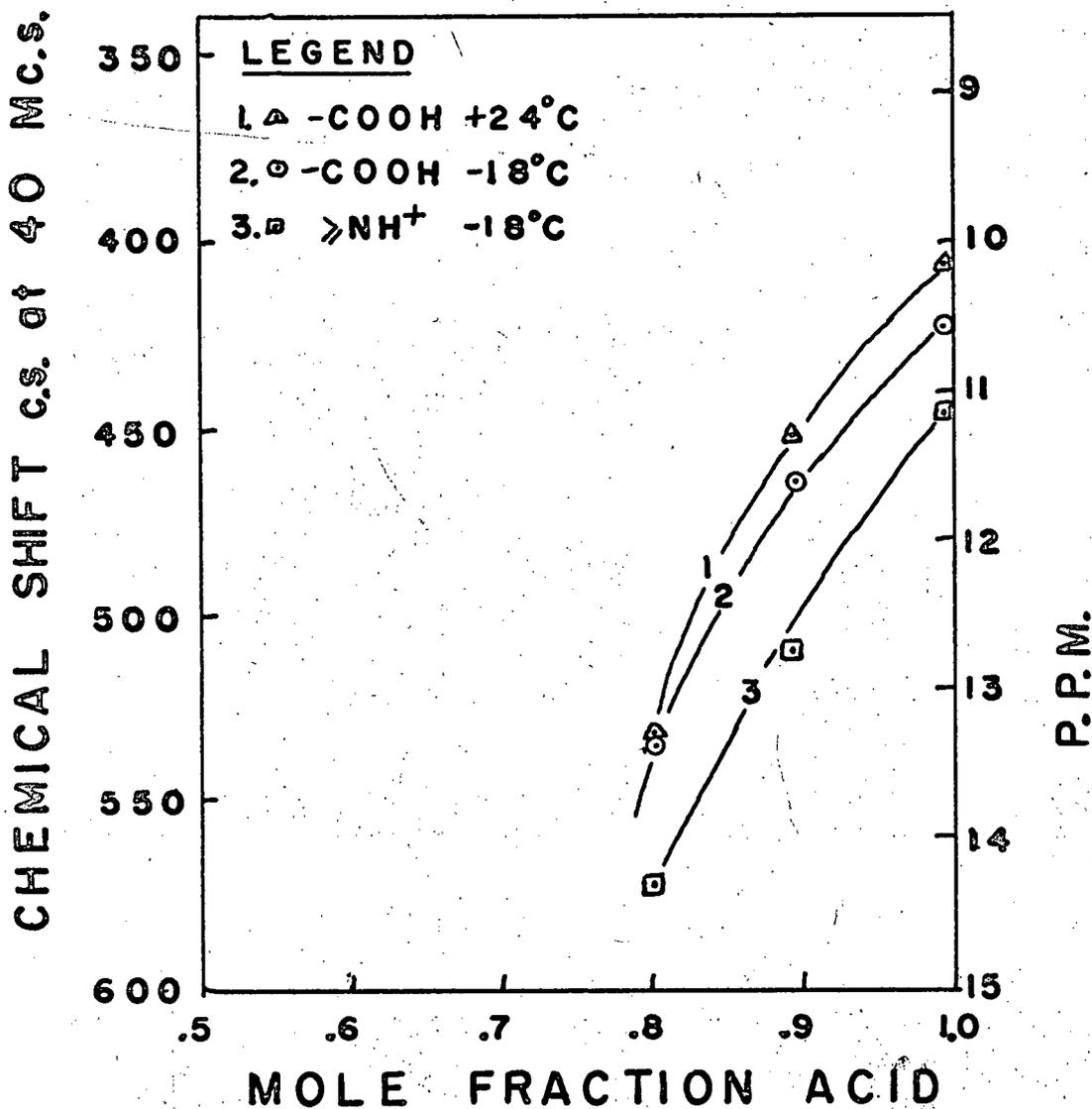
When trifluoroacetic acid is added to quinoline, the spectrum of quinoline is modified considerably and ring proton positions are

FIGURE V

POSITION OF COOH AND NH⁺ PEAKS

SOLVENT: DICHLOROMETHANE

REFERENCE: CYCLOHEXANE



difficult to assign. This is due in part to exchange broadening but the greatest difficulty in assigning these peaks results from the concentration dependence of the ring-protons. The peaks overlap as the concentration of acid and base varies and their assignments become ambiguous. However the concentration dependent shifts of the ring protons shown in Fig. VI were obtained by observing the spectra of several trifluoroacetic acid-methylquinoline solutions and observing an absence of a signal compared with a spectrum of trifluoroacetic acid-quinoline using solutions of the same relative acid-base mole ratio. Once a peak was assigned, its chemical shift displacement was followed as more quinoline was added. In Fig. VI hexamethyldisiloxane is the internal reference. The acid-base mixtures were dissolved in acetonitrile and the spectra taken at 40 M.c.s. The three protons in the hetero-ring move to low field as more quinoline is added with the γ proton experiencing the largest shift. In all three cases, the maximum low field shift occurs at an approximately 2:1 acid to base mole ratio.

Room temperature measurements of the line width of the exchange averaged peak are plotted as a function of concentration for the pure acid-base system in Fig. VII. The line widths were obtained using a Varian A-60 spectrometer and calibrated by placing tetramethylsilane (internal) side bands on either side of the peak. In this manner, the full line width at half the peak amplitude was directly obtained in cycles per second. In all cases, minimum sweep fields were used on the A-60. This produced a symmetrical trace expanded so as to cover the entire length of the chart paper with sidebands placed at either end.

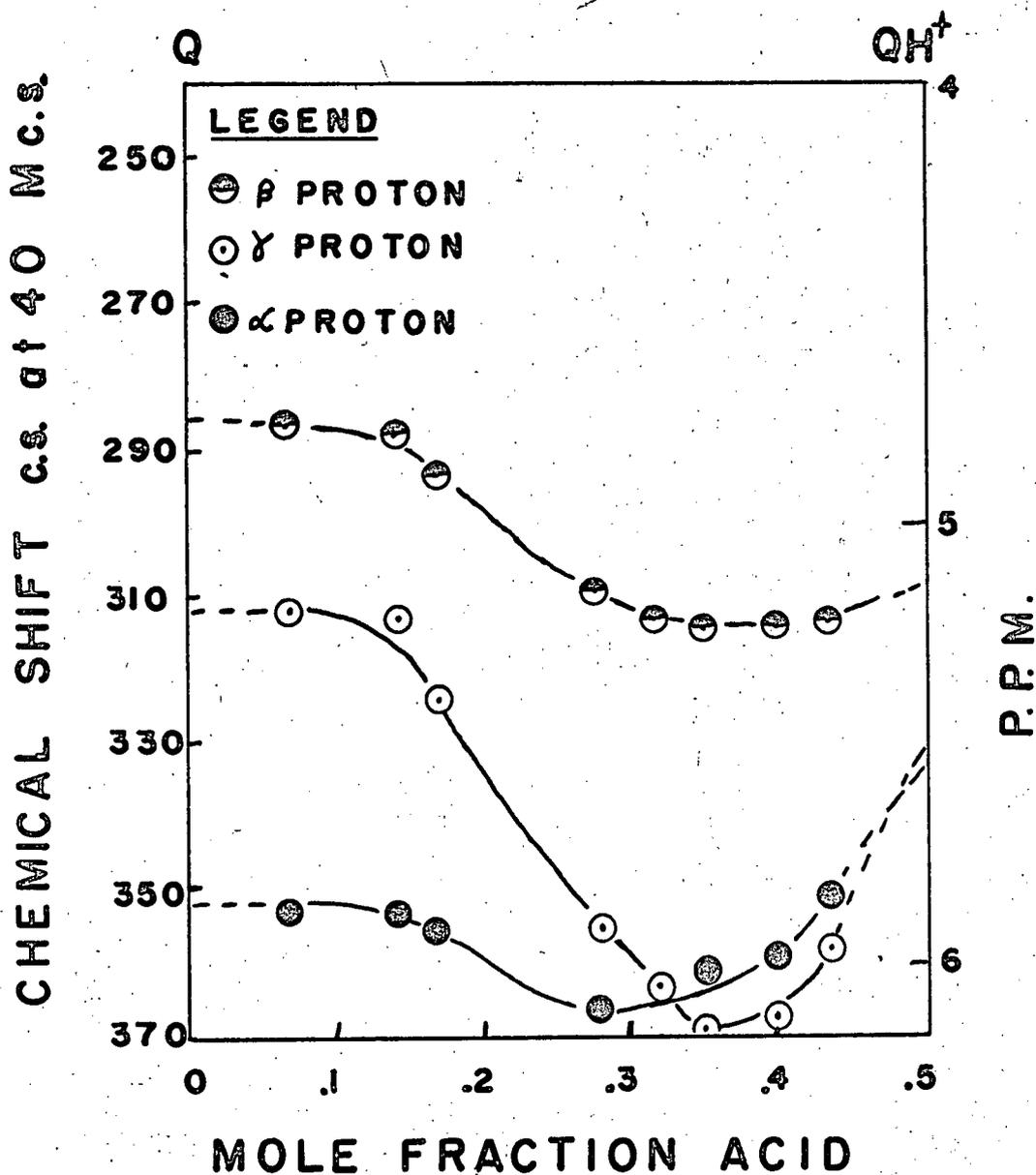
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FIGURE VI

POSITION OF THE RING PROTONS

SOLVENT: 50% ACETONITRILE

REFERENCE: HEXAMETHYLDISILOXANE

TEMPERATURE: +26°C



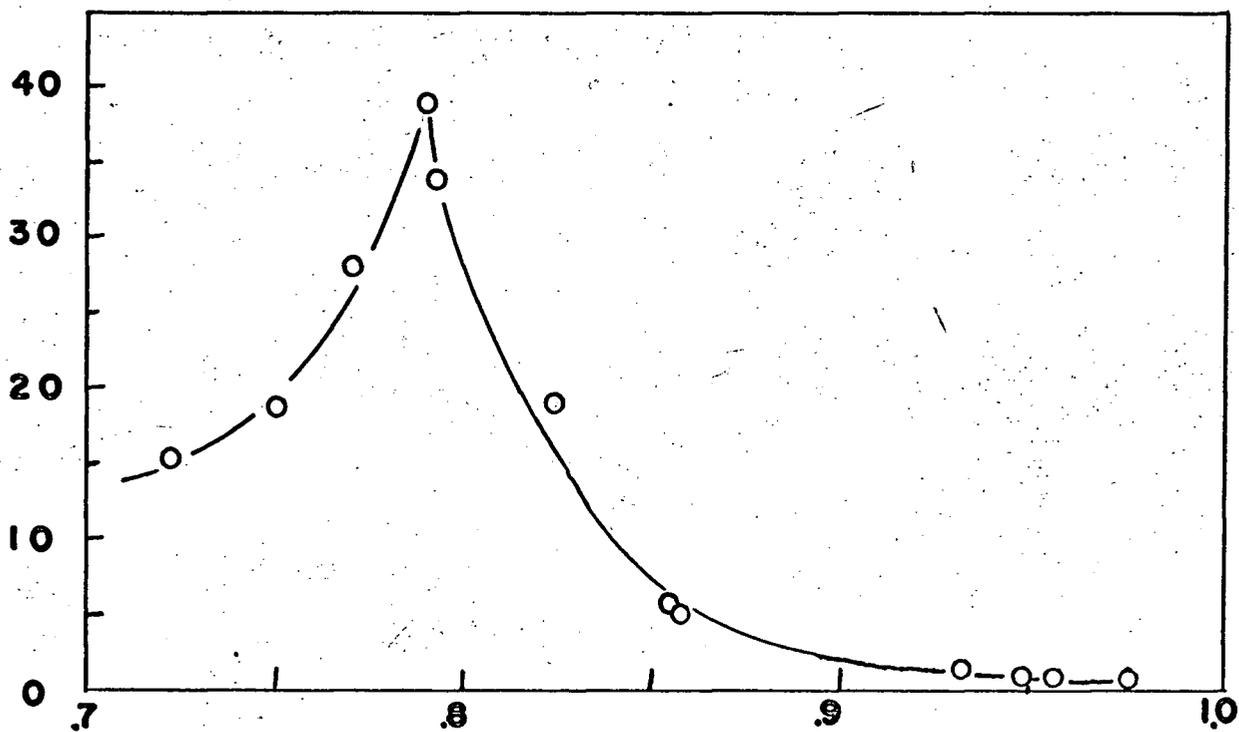
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FIGURE VII

LINE WIDTH OF THE EXCHANGE AVERAGED PEAK

TRIFLUOROACETIC ACID - QUINOLINE
NO SOLVENT

LINE WIDTH c.s. at 60 Mc.s.



MOLE FRACTION ACID

Since the sidebands were put down at the same time as the trace was obtained, deviations from the linearity of the sweep were minimized so that the line widths, obtained in this way, are accurate, to within 0.5 c.s. The results of a similar line width study of the acid-base system in 50 mole % acetonitrile solution are shown in Fig. VIII. A comparison of Figs. VII and VIII indicate that the maximum in the line width occurs at different concentrations of the acid-base mixture as well as the maximum line width in the acetonitrile solutions being less than in the pure acid-base mixtures.

Attempts to do low temperature (0 to -60°C) experiments on a 50-50 acid to base mole ratio solution in order to obtain a sharp acid peak and a broadened $\gg\text{NH}^+$ signal were unsuccessful due to crystallization of the salt even in acetonitrile solutions. No suitable solvent which has a low enough freezing point and could dissolve the salt without the danger of itself being protonated by the trifluoroacetic acid could be found.

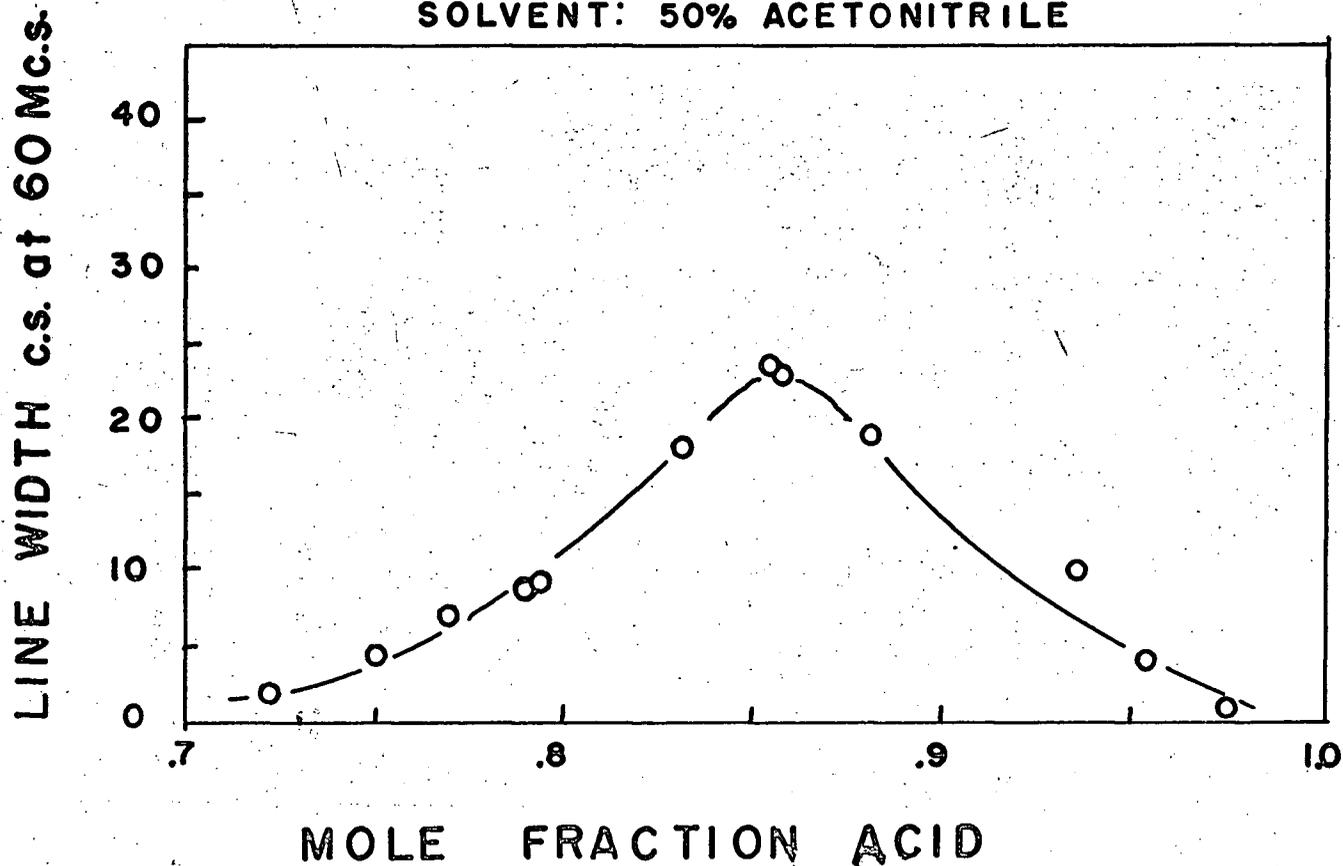
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FIGURE VIII

LINE WIDTH OF THE EXCHANGE AVERAGED PEAK

TRIFLUOROACETIC ACID - QUINOLINE

SOLVENT: 50% ACETONITRILE



B) Methanol - Orthochlorophenol

(i) Influence of Temperature

A low temperature investigation of a 0.47 - 0.53 mole ratio orthochlorophenol to methanol solution was carried out in order to study the line widths of the methanol -OH and phenol -OH resonances in the region where the two proton resonance peaks are distinct. The low melting point of methanol (-97.8°C) allows for investigation of the two component system between -5.5°C and -41.1°C below which the solution becomes too viscous for any accurate line width measurements. All chemical shifts are referenced to the single high field $-\text{CH}_3$ peak of the methanol.

The room temperature n. m. r. spectrum of this solution consists of a single $-\text{CH}_3$ peak of the methanol and a complex series of peaks from the aromatic ring protons of the phenol. Rapid exchange averages out the separate -OH resonances into a single very broad peak which lies directly under the aromatic spectrum. The estimated half width of this peak is 100 c.s.

As the temperature of the sample is decreased to -5.5°C , single very broad peaks appear to the low and high field sides of the ring proton spectrum. Previous investigations of several cooled samples containing varied concentrations of the two components, enabled the assignment of the low field peak to the -OH proton of the phenol. A further decrease in the temperature results in the peaks being chemically shifted slightly away from the aromatic spectrum but of more importance

is the decrease in the line width to a minimum of ~ 14 c.s. at -41.1°C . Below this temperature an increase in the viscosity of the solution broadens all peaks in the spectrum. The chemical shift and line width data are given in Table I.

TABLE I
CHEMICAL SHIFTS* AND LINE WIDTHS OF THE SEPARATE -OH PEAKS

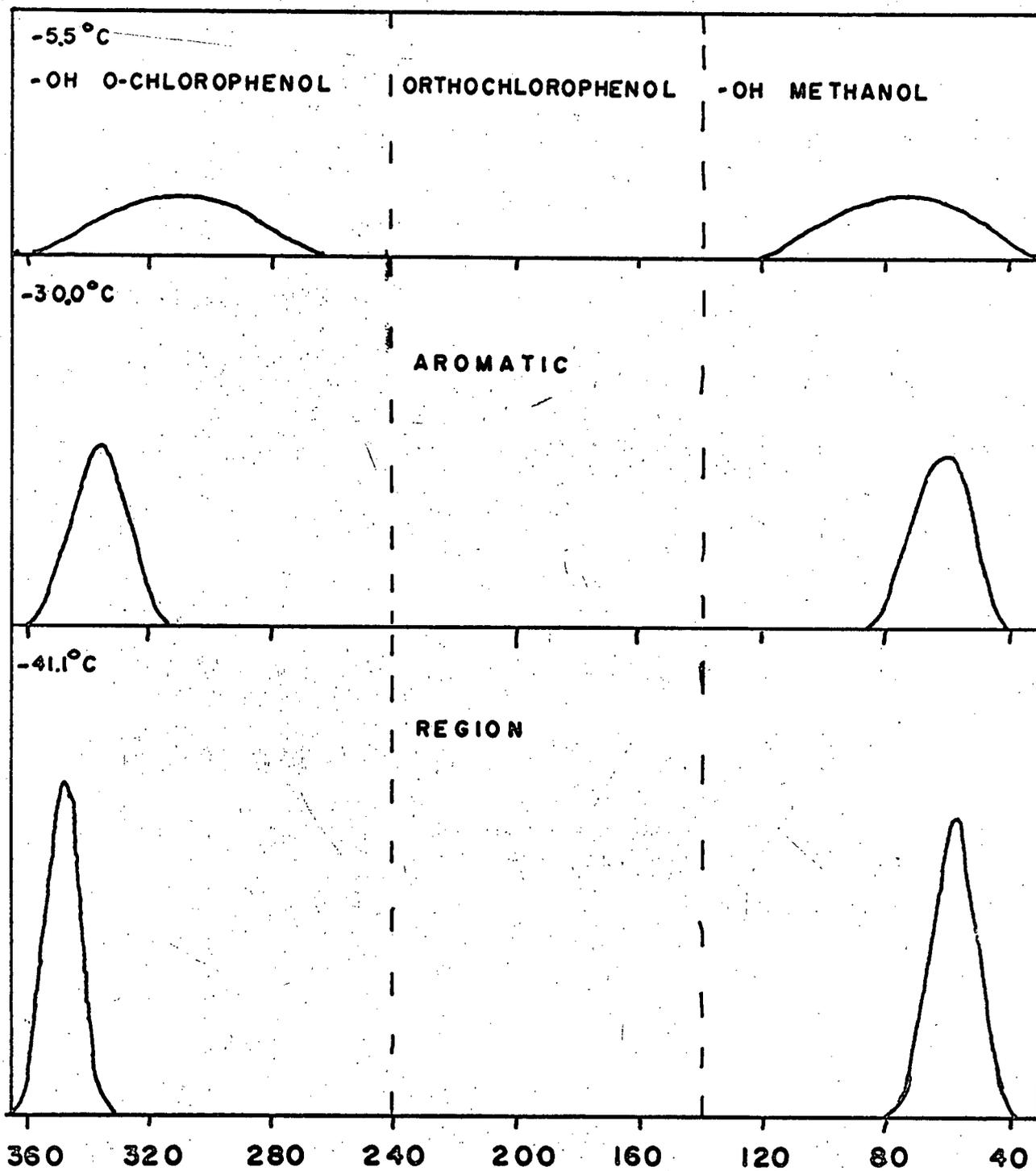
TEMP.	δ_{PHENOL}	δ_{ALCOHOL}	$\Delta\nu_{\frac{1}{2}\text{PHENOL}}$	$\Delta\nu_{\frac{1}{2}\text{ALCOHOL}}$
$^\circ\text{C}$.	c.s.	c.s.	c.s.	c.s.
- 5.5	310.5	75.3	55.5	61.4
- 7.1	313.4	72.7	52.4	60.5
-30.0	336.0	60.8	20.8	25.0
-35.5	342.6	59.8	15.6	22.5
-41.1	348.2	56.8	13.5	19.3

* referenced to the $-\text{CH}_3$ signal of methanol at $H_1 = 60$ M.c.s.

Figure IX illustrates schematically the effect of lowering the temperature on the line width and chemical shift of the separate -OH resonances. The aromatic spectrum undergoes some modification as the temperature is decreased but its analysis is very involved and of no direct consequence to this investigation.

The separate -OH resonance signals between -5.5°C and -41.1°C permit use of the slow exchange solutions of the modified Bloch equations (1)(8)(16). In this region, $\tau_A, \tau_B \gg (\omega_A - \omega_B)^{-1}$ where τ is the lifetime of the nucleus in sites A and B and $(\omega_A - \omega_B)$ is

FIGURE IX



CHEMICAL SHIFT c.s. at 60 Mc.s.

the chemical shift, in radians per second, between these two sites. Neglecting the natural relaxation time of the proton in site A, the line widths are determined entirely by the exchange process. The inverse of the first order lifetime, τ_A^{-1} , of the proton is given by:

$$\frac{1}{\tau_A} = \pi \Delta \nu_{\frac{1}{2}A} \quad (25)$$

A similar expression applies for the proton in site B. τ_A (SEC) is the lifetime of the proton in site A and is equal to the inverse of the first order rate constant for a transfer of a proton out of site A. $\Delta \nu_{\frac{1}{2}A}$ (c.s.) is the full line width at half peak amplitude in site A.

Table II summarizes the results which have been computed from line width measurements of the separate -OH signals.

TABLE II
PROTON LIFETIMES AND POPULATIONS IN EACH SITE

TEMP °C.	$\text{LOG}_{10} \frac{1}{\tau_A}^*$	τ_A msec.	$\text{LOG}_{10} \frac{1}{\tau_B}$	τ_B msec.	P_A	P_B
25	2.6760	2.11	2.7620	1.73	0.45	0.55
- 5.5	2.2408	5.75	2.2851	5.19	0.47	0.53
- 7.1	2.2159	6.07	2.2788	5.26	0.46	0.54
-30.0	1.8156	15.3	1.8949	12.7	0.45	0.55
-35.5	1.6902	20.4	1.8488	14.2	0.41	0.59
-41.1	1.6274	23.6	1.7825	16.5	0.41	0.59

- A = orthochlorophenol site
- B = methanol site
- * computed from equation (25)

As a further test of the consistency of the line width measurements a calculation of the population ratio, $p_A:p_B$ of orthochlorophenol to methanol is also given in the last two columns of table II. These values were computed from nuclear lifetimes in each site using the relation

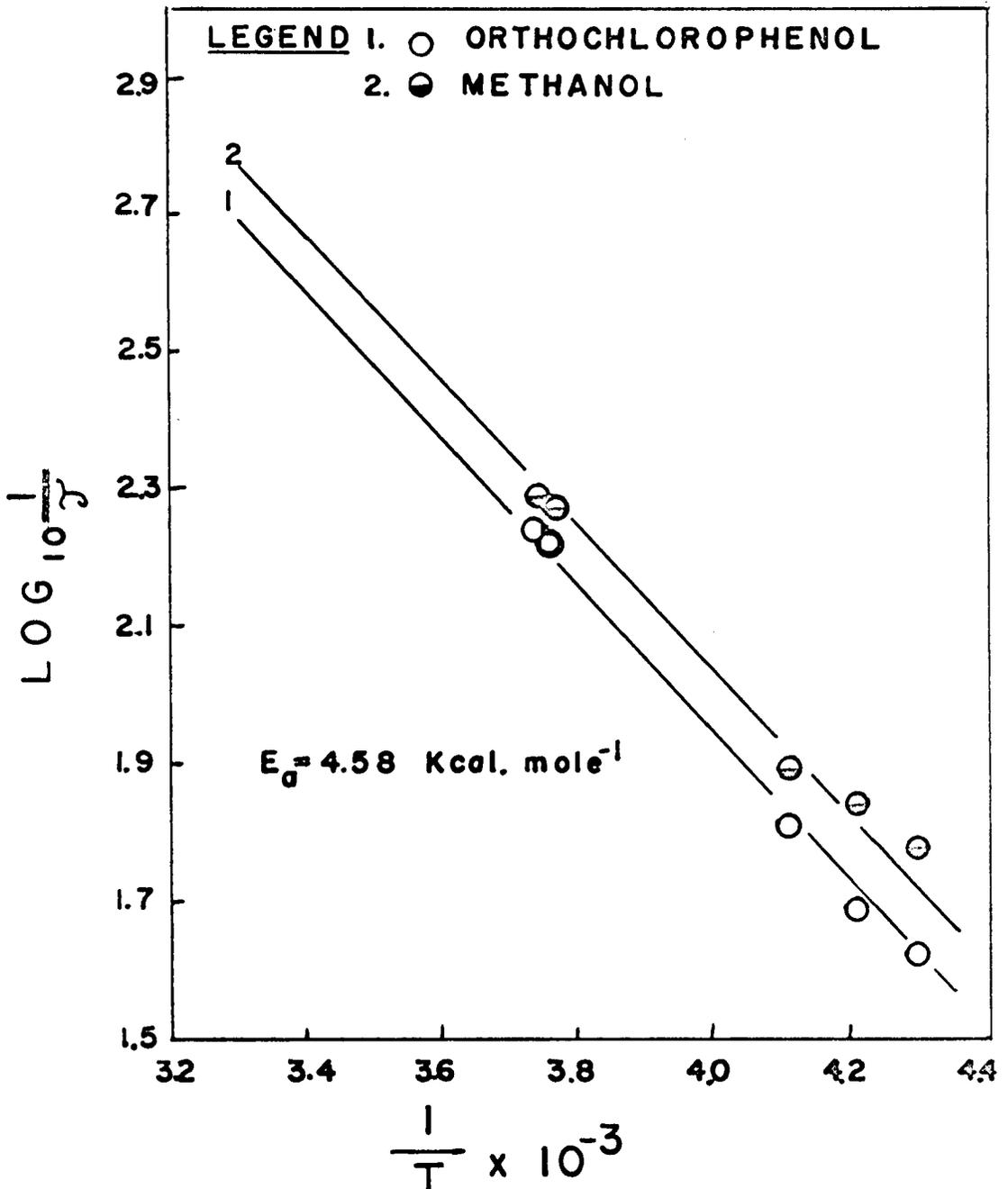
$$p_A \mathcal{T}_A = p_B \mathcal{T}_B \quad (26)$$

- p_A is the fraction of protons in the phenol site
- p_B is the fraction of protons in the methanol site

The sample under investigation was originally made up in the ratio 0.47:0.53 orthochlorophenol to methanol. The values of p_A and p_B in table II are in good agreement with the known fractional population.

Piette and Anderson (16) have indicated that a measurement of the change in line width over a range of temperatures in the slow exchange limit may be used in determining the activation energy, E_a , for the system. In Fig. X a plot of $\log_{10} (\pi \Delta \nu_{\frac{1}{2}})$ or $\log_{10} 1/\gamma$ (Table II) versus the reciprocal of the absolute temperature is given. Two parallel straight lines are obtained whose slope is equal to $-E_a/2.3R$. The computed activation energy for the intermolecular exchange system is 4.58 Kcal. mole⁻¹. Figure X has also been used to obtain room temperature values for \mathcal{T}_A and \mathcal{T}_B given in Table II.

FIGURE X
METHANOL— ORTHO CHLOROPHENOL
ENERGY OF ACTIVATION



In the fast exchange region, the separate -OH resonance peaks observed at a lower temperature coalesce and form a broad exchange averaged peak. The transition from the slow to fast regions occurs over a very narrow temperature range near 0°C. The line width in the fast exchange region, neglecting natural relaxation times, is given by:

$$\frac{1}{T_2'} = p_A^2 p_B^2 (\omega_A - \omega_B)^2 (\gamma_A + \gamma_B) \quad (19)$$

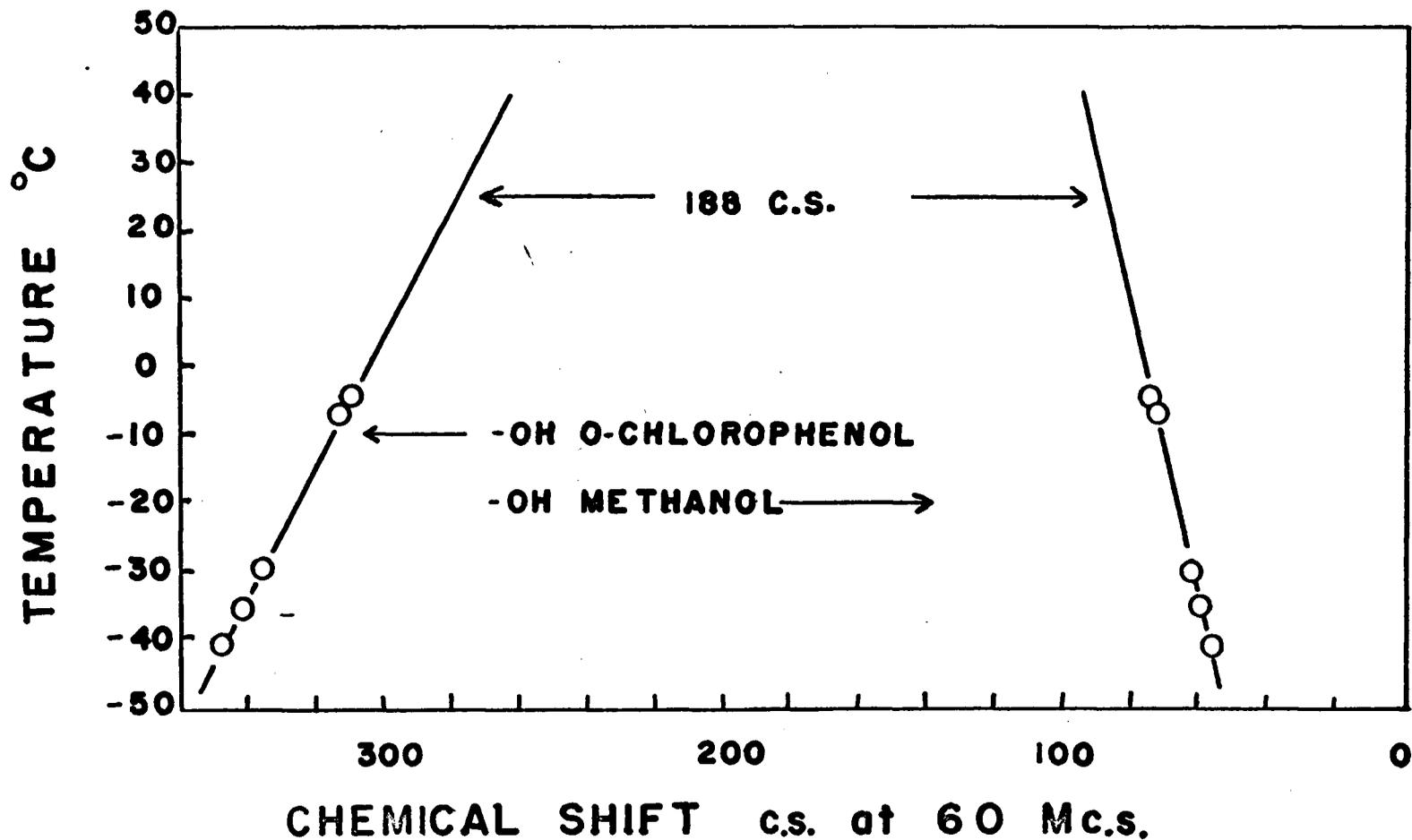
$\frac{1}{T_2'}$ is the half line width in the presence of exchange.

The exchange averaged -OH signal could not be determined because of peak overlap with the aromatic spectrum. However the line width of this signal is estimated to be 100 c.s. In order to use equation (19), the value for $(\gamma_A + \gamma_B)$ at 25°C was obtained from Table II. $(\omega_A - \omega_B)$ was obtained directly from an extrapolation to room temperature of the chemical shift of the -OH resonances versus temperature. This is indicated in Fig. XI from which $(\omega_A - \omega_B) = 2\pi(\nu_A - \nu_B) = 188$ c.s. Since the chemical shifts appear to be linear with temperature (Fig. XI), the error in the extrapolated value of 188 c.s. is probably ± 3 c.s. The mole ratio of the two component system is known so that equation (19) yields a value for $1/T_2'$. Using equation (25) the line width is computed as 104 c.s. in sensible agreement with observation.

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FIGURE XI

POSITION OF THE SEPARATE -OH RESONANCE PEAKS



REFERENCE: METHANOL-CH₃ PEAK

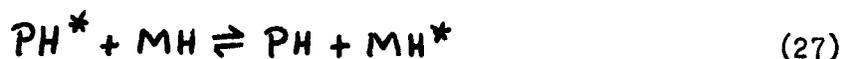
(ii) Influence of Water

Both methanol and orthochlorophenol are hygroscopic. Preliminary investigations indicated that the presence of a trace of water added to the two component system affected the line width of the OH signal at room temperature. A quantitative study of the influence of a small amount of added water to the two component system has been carried out. As a result of this study, the concentration dependence of the line width of the coalesced signal has also been investigated. The results are illustrated in Fig. XII.

Three solutions showing relative concentrations of methanol to orthochlorophenol of 0.879:0.121, 0.802:0.198, and 0.695:0.305 mole ratios have been prepared. The chemical shift of the coalesced -OH signal at room temperature is concentration dependent. The signal is very broad and buried under the aromatic spectrum in an equimolar solution. As the relative concentration of methanol to orthochlorophenol is increased, the line width of the signal decreases and the position of the signal is chemically shifted to high field. As a result the n. m. r. spectrum of the above three solutions consists of three peaks, with the coalesced -OH signal bracketed by the aromatic spectrum and the single methyl resonance. The position of the -OH peak in these solutions simplified the task of measuring line widths with no interference from the aromatic peaks. All line widths were measured on the A-60 spectrometer, using the methyl sidebands to calibrate the spectra. The use of minimum sweep fields and the slowest sweep rate make the data accurate to within ± 0.5 c.s.

The amount of water added to each solution is expressed in terms of its mole fraction in the three component system (Fig. XII) and is plotted as the abscissa. The line widths in the absence of water can be read from the intercept on the ordinate.

Proton exchange between methanol and orthochlorophenol is a second order rate process represented simply as:



The rate equations are:

$$\frac{d[PH^*]}{dt} = -k_I [PH^*][MH] = \chi_I [PH^*] \quad (28)$$

$$\frac{d[MH]}{dt} = -k_{II} [PH^*][MH] = \chi_{II} [MH] \quad (29)$$

$[PH^*]$ is the concentration of orthochlorophenol

$[MH]$ is the concentration of methanol

χ_I, χ_{II} are pseudo first-order rate constants describing the rate of proton transfer from the phenol and methanol sites respectively.

$$\chi_I = \frac{1}{\tau_A} \quad \chi_{II} = \frac{1}{\tau_B} \quad (30)$$

In equations (28) and (29)

$$k_I = k_{II}$$

$$\chi_I + \chi_{II} = k_I ([PH^*] + [MH]) = \frac{\tau_A + \tau_B}{\tau_A \tau_B} = \text{constant} \quad (31)$$

$\frac{\tau_A + \tau_B}{\tau_A \tau_B}$ should then be independent of concentration. (TABLE III)

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FIGURE XII

INFLUENCE OF WATER ON THE LINE WIDTH OF THE EXCHANGE AVERAGED PEAK

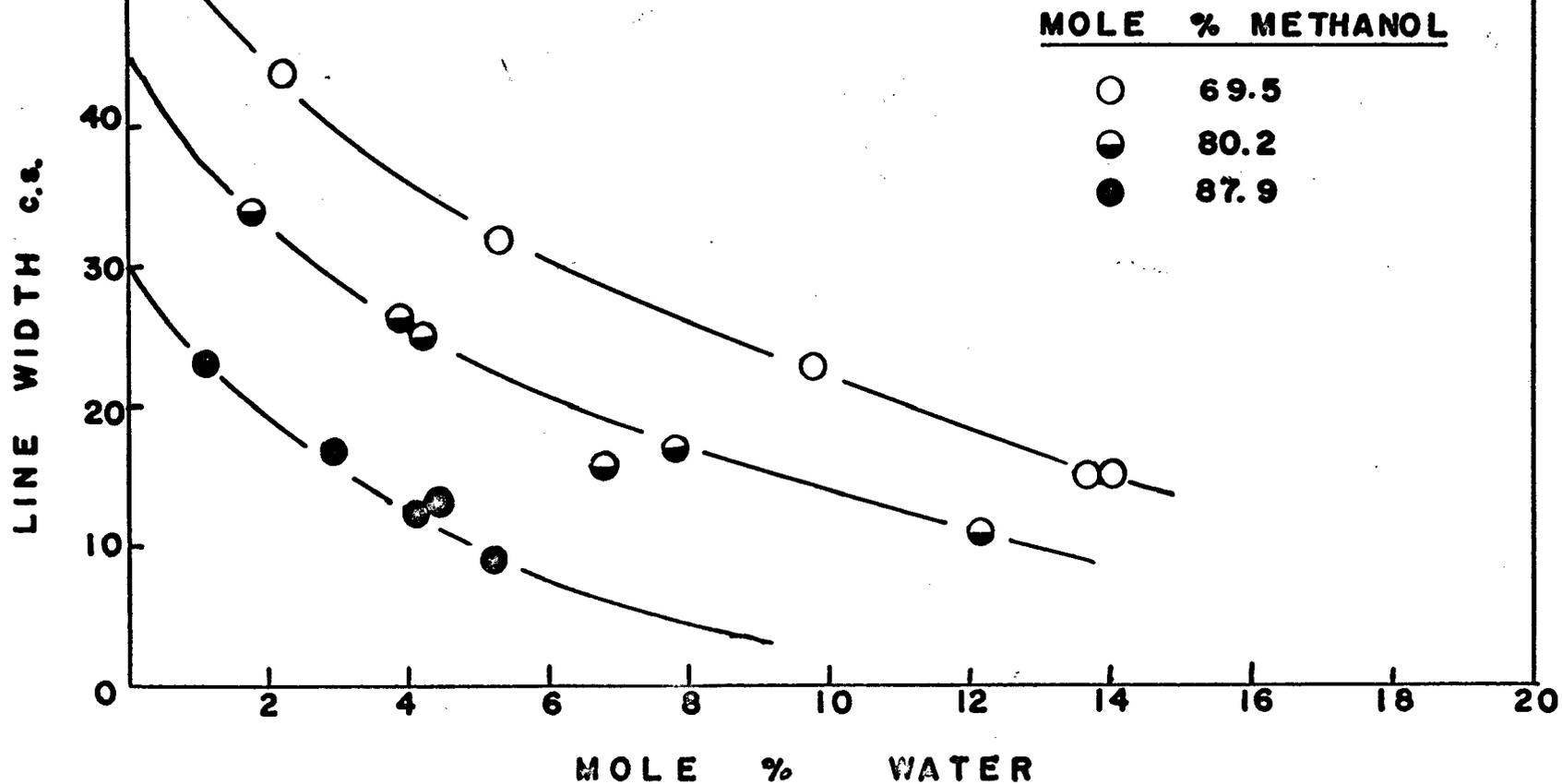


TABLE III
CONSISTENCY OF LINE WIDTH MEASUREMENTS

P_A	P_B	$\Delta\nu_{\frac{1}{2}}$ ^a	$(\gamma_A + \gamma_B)$ ^b	γ_A ^c	γ_B ^c	$\frac{\gamma_A + \gamma_B}{\gamma_A \gamma_B}$ ⁻¹
PHENOL	METHANOL	c.s.	SEC.	SEC.	SEC.	SEC.
0.121	0.879	30.0	0.00606	0.00532	0.00074	1.54×10^3
0.198	0.802	45.0	0.00396	0.00318	0.00078	1.60×10^3
0.305	0.695	57.5	0.00296	0.00207	0.00089	1.60×10^3
0.470 ^d	0.530	104.0	0.00243	0.00126	0.00117	1.64×10^3

a) extrapolated value of line width (Fig. XII)

b) computed from equation (26)

c) computed from $P_A = \gamma_A / (\gamma_A + \gamma_B)$; similarly for P_B

d) low temperature data extrapolated to room temperature (Table II) (Fig. X).

The addition of a small amount of water increases the exchange rate between the methanol and orthochlorophenol. This is seen by a decrease in the line width of the signal as the water concentration is increased.

Investigation of the protolysis kinetics of methanol (46) have indicated a rapid proton exchange rate between water and methanol. This was confirmed by cooling the solutions and observing their n. m. r. spectrum. Two signals emerged from the coalesced peak now exchange averaged for rapid proton transfer between methanol, water and the phenol. The low field resonance peak was identified as the -OH proton of the phenol and the high field signal was the collapsed line for the methanol-water mixture.

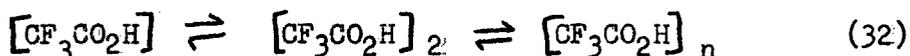
DISCUSSION

CHAPTER IV

A) Trifluoroacetic acid - Quinoline(i) Chemical Shift of the Exchange Averaged Peak:

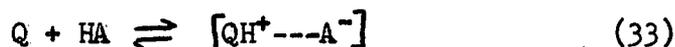
When trifluoroacetic acid, a moderately strong acid (38), is added to quinoline, a weak base which has a lone pair of electrons on the nitrogen atom, an intermolecular $\bar{O}-H-\overset{+}{N}$ hydrogen bond is formed. The strength of this bond is indicated by the extreme low field shift of the proton resonance in concentrated acid solutions (Fig. III and Fig. IV) (1).

Pure trifluoroacetic acid consists of a mixture of monomers, dimers and chain like hydrogen bonded polymers (32) whose proton resonance is concentration dependent due to equilibria among these species.

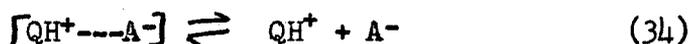


When quinoline is added to the acid, a hydrogen bonded ion pair, $[QH^+ \cdots A^-]$ of the conjugate acid and base is formed and the proton resonance of the exchange averaged signal between trifluoroacetic acid and the quinolinium ion, now is chemically shifted to low field. Although it is difficult to predict the extent of protonation in solution, the maximum low field shift occurs for a 50-50 acid to base mole ratio mixture, in which case almost all acid molecules are involved in ion pair formation with the quinoline. Crystallization of

the salt in the 20-60 mole % acid region prevents measurement of the proton chemical shift but the minimum position of the curve for the acid-base mixture dissolved in acetonitrile indicates complete association of the ion-pairs at this point. The formation of these hydrogen bonded species and the position of the exchange averaged peak in concentrated acid solution is indicative of the equilibrium (75)



In solutions, having an excess of quinoline, the hydrogen bonded complex is dissociated and the proton resonance is chemically shifted to high field.

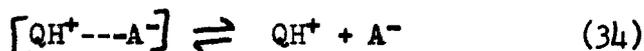


Proton exchange between the trifluoroacetate anion and quinoline can occur via the path of the hydrogen bond in the ion pair. As such only a small quantity of quinoline is needed for equilibrium 33.

Comparison of Figs. III and IV indicate less of an association shift (2) of the proton resonance after the pure acid-base mixtures are dissolved in acetonitrile. This is due, in part, to the dilution of the acid and base in a large amount of solvent (25)(28) and to the increased dielectric constant of the medium (32) favouring dissociation of the hydrogen bonded complex into ion pairs.

Fig. V shows the concentration dependence of the two contributing resonances to the exchange average signal. The experiment was performed at -18°C and the concentration dependence of the chemical shift of both species suggests that the shifts are not related in any simple manner to the change in charge density on the ring atoms due to protonation of the quinoline (74). A more detailed consideration of this problem is presented in the next section of this discussion. Further, the appearance of two distinct resonance signals at a lower temperature suggests that the trifluoroacetic acid and the quinolinium ion are the only contributing factors to the room temperature exchange averaged signal. This appears to be valid even though the crystallization of the salt prevented a measurement of the proton shift in the equimolar region of the pure acid-base system. Fig. III suggests that the proton is chemically shifted -18 to -19 parts per million from tetramethylsilane. This value is in good agreement for shifts found in symmetrical hydrogen bonds by Forsen (76).

The high field shift in dilute acid solutions has been attributed to the dissociation of the hydrogen bonded complex into the ions QH^+ and A^- . Therefore the infinite dilution chemical shift (Fig. III) extrapolates to -9.4 p.p.m. which can be taken as the chemical shift of the quinolinium cation (QH^+) in quinoline. Further the proton resonance shift of the fully associated species $[\text{QH}^+ \cdots \text{A}^-]$ is taken as -18.5 p.p.m. from tetramethylsilane. On the basis of work done by Gutowsky and Saika (10), it is possible to evaluate the equilibrium constant for



from the linear dependence of the chemical shift on the concentration in the region 0.04 to 0.12 mole fraction acid. In this region the contributing factors to the measured chemical shift, δ_M , are the QH^+ and $[\text{QH}^+ \cdots \text{A}^-]$ species.

Assume that $\delta_{\text{QH}^+} = 0$ (10) so that

$$\delta_M = \chi_{[\text{QH}^+ \cdots \text{A}^-]} \delta_{[\text{QH}^+ \cdots \text{A}^-]} \quad (35)$$

$\chi_{[\text{QH}^+ \cdots \text{A}^-]}$ is the mole fraction of the quinolinium ion bonded to the anion $\delta_{[\text{QH}^+ \cdots \text{A}^-]}$ is the chemical shift of the quinolinium ion in the associated ion pair form.

In a 10 mole % acid solution, $\delta_M = -13.6$ p.p.m. from tetramethylsilane or $[-13.6 - (-9.4)] = -4.2$ p.p.m. from QH^+ and calculating $\delta_{[\text{QH}^+ \cdots \text{A}^-]}$ to be $[-18.5 - (-9.4)] = -9.1$ p.p.m. from QH^+ , then equation (35) can be used to obtain a value of 0.462 mole fraction for the quinolinium ion bonded to the anion. The equilibrium constant in total mole fraction units is evaluated using the total number of moles in solution. As such assume that there are 100 moles present before association. In a 10 mole % acid solution, at equilibrium, there are 80 moles of quinoline, 4.62 moles of $[\text{QH}^+ \cdots \text{A}^-]$, 5.38 moles of QH^+ and 5.38 moles of A^- . The value of the equilibrium constant in mole fraction units is 6.5×10^{-3} .

(ii) Chemical Shift Changes in the Ring Protons

Although chemical shifts for the hetero-ring protons were difficult to measure due in part to the complexity of the n. m. r. spectrum of quinoline, as well as the many modifications in the spectrum when the quinoline is protonated, nevertheless the complete concentration range of acid to base could be studied for the system in 50 mole % acetonitrile. The results are shown in fig. VI. Smith and Schneider (74) have carried out a less involved but related study of the protonation of pyridine using trifluoroacetic acid in solution of high acid concentration. In agreement with their results, there is a small low field chemical shift of the β proton, a large shift for the δ proton and an almost as large a shift for the α proton. Below 0.15 mole fraction of acid, the curves level off. In this region, since there are so few acid molecules in solution the rapid exchange of the proton among the quinoline molecules averages out any chemical shift changes due to protonation.

A low field chemical shift corresponds to a deshielding of the nucleus by its electron environment. In protonation studies of pyridine by trifluoroacetic acid, Smith and Schneider (74) have attributed the low field displacements of the ring protons to the decrease in electron charge density at the individual carbon nuclei caused by the presence of the proton at the nitrogen atom. Further, assuming a simple proportionality between the proton resonance displacement (60) and the electron charge deficiency on the carbon and nitrogen atom to which the proton is bonded, an assignment of the charge densities in pyridinium ion are given.

The chemical shift versus concentration curves in Figure VI may be interpreted by considering the measured chemical shift of the ring protons, δ_{MR} , as a function of the free quinoline molecules in solution, $[Q]$ the cation QH^+ and the hydrogen bonded ion pair species $[QH^+ \cdots A^-]$ so that (9):

$$\delta_{MR} = x_Q \delta_Q + x_{QH^+} \delta_{QH^+} + x_{[QH^+ \cdots A^-]} \delta_{[QH^+ \cdots A^-]} \quad (36)$$

where x is the mole fraction of the species indicated and

$$x_Q + x_{QH^+} + x_{[QH^+ \cdots A^-]} = 1 \quad (37)$$

At infinite dilution in the acid-acetonitrile solution, the measured chemical shift is that for the ring proton in the species QH^+ . On the other side of the curve, at infinite dilution in the base-acetonitrile solution, the chemical shift, δ_{MR} , is that for the ring protons in quinoline (1), dissolved in acetonitrile. Comparing the differences in these two values for the three ring protons, it is seen that the β and δ protons experience a low field shift while the α proton shifts to high field in going from Q to QH^+ . Recent investigations of quinoline diluted in different solvents (77) and the work done by Reeves and Strømme (73) on substituted quinolines indicate that the chemical shifts of the ring protons are dependent upon their medium. It is seen, in the present study, that the shifts for the ring protons in the quinolinium ion are obtained in an acid-solvent medium while the ring proton shifts for the free quinoline molecules are obtained in a quinoline solvent medium. It appears that the magnitude of the low field shift of the ring protons is determined by the rapid equilibria in solution

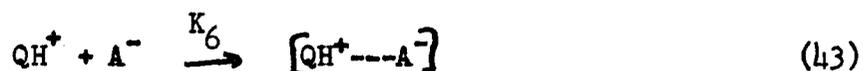
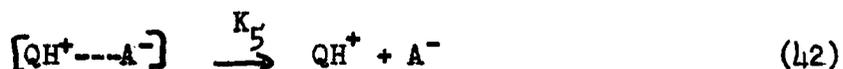
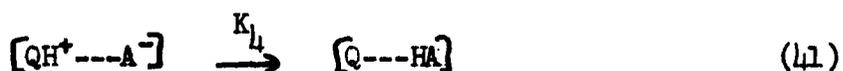
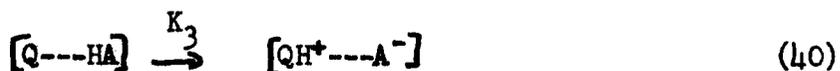
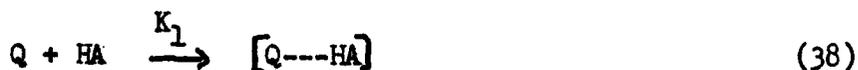
rather than by charge densities on the carbon atom and the fact that the shifts of the ring protons in the quinolinium ion are dependent upon the medium negates any arguments concerning charge densities at various carbon atoms in the ion.

The pronounced concentration dependent low field chemical shift of the ring protons in concentrated acid solutions is due to the formation of the hydrogen bonded ion-pair $[QH^+ \cdots A^-]$ so that as more quinoline is added to the acid, the term $\chi_{[QH^+ \cdots A^-]} \delta_{[QH^+ \cdots A^-]}$ in equation (36) becomes important. The acceptance of the proton by the quinoline molecule to form the cation appears to affect the α and δ protons much more than the β ring proton (78). In dilute acid solutions, the displacement of the curves to high field are accounted for in terms of the dissociation of the hydrogen bonded ion-pair giving more weight to the term $\chi_Q \delta_Q$ in equation (36).

(iii) Line Widths of the Exchange Averaged Signal:

In high resolution nuclear magnetic resonance, the full line width of the resonance signal at half the peak amplitude, may be used as a means of investigating the exchange processes taking place in a chemical system. Figure VII shows the graph obtained as a result of plotting the line width of the $\gg NH^+ - COOH$ signal, exchange-averaged at room temperature, as a function of the mole fraction acid in the pure acid-base mixture. Fig. VIII shows the same type of plot after the solutions had been dissolved in acetonitrile. In figure VII, crystallization of the salt below 72 mole % acid in the pure acid-base system prevented any further measurement of the line width.

In the two component, trifluoroacetic acid-quinoline system, it is suggested, on the basis of the experimental evidence presented, that the following processes occur in solution



Most hydrogen bonds are very short-lived so that the making and breaking of these bonds is very fast on the proton magnetic resonance time scale. In this regard, processes 38), 39), 42) and 43) are in the fast exchange limit (12). However, most of the quinoline will be fully protonated by the acid so that the concentration of the species $[Q\cdots HA]$ in mechanisms 38) and 39) will be negligibly small. As previously indicated, the position of the exchange averaged peak when ion pair association is complete is at maximum low field compared to the proton resonance position of the free trifluoroacetic acid. Therefore the average chemical shift for the proton in processes 38) and 39) is very nearly equal to that for the pure acid whose proton resonance position

is an average for the concentration of monomers, dimers and polymers existing in equilibrium. The mean chemical shift resulting from the rapid processes 42) and 43) lie between that of the higher field position of the QH^+ ion (see Fig. V) and the extreme low field shift of the species $[\text{QH}^+ \cdots \text{A}^-]$.

The concentration dependence of the line width, indicated in Figures VII and VIII may be accounted for in terms of the slow processes 40) and 41). These are the rate determining steps and describe the exchange of the proton between two chemically different environments. In each of these sites, the proton precesses with a slightly different Larmor frequency. This is reflected in the appearance of the two resonance signals at -18°C . At room temperature, however, proton transfer along the path of the hydrogen bond is rapid so that an exchange averaged signal results. Therefore, in one site, i.e. HA, the proton spends most of its time in an intermolecularly hydrogen bonded environment with other acid molecules. The proton transfers to its second site by bonding to the nitrogen atom of quinoline and forming the quinoline cation. In this site, depending upon the concentration of acid to base, the proton chemical shift is exchange averaged between the conjugate acid (QH^+) and the ion pair form.

Nuclei with spin greater than one-half possess an electric quadrupole moment (1). In the quinolinium ion, the proton is bonded to a nitrogen atom whose nuclear spin, $I = 1$. As a result the spin-lattice relaxation time of the proton, T_2 , which is directly related to the line width, is influenced strongly by

quadrupolar relaxation due to $I \cdot I$ interaction with the nitrogen. The n. m. r. spectrum of the two component system at -18°C shows the exchange broadened peak of the NH^+ resonance to the low field side of the resonance found for the proton in its alternate site. The additional broadening of the QH^+ signal is attributed quadrupole effects. Attempts were made to study a 50-50 acid-base mixture at -60°C . At this temperature, the chemical shift difference for the proton in its two possible sites would be a maximum, and with equal populations in both environments, McConnell's (13) exchange modification of the Bloch (8) equations could be applied in determining the contribution of the quadrupole moment to the line width of the QH^+ signal. However crystallization of the salt, even in solutions of acetonitrile, prevent such an investigation.

The position of the maximum line width, which corresponds to the slowest exchange rate at room temperature, occurs at 79 mole % in the pure acid-base system and at 85 mole % after dissolution in acetonitrile. (Figs. VII and VIII). In the rapid exchange limit, i.e. reflected by the room temperature coalesced signal, the following expression is valid: (1)

$$\frac{1}{T_2'} = \frac{P_A}{T_{2A}} + \frac{P_B}{T_{2B}} + P_A^2 P_B^2 (\omega_A - \omega_B)^2 (\gamma_A + \gamma_B) \quad (19)$$

P_A, P_B are the fractional populations of the two sites

T_2 is the natural relaxation time

T_2' is the natural relaxation time plus relaxation due to exchange =

$$T_2' = 1/\pi \Delta \nu_{1/2}$$

$\Delta \nu_{1/2}$ is the full line width at the half amplitude (c.s.)

τ is the mean lifetime of a proton in each site

$(\omega_A - \omega_B)$ is the chemical shift difference between the proton
in both of its environments.

From equation (19) it is seen that the line width is related to the square of the chemical shift difference between the two sites. The occurrence of a maximum line width at different concentrations of acid to base in the pure system and in the acetonitrile solutions may therefore be accounted for in terms of the chemical shift change of the exchange averaged peak in the two media.

B) Methanol-Orthochlorophenol

Previous n. m. r. investigations of the protolysis kinetics of methanol (46) have indicated that the exchange rate of the hydroxyl proton between alcohol molecules is very rapid. Quantitative measurements of the proton transfer rate have been made on a number of methanol-water mixtures in order to determine the influence of water on the exchange mechanism. The results indicated that in neutral methanol the rate of exchange increased somewhat with water content. There was no evidence as to whether this should be ascribed to an exchange mechanism with water given by



or whether it is an increase in rate of the reaction



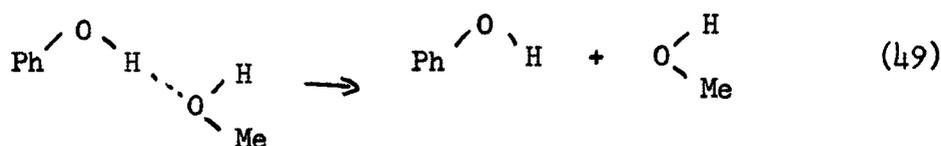
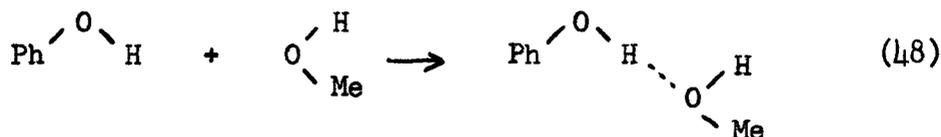
as a result of a change in medium.

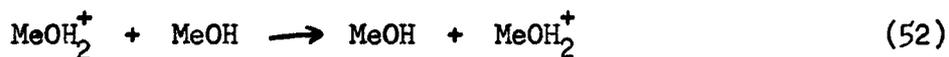
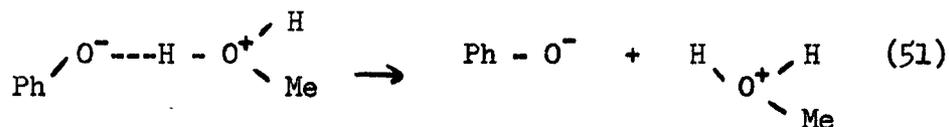
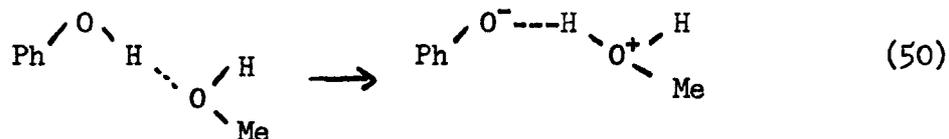
Orthochlorophenol contains a proton involved in an intramolecular hydrogen bond. Allan and Reeves (34), in this laboratory, have measured the equilibrium constant for the cis-trans conversion in orthochlorophenol and it has been shown (79) (80) that in dilute non-polar solvents, there is a small concentration of the trans form which is hydrogen bonded to a cis molecule to produce a dimer (81).

In a mixture of methanol and orthochlorophenol, the relative values of the pK_A 's of the two components in water is an indication of the small concentration of protonated species which is responsible

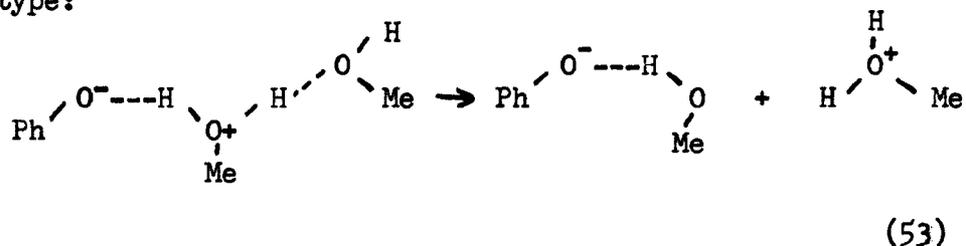
for transferring a proton from the phenol to methanol. The pK value of phenol in water is 8.49 (82). The value for methanol in water is much higher since methanol is a weaker acid because of the inductive effect of the methyl group.

Proton transfer along the path of a hydrogen bond in an ion pair has been discussed in the trifluoroacetic acid-quinoline system (75). In a somewhat analogous manner, proton exchange in solutions of orthochlorophenol and methanol will occur along a hydrogen bond in an ion pair composed of some protonated methanol and the phenoxide anion. This is based upon the fact that in concentrated solutions of polar solvents which have donor centers such as methanol the trans form of orthochlorophenol is favoured because the intramolecular hydrogen bond is very weak (34) ($\Delta H_f = 2356 \text{ cal. mole}^{-1}$) and the intermolecular O-H...O hydrogen bond is much stronger ($> 5000 \text{ cal. mole}^{-1}$) (81) (83). Assuming the contributions of the intramolecular hydrogen bond in the phenol are negligible, proton transfer between the two components will occur along the intermolecular hydrogen bond. The kinetic scheme for the proton transfer is:





Step 51 may be replaced by a mechanism involving transfer of the type:



As the mole ratio of methanol to orthochlorophenol is increased, the position of the exchange average -OH signal is chemically shifted to low field. The low field shift indicates the formation of a hydrogen bond. Processes 48) and 49) are in the fast exchange limit (75) but the rate determining step involves proton transfer in the hydrogen bonded ion pair (process 50).

The weak internal hydrogen bond in the phenol does not hinder proton transfer between the two components. However, it is known that strong intramolecular hydrogen bonds remain unbroken even in polar solvents (84). In such systems, the effect of an internal hydrogen bond on the intermolecular proton exchange must be considered.

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