The University of Manitoba

# A PROTON MAGNETIC RESONANCE STUDY OF SOME LONG-RANGE COUPLING CONSTANTS, PROTON EXCHANGE REACTIONS AND INTRAMOLECULAR HYDROGEN BONDS IN SOME BENZENE DERIVATIVES

by

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-TO MY PARENTS-

To strive, to seek, to find,

and not to yield.

(Alfred Lord Tennyson "Ulysses", 1842)

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-ABSTRACT-

Tickling and decoupling (triple resonance) techniques show that the ortho, meta and para ring proton coupling constants ($J^{o}_{H,H}$; $J^{m}_{H,H}$ and $J^{p}_{H,H}$ respectively) have the same sign in 2-bromo-5-chlorotoluene and are positive since $J^{o}_{H,H}$ is positive. Decoupling experiments also show that the methyl proton coupling to the ring protons in the ortho and para position to the methyl group ($J^{o}_{H,CH_3}$ and $J^{p}_{H,CH_3}$) is negative while that to the meta position ($J^{m}_{H,CH_3}$) is positive. The signs of the long-range couplings and $J^{p}_{H,H}$ are in agreement with the $\sigma$-$\pi$ exchange mechanism and the theoretical basis developed by McConnell. Studies of other polysubstituted toluenes show that substituents have almost a negligible effect on the magnitudes of the long-range coupling constants. They are also solvent independent. An exception is 2-hydroxy -3,5-dinitrotoluene for which the observed coupling $J^{o}_{H,CH_3}$ is $-0.86\pm0.02$ cps. The large magnitude of this coupling may be attributed to an increase in the mobile bond order of the ortho C-C bond induced by a quinoid resonance structure. The $J^{o}_{H,H}$ coupling constants correlate with the electronegativities of the heteroatoms substituted ortho to one of the coupling protons while the $J^{m}_{H,H}$ and $J^{p}_{H,H}$ values show no trends with substituent effects. A correlation is observed between the methyl proton shifts and the sum of the Hammett sigma constants for the ring substituents.

One side-chain substituted toluene, 3,4-dichlorobenzylchloride, is studied. The magnitudes of $J^{o}_{H,CH_2Cl}$ and $J^{m}_{H,CH_2Cl}$ decrease by about 0.2 cps from the corresponding $J^{o}_{H,CH_3}$ and $J^{m}_{H,CH_3}$ values. Several reasons for this are discussed.

A proton magnetic resonance study is carried out on the intramolecular hydrogen bond and the intermolecular proton exchange reactions in benzene solutions of 3,5-dichlorosalicylaldehyde. The results indicate that the exchange process is bimolecular with respect to the solute molecules. The magnitude of the second order proton exchange rate constant is $16.8 \pm 4.8$ liters $mole^{-1}$ $sec.^{-1}$ The magnitudes of the activation parameters are listed in Table 3-XVIII. The activation energies may be explained by the energies required to break the intramolecular hydrogen bond and to twist the phenolic (and perhaps the aldehydic) group out of the plane of the ring. The exact nature of the transition state and hence the proton transfer mechanism is not known except that it must involve the formation of a stereospecific dimer between two solute molecules. The concentration and temperature effects on the ring proton, aldehydic and phenolic proton shifts indicate the presence of a weak interaction between the solute and solvent molecules. Therefore the proton exchange reaction is thought to be solvent-assisted. This is the first extensive study of a proton exchange reaction between molecules in which the exchangeable protons are intramolecularly hydrogen-bonded.

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# Chapter I

## INTRODUCTION

This thesis is concerned with the application of proton magnetic resonance techniques to the study of two main areas of interest, namely:

1. long-range coupling constants and

2. proton exchange reactions and intramolecular hydrogen bonds.

For this reason the thesis is subdivided into two sections, each independent of the other and treated as a thesis in itself. The bibliography is at the end of each chapter.

Chapter 2 is concerned with the study of the signs and magnitudes of the long-range coupling constants in ring-substituted toluenes, and one side-chain-substituted toluene. This section also contains a short introduction to the theory of the nuclear magnetic resonance experiment. Chapter 3 describes the study of the intramolecular hydrogen bond, of proton exchange reactions, and of the associated activation parameters in 3,5-dichlorosalicylaldehyde in benzene solution. A more extensive introduction to each topic is found in the separate sections.

# Chapter II

## A STUDY OF LONG-RANGE PROTON-PROTON COUPLING CONSTANTS IN POLYSUBSTITUTED TOLUENES

1.

# INTRODUCTION

The object of this research was to study the signs and magnitudes of long-range coupling constants in polysubstituted toluenes, their dependence on substituents and solvents, and to compare this data with existing theoretical calculations.

This chapter is subdivided into several parts. In the Introduction the nuclear magnetic resonance (n.m.r.) phenomenon is introduced and two of the parameters obtained from an n.m.r. spectrum, namely the chemical shift and coupling constant, are discussed. A discussion of factors affecting line widths, relaxation times and exchange processes is reserved for the next chapter. A long-range coupling constant is then introduced and a review of the existing literature on these couplings in benzylic systems as well as on their theoretical interpretation follows. This section is concluded with a description of the determination of absolute signs of coupling constants in aromatic systems and the nuclear magnetic double resonance technique of obtaining relative signs of coupling constants.

The rest of the chapter deals with the long-range coupling constants of polysubstituted toluenes in the normal manner, i.e., Nature of the Problem, Experimental Methods and Results, followed by a Discussion and Summary with Conclusions. Several other experiments which I had hoped to carry out are described in the section entitled Recommendations for Future Research. This chapter concludes with a Bibliography.

2.

## THEORETICAL DISCUSSION

## A. THE NUCLEAR MAGNETIC RESONANCE EXPERIMENT

The theory of nuclear magnetic resonance (n.m.r.) spectroscopy has been developed in detail in several monographs (1 - 8). Hence, only a brief review will be presented in this chapter.

Many nuclei possess magnetic moments associated with an intrinsic angular momentum. These magnetic moments can interact with both intrinsic and externally applied magnetic fields in the presence of which they experience a torque and tend to line up in the direction of the field. The magnetic moments thus behave as small bar magnets or the so-called nuclear magnets. If an oscillating magnetic field in the radiofrequency region is applied to a sample containing nuclear magnetic moments, an absorption of energy can be detected. Thus, the nuclear magnetic moment is used as a probe in a study of the local magnetic effects within a molecule. This is known as the nuclear magnetic resonance experiment.

In order for a nucleus to possess a magnetic moment, it must possess the property of spin which results from a circulation of mass about a given axis. The spin, or spin angular momentum vector is designated by the symbol $\underline{I}$ and is measured in units of $\hbar$ . $m_I$, known as the nuclear spin quantum number, is the maximum measurable component of the angular momentum in any given direction. For all nuclei with odd mass number, the value of the spin $\underline{I}$ is an odd integral multiple of $\frac{1}{2}$. For nuclei with even mass numbers the spin is zero for an even atomic number and integral for odd atomic numbers. This study is concerned solely with protons which have a spin of $\frac{1}{2}$.

The circulation of mass has an associated circulation of charge giving rise to the nuclear magnetic moment $\underline{\mu}$ which is proportional to the magnitude and direction of spin:

2-1 $$\underline{\mu} = \gamma_N \hbar \underline{I} = g_N \beta_N \underline{I}$$

where $\gamma_N$ is the nuclear magnetogyric ratio, $g_N$ the nuclear g factor and $\beta_N$ the nuclear magneton. The nuclear magneton is defined in terms of the proton mass $M_p$,

2-2 $$\beta_N = \frac{e\hbar}{2M_p c}$$

and is numerically equal to $5.05 \times 10^{-24}$ erg/gauss. $\hbar$ is Planck's constant divided by $2\pi$ while e and c are respectively the charge of the proton and the velocity of light. Nuclei are thus distinguished from each other by different values of spin and magnetogyric ratios.

In field-free space the orientations of the spinning nuclei will be random but the spin angular momentum vector must still be such that its components in any given direction can only take up one of a set of discrete values which are +I, (I -1), ...-(I-1)-I. The energies of these 2I + 1 orientations are degenerate. For a proton with $I = \frac{1}{2}$, the nuclear spin quantum number $m_I$ may have the values $+\frac{1}{2}$ and $-\frac{1}{2}$. The application of a steady external magnetic field $\underline{H}_o$ defines the reference direction and lifts the degeneracy of the two energy levels. The external field exerts a torque $\underline{L}$ on the magnetic moment vector and thus tends to align it parallel to the field

2-3 $$\underline{L} = \underline{\mu} \times \underline{H}_o .$$

The energy of interaction is represented in terms of the Hamiltonian

2-4 $$\mathcal{H}^o = + \underline{\mu} \cdot \underline{H}_o$$

The direction of $\underline{H}_o$ (axis of quantization) is normally chosen as the negative Z direction. The Hamiltonian for the interaction then becomes

2-5 $$\mathcal{H}^o = + \gamma_N \hbar I_Z H_o = +g_N \beta_N I_Z H_o$$

where $I_Z$ is the nuclear spin quantum number corresponding to the allowed component of the nuclear spin in the Z direction. It is also designated as $m_Z$. The separation between adjacent nuclear energy levels is

2-6 $$\Delta E = \gamma_N \hbar H_o = g_N \beta_N H_o .$$

The units of energy are in ergs when $H_o$ is in gauss.

Transitions between these two nuclear spin levels are induced by the application of an oscillating electromagnetic field of frequency $\nu$ satisfying the equation

2-7 $$\Delta E = h\nu = \gamma_N \hbar H_o = g_N \beta_N H_o .$$

Classically the magnetic moment vector $\underline{\mu}$ precesses about $\underline{H}_o$ as a result of the torque $\underline{L}$ exerted by $H_o$. The angular frequency of precession $\omega$ is

2-8 $$\omega = \gamma H_o = 2\pi\nu$$

Hence, the resonance equation for the nuclear magnetic resonance phenomenon is

2-9 $$\nu = \frac{\gamma_N H_o}{2\pi} = \frac{g_N \beta_N H_o}{h}$$

So far in the discussion it has been assumed that the nuclei are bare and in free space — an ideal situation. However, the n.m.r. experiment is carried out on nuclei in molecules in which case the resonance magnetic field and the external magnetic field $H_o$ are not

the same. The resonance magnetic field must be replaced by an effective magnetic field $H_{local}$ which varies according to the chemical environment of the proton. This change in the resonance field between a bare proton and a proton in a molecule (assuming a constant frequency $\gamma$ ) arises from the extranuclear electrons which when placed in a magnetic field also undergo a precession. This precession has associated with it a magnetic field which causes a small shift in the value of the external field required for resonance. This difference in the resonance fields is known as the screening effect or the "chemical shift" and will be discussed briefly in the next section.

The n.m.r. spectra of molecules possessing several nuclei with magnetic moments are also complicated by the interaction of these moments with each other. This effect is also characteristic of the molecular environment of the nuclei and is known as the electron-coupled nuclear spin-spin interaction. It is discussed in Section C of this chapter.

Two other effects influence n.m.r. spectra. The first occurs for some nuclei with spins of <u>one</u> or more since they possess an electric quadrupole moment. An electric quadrupole moment arises from the non-spherical distribution of electric charge density at the nucleus. Various complications arise in the n.m.r. spectra when the nuclei are present in a molecule. In the presence of an electric field gradient these quadrupole moments undergo precession which displaces the nuclear magnetic levels. This provides an efficient relaxation mechanism leading to a broadening of the resonance lines. This effect will not be considered further since in proton magnetic resonance studies it does

not arise. The widths of n.m.r. absorption lines are also affected by the lifetimes of the spin states which in turn are governed by the relaxation times of the various nuclei. Molecular motions such as hindered rotations and nuclear exchange reactions also govern the line widths. These phenomena will be considered in Chapter III.

## B. THE CHEMICAL SHIFT

### 1. General Introduction

The resonance frequency of a particular nucleus varies depending on its environment in a molecule and differs from that of a free nucleus. The actual magnetic field $H_{local}$ at the nucleus is

2-10 $$H_{local} = H_o (1 - \sigma)$$

where $\sigma$ is the shielding constant of the nucleus under consideration. It is a positive quantity which arises from the magnetic field produced at a nucleus by the precession of the neighbouring electrons about the magnetic field direction $H_o$. This induced field opposes $H_o$ and is proportional to it. Thus the resonance frequency of a particular nucleus will vary from one environment to another. The Hamiltonian for the interaction between the nuclear magnetic moment and the external field (Zeeman energy) becomes

2-11 $$\mathcal{H}^\circ = \gamma_N \hbar I_Z H_{local} = \gamma_N \hbar I_Z H_o (1 - \sigma).$$

Since it is more convenient to express all energies in cycles per second rather than ergs, the above equation becomes (dividing by h)

2-12 $$\mathcal{H}^\circ = \frac{\gamma_N}{2\pi} I_Z H_o (1 - \sigma).$$

For a set of nuclei with magnetogyric ratios $\gamma_i$ and screening constants $\sigma_i$ equation (2 - 12) becomes

2-13 $$\mathcal{H}^\circ = \frac{H_o}{2\pi} \sum_i \gamma_i I_Z (i) (1 - \sigma_i),$$

where $\gamma_i$ depends only on the nuclear species and is the same for all protons.

From these equations it is seen that a resonance for a particular nucleus will appear at a higher field (at constant frequency $\nu$ ) than that of a bare nucleus due to the screening effect. This screening effect is the "chemical shift".

It is seldom necessary to know the absolute field strength of a nuclear resonance signal with great precision and most n.m.r. measurements are concerned only with the difference in the field strengths of signals, usually in frequency units. N.M.R. spectra are thus calibrated with respect to some reference, the most common of which in proton magnetic resonance spectroscopy today is tetramethylsilane (TMS).

The position of a peak is often specified in terms of its chemical shift from that of a reference by a dimensionless quantity $\delta_{rs}$ expressed in units of parts per million (ppm).

2-14 $$\delta_{rs} = \frac{H_s - H_r}{H_r}$$

where $H_s$ and $H_r$ are the resonant fields of the sample and reference respectively. The chemical shift is also expressed in terms of the shielding constants of the sample $\sigma_s$ and the reference $\sigma_r$ as

2-15 $$\delta_{rs} = \frac{H_o (1 - \sigma_s) - H_o (1 - \sigma_r)}{H_o (1 - \sigma_r)}$$

$$= \frac{\sigma_r - \sigma_s}{1 - \sigma_r}$$

$$\cong \sigma_r - \sigma_s, \text{ since } \sigma_r << 1.$$

There is a change in the sign convention in going from definitions (2 - 14) to (2 - 15) since a largest shielding constant implies

that the resonance for that particular nucleus will occur at highest field. However, no problems arise because of this since all authors state the reference and the shift in parts per million or in frequency units with respect to it.

The above definitions and discussion are found in all the standard references mentioned previously.

## 2. Origins of the Chemical Shift

All theoretical attempts so far have been concerned with the mathematical formulation of $\sigma$, the shielding constant. Following a recent method (9), $\sigma$ can be written as

2-16 $$\sigma = \sigma_G + \sigma_{medium}$$

where $\sigma_G$ is the contribution to the screening constant arising from an isolated gaseous molecule and $\sigma_{medium}$ is the contribution arising from solvent effects on the particular nucleus when in solution. Buckingham, Schaefer and Schneider (10) first systematized the different contributions to the shielding constant arising from medium effects, and write

2-17 $$\sigma_{medium} = \sigma_b + \sigma_a + \sigma_w + \sigma_E + \sigma_H$$

where $\sigma_b$, $\sigma_a$, $\sigma_w$, $\sigma_E$ and $\sigma_H$ are the respective contributions to $\sigma_{medium}$ arising from the bulk diamagnetic susceptibility of the solvent, the anisotropy in the susceptibility of the solvent, the van der Waals interactions between solute and solvent molecules, the reaction field of the solvent (important for polar solute molecules and known as the "polar effect") and the contribution due to complex

formation. The effects of $\sigma_{medium}$ on $\sigma$ can be minimized or essentially held constant by the proper choice of solvents, internal references, extrapolation of shifts to infinite dilution and other experimental devices. The various contributions to $\sigma_{medium}$ have been discussed previously (11) and will therefore not be discussed further.

The shielding constant $\sigma_G$ can be written as a sum of four contributions (3, 12) namely:

2-18 $$\sigma_G = \sigma_{GG}^{d} + \sigma_{GG}^{P} + \sum_{G \neq B} \sigma_{GB} + \sigma_{G,ring}$$

where $\sigma_{GG}^{d}$ is the diamagnetic screening from the circulation of electrons on the same atom as the nucleus in question; $\sigma_{GG}^{P}$ is the contribution to $\sigma_G$ arising from paramagnetic currents on the same atom; $\sigma_{GB}$ is the contribution from the B substituent anisotropy and is the combined effect of the diamagnetic and paramagnetic currents on other atoms while $\sigma_{G,ring}$ is the contribution to $\sigma_G$ arising from electronic currents flowing around closed rings of atoms, or ring currents. These four contributions will be discussed separately.

(a) Atomic Shielding Constant

The shielding constant term $\sigma_{GG}^{d}$ was first evaluated by Lamb (13). He considered the simplest system, namely a free atom with no resultant orbital or spin angular momenta. Placing the atom in a magnetic field produces a diamagnetic circulation of electrons about the nucleus which in turn produces a magnetic field opposing the applied external field. The nucleus thus experiences a reduced field and the effect

is larger for larger diamagnetic currents. Lamb's formula may be written as

$$2\text{-}19 \qquad \sigma_{GG}^{d} = \frac{4\pi e^2}{3mc^2} \int_0^\infty r\,\rho\,(r)dr$$

where e and m are respectively the charge and mass of the electron, c is the velocity of light, and $\rho$ (r) is the electron density at a distance r from the nucleus.

(b) Paramagnetic Currents

When a nucleus is no longer free but forms part of a molecule the electrons are no longer completely free to precess about the direction of $\underline{H}_o$. Two problems arise; first the secondary induced field seen by the nucleus is not necessarily parallel to $\underline{H}_o$ and second; a term additional to the Lamb term arises for the theoretical expression for the shielding constant.

Ramsey (14) has derived an expression for the magnetic field at a nucleus resulting from the application of an external magnetic field to a polyatomic molecule which has no resultant electron orbital or spin angular momenta in the absence of the external field. A simple but less exact form of Ramsey's equation in terms of the screening constant is (1)

$$2\text{-}20 \qquad \sigma_{ZZ} = \frac{e^2}{2mc^2} \int \frac{x^2 + y^2}{r^3}\,\rho\, d\tau + \frac{e^2\hbar^2}{m^2c^2\,\Delta E} \left\langle 0 \left| \sum_{j,k} r_k^{-3} \frac{\partial^2}{\partial\phi_j\,\partial\phi_k} \right| 0 \right\rangle$$

where $\Delta$ E is the mean excitation energy used in the approximation to Ramsey's equation instead of the sum over $n$ for all excitation energies $E_n - E_o$. The above expression involves only the ground-state wave functions.

The shielding constant is $\sigma_{zz}$, $\hbar$ is Planck's constant $h$ divided by $2\pi$, $\frac{\partial}{\partial\phi}$ is the angular momentum operator about the Z-axis, and the other constants were defined previously for Lamb's equation.

The first term is similar to the Lamb formula for atoms and becomes identical with it when averaged over all directions. It is known as the "diamagnetic" shielding term. The integrals are taken over all the electrons in the molecule so that this term corresponds to the shielding arising from a simple circular diamagnetic circulation of the electrons about the nucleus of interest. The second term, known as the "paramagnetic" shielding term, effectively corrects for the hindrance to this free electronic rotation and arises from the lack of spherical symmetry in the molecule.

The Lamb term $\sigma_{GG}^{d}$ is easier to estimate theoretically since it depends only on the electron distribution in the ground state. The paramagnetic term or $\sigma_{GG}^{P}$ in the original Ramsey equation requires the detailed knowledge of the energies as well as the wave functions of the ground and excited states. These are seldom known. Even when Ramsey's simplified equation (2 - 20) is used where the integrals are only over the ground state wave functions, a good method for obtaining the appropriate $\Delta E$ is not available unless it is estimated experimentally.

Furthermore the second term is difficult to evaluate reliably since it depends on the second derivative of the wave functions. Consequently it is very sensitive to errors in this derivative as Ramsey (14) illustrates with an example from the literature (15). Wick (15) found that by taking two somewhat different wave functions in his calculations

of the rotational magnetic moment of $H_2$ he could obtain results for a term analogous to the Ramsey paramagnetic term which differed from each other by more than a factor of eight.

The two terms in Ramsey's equation (2 - 20) are often of comparable magnitudes but of opposite sign. Hence this equation has been mainly applied to small molecules. In proton magnetic resonance the diamagnetic term is predominant whereas fluorine chemical shifts are largely dominated by the paramagnetic term. Due to the problems arising from the use of Ramsey's equation in dealing with larger systems, the contribution to the total shielding must be subdivided into local contributions. This is discussed in the next two sections.

(c) The Neighbour Anisotropy Effect

Further work on the evaluation of the contributions to $\sigma$ was carried out by Saika and Slichter (16). After completing a study of fluorine resonance shifts, they found it convenient to subdivide the shielding constant into three terms. The first two terms were found to be equivalent to the diamagnetic and paramagnetic terms discussed by Ramsey. The third term was the combined effect of the diamagnetic and paramagnetic currents arising from other atoms on a particular nucleus. This effect is largest if the electrons on a near neighbour atom have a large and anisotropic magnetic susceptibility. This term corresponds to $\sum_{G \neq B} \sigma_{GB}$ in equation (2 - 18). It is particularly important for molecules like acetylene with an anisotropic triple bond and for the hydrogen halides.

Magnetic anisotropy originates from the circulation of electrons

on neighbouring atoms. These circulations are induced by the applied field and may be either diamagentic or paramagnetic. They may arise on the neighbouring atom or the bond joining the neighbouring atom to the nucleus in question.

The mathematical treatment has been developed by McConnell (17) and Pople (18). 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 nucleus in question is then investigated. This effect would be averaged to zero over all orientations of the molecule with respect to the field if the magnitudes of the induced currents were independent of orientation. However, if the electrons on the neighbouring atom have a local anisotropy in the magnetic susceptibility the component of the secondary field at a neighbouring nucleus will not be averaged to zero.

Hence a secondary field is produced at the nucleus due to these distant currents and will contribute to the measured chemical shift. For a diatomic molecule H-X with cylindrical symmetry the contribution $\Delta\sigma$ to the shielding of the proton due to the neighbouring anisotropy effect is

2-21 $$\Delta\sigma = \frac{\chi_{//} - \chi_{\perp}}{3R^3} \quad (1-3\,\mathrm{Cos}^2\,\theta) \,.$$

This equation was first derived by McConnell (17). R is the separation between proton H and the point dipole on X, $\theta$ is the angle between the R vector and the anisotropy axis, $\chi_{//}$ and $\chi_{\perp}$ are the magnetic susceptibilities parallel to and perpendicular to the bond

axis. They are negative when we are dealing with diamagnetic currents and positive when paramagnetic currents are involved. The anisotropy in the magnetic susceptibility is $\Delta\chi$.

McConnell's derivation makes several assumptions; namely, that the group which is studied is distant enough from the proton in question, that the moment induced by the applied field may be represented by a point dipole and that the secondary field at the proton may be calculated on this basis. Equation (2 - 21) may be extended to calculate the effect of several groups in one molecule on a particular nucleus.

Pople has studied the diamagnetic anisotropy of the triple bond in acetylene. A large paramagnetic current in the carbon atoms of the triple bond is induced when the field is perpendicular to the molecular axis but this effect is zero when the field lies along the bond axis. Hence $\chi_{//} - \chi_{\perp}$ is large and negative and since $\cos\theta = \cos o$ is positive, $\Delta\sigma$ is approximately + 10 ppm. This increased shielding is large enough to displace the acetylene resonance signal from where one would expect it on the basis of acidity (low field of ethylene) to its observed position near ethane.

An excellent review has recently appeared which correlates all the data and gives a good discussion of the diamagnetic anisotropy of electron groups (19).

(d) Ring Current Effect

Electronic currents will flow around closed rings of atoms with the best example being the "ring currents" arising from the pre-

cession of the $\pi$ electrons around the direction of an externally applied magnetic field in aromatic systems. This approach was first suggested by Pauling (20). On this model it is possible to compare the shielding constant between an aromatic and an ethylenic proton.

When a magnetic field is applied perpendicular to the plane of the benzene ring the induced magnetic moment is diamagnetic. There is no free electron current if the magnetic field lies in the plane of the ring. Pople (21) has made a simple estimate of the magnitude of the secondary magnetic field at the benzene protons due to the induced magnetic moment at the centre of the ring. On this basis he has calculated the difference in the shift between benzene and ethylene protons to be -1.75 ppm as compared to the experimental value of -1.4 ppm. The induced magnetic moment has a deshielding effect on the ring protons since the magnetic lines of flux at the protons are paramagnetic.

Musher (22, 23) has challenged the whole idea of a ring current model. However, many authors still argue that the ring current model is of great practical use. Gaidis and West (24) have shown that this model accounts for the observed high-field proton shifts above the plane and inside the ring of an aromatic system. Pople and Untch (25) have applied this model to conjugated monocyclic polyenes and predicted paramagnetic circulations for molecules with $4n$ $\pi$ electrons and diamagnetic circulations for $4n + 2$ systems. Their predictions appear to be in reasonable agreement with the observed proton shifts in the relevant molecules. The number of experimental descriptions in terms of "ring currents" in the NMR literature is very large (24, 25 and references

therein).

The theory and calculation of the chemical shift has recently been reviewed and discussed (23, 26) in full detail.

## C. THE ELECTRON-COUPLED SPIN-SPIN COUPLING CONSTANT

A nucleus in a molecule experiences a contribution to the magnetic field arising from the magnetic moments of neighbouring nuclei. This interaction manifests itself as a broadening of the resonance line in solids and as hyperfine structure in liquids and gases. The former is due to direct dipole-dipole interaction and will not be considered further. The hyperfine structure in liquids and gases arises from, and is known as the electron-coupled spin-spin interaction. Studies of these spin-spin interactions are very important in nuclear magnetic resonance spectra since they strongly depend on the electronic environments of the coupled nuclei (27).

This energy of interaction is equal to $hJ_{ij}\underline{I}(i).\ \underline{I}(j)$ where h is Planck's constant and $J_{ij}$ is the coupling constant (in cps) between nuclei i and j having nuclear spins $\underline{I}(i)$ and $\underline{I}(j)$ respectively. Hence the total Hamiltonian for a molecule in the liquid state in the field $\underline{H}_o$ may be obtained by including the spin-spin interaction term in equation (2 - 13) which now becomes

$$2\text{-}22 \qquad \mathcal{H}^{\circ} = \frac{H_o}{2\pi} \sum_i \gamma_i I_Z(i)\ (1-\sigma_i) + \sum_{i<j} J_{ij}\underline{I}(i).\ \underline{I}(j).$$

The summations are over all the nuclei and $I_Z$ (i) is the Z component of the spin I or the nuclear spin quantum number.

The theory of nuclear spin-spin coupling has recently been reviewed by Barfield and Grant (27). Their review article will be mainly followed in this discussion.

Field independent splittings of the n.m.r. spectra were first discovered by Gutowsky and McCall (28) and by Hahn and Maxwell (29). Gutowsky et al (30) suggested that the orbital motions of the electrons may so shield the direct interaction between nuclei that the local fields might not be averaged to zero when averaged over all orientations by the rapid tumbling motions in liquids. This interaction between nuclear spins and the orbital motions of the electrons was shown (31) however to be smaller by an order of magnitude than the observed coupling constants. Another mechanism proposed by Ramsey and Purcell (32) assumes that nuclear spins interact through the magnetic polarization of the spins of the nearby electrons. This theory, developed in more detail by Ramsey (31) is much more successful and forms the physical basis on which theoretical studies of spin-spin coupling constants are based.

Ramsey's (31) theory took into account all possible interactions between nuclear spins in a molecule and showed that the indirect coupling, which occurs by a polarization of the electronic environment, may occur by three mechanisms:

a) one nuclear magnetic moment induces orbital electronic currents which in turn produce magnetic fields at the site of a second nucleus.

b) the dipole interaction between the magnetic moment of one nucleus and the electron spin produces an electron spin polarization so that there are nonvanishing magnetic fields acting on other nuclei.

c) there is a coupling involving the Fermi contact interaction between nuclear moments and electron spins in s-orbitals.

Since protons have only a single 1s electron mechanism c constitutes the most important contribution to the total coupling mechanism.

Qualitatively, the Fermi contact coupling mechanism may be discussed as follows. It is proposed that the spin-spin interactions are transmitted via the bonding electrons between the nuclei, and not through space. Consider two nuclei A and B joined by a pair of bonding electrons. To a first approximation, it is very likely that one electron will be associated with one nucleus A and the other electron with nucleus B. Energetically the most stable state is the one in which the electron spin is opposed to that of its own nucleus. But the Pauli principle states that the two electron spins must also be paired (i.e. antiparallel). Hence the most stable state will be the one in which nucleus A-electron a-electron b-nucleus B spins alternate. Preferentially nuclear spins A and B will tend to be antiparallel (paired). Thus the bonding electrons are responsible for letting one nucleus know the spin state of a neighbouring nucleus. This is the Fermi contact potential or interaction. For an s-electron there is a probability of the electron being found right at the nucleus and the contact interaction is proportional to the electron density at the nucleus. For this reason it is so important for proton-proton coupling. The calculation of the Fermi contact interaction is actually a relativistic problem since the potential energy of the system becomes very large when the electron is near the nucleus.

Ramsey's approach to the spin-spin coupling theory was developed

using quantum-mechanical perturbration theory. He showed that the Hamiltonian for electrons moving in a field of nuclei which have magnetic moments is (33)

2-23 $$\mathcal{H} = \mathcal{H}_1 + \mathcal{H}_2 + \mathcal{H}_3,$$

where $$\mathcal{H}_1 = \sum_k \frac{1}{2m}\left(\frac{\hbar}{i}\nabla_k + \frac{e}{c}\sum_N \hbar\gamma_N \underline{I}_N \times \frac{\underline{r}_{kN}}{r^3_{kN}}\right)^2 + V + \mathcal{H}_{LL} + \mathcal{H}_{LS} + \mathcal{H}_{SS};$$

$$\mathcal{H}_2 = 2\beta\hbar\sum_k\sum_N \gamma_N\left[3(\underline{S}_k\cdot\underline{r}_{kN})\frac{(\underline{I}_N\cdot\underline{r}_{kN})}{r^5_{kN}} - \frac{\underline{S}_k\cdot\underline{I}_N}{r^3_{kN}}\right],$$

$$\mathcal{H}_3 = \frac{16\pi\beta\hbar}{3}\sum_k\sum_N \gamma_N \delta(\underline{r}_{kN})\underline{S}_k\cdot\underline{I}_N.$$

$\mathcal{H}_1$ - the term involving $\sum_k$, gives the total electronic kinetic energy and magnetic interactions between electronic orbital motions and nuclear moments (coupling mechanism a)

$V$ - electrostatic potential energy

$\mathcal{H}_{LL}$ - electron orbital-orbital interactions

$\mathcal{H}_{LS}$ - electron orbital-spin interactions

$\mathcal{H}_{SS}$ - electron spin-spin interactions .

These four quantities are not involved with the nuclear spin vector $\underline{I}_N$.

m - electron mass

e - electron charge

$\gamma_N$ - magnetogyric ratio of nucleus N

$\hbar$ - Planck's constant divided by $2\pi$

c - velocity of light

$\underline{I}_N$ - nuclear spin vector

$\underline{r}_{kN} = \underline{r}_k - \underline{r}_N$ where $\underline{r}_k$ designates the coordinates of the k'th electron and $\underline{r}_N$ the coordinates of the n'th electron.

$\mathcal{H}_2$ - gives the magnetic dipolar interactions between electrons in non - s orbitals and nuclear moments (coupling mechanism b).

$\beta$ - Bohr magneton = $\frac{e\hbar}{2mc}$

$\underline{S}_k$ - electron spin vector .

$\mathcal{H}_3$ - represents the Fermi contact interaction between electron spins in s - orbits and nuclear spins (coupling mechanism c).

The Dirac delta function $\delta(\underline{r}_{kN})$ has the properties

$$\int_{-\infty}^{+\infty} \delta(x)\, dx = 1; \qquad \int_{-\infty}^{+\infty} f(x)\ \delta(x-a)\, dx = f(a).$$

Its presence in the term implies that the interaction depends on the probability of the electrons being at the nucleus. This term was introduced by Fermi to explain the hyperfine structure in atomic spectra.

The total Hamiltonian for a molecule is derived by Hameka (34) and will not be considered further.

For protons the Fermi contact term ($\mathcal{H}_3$) makes the largest contribution to the total Hamiltonian since it corresponds to the electrons being closest to the nuclei. The interaction of the nuclear magnetic moments with the electron orbital motion ($\mathcal{H}_1$ term) and the electron-dipole ($\mathcal{H}_2$ term) are usually neglected (31, 35). The presence of the large Fermi contact term is also evidence against a coupling mechanism which would occur between nuclear spins through space rather than through the electronic structure of the intervening bonds. Experimental evidence indicates that the magnitude of the coupling constant betwen two nuclei attenuates with an increasing number of

bonds separating these two nuclei and an attenuation factor of ten for each additional intervening saturated bond has been suggested by McConnell (36).

The coupling constant $J_{NN'}$ between nuclei N and N' may be calculated from the total Hamiltonian. A rigourous evaluation of $J_{NN'}$ requires the wave functions for the electronic ground state and all the excited states. These are seldom known. An approximation is usually made in which the sum of $(E_N - E_0)$, where $E_N$ is the energy of the n'th excited state and $E_0$ is the ground state energy, is replaced by an average excitation energy $\Delta$ E (average energy approximation). The contact contribution $J_{NN'}^{(3)}$ to the total coupling constant $J_{NN'}$ is found to be (1, 31)

2-24
$$J_{NN'}^{(3)} = \frac{-2}{3h}\left(\frac{16\pi\beta\hbar}{3}\right)^2 \gamma_N \gamma_{N'} \frac{1}{\Delta E} \times \left\langle 0 \left| \sum_k \sum_j \delta(\underline{r}_{kN}) \delta(\underline{r}_{jN'}) \underline{S}_k \cdot \underline{S}_j \right| 0 \right\rangle .$$

This evaluation requires only a knowledge of the wave functions for the electronic ground state. The k and j refer to summations over electrons.

This approach also has difficulties. The evaluation of $\Delta$ E is nearly as difficult as the evaluation of the coupling constant itself. Due to the average energy approximation, calculations of spin-spin coupling constants must have elements of empiricism (27).

In equation 2 - 24 it is seen that $J_{NN'}$ is proportional to the product of the magnetogyric ratios $\gamma_N \gamma_{N'}$. This gives a simple relation between the spin coupling constants involving various isotopes of the same nuclear spins. A slight departure from strict proportionality

might be expected in two molecules differing isotopically due to different amplitudes of zero-point vibration and to different electronic reduced masses, but these are very small (37).

The above theory was first applied to the coupling in the hydrogen molecule. In practice the spin coupling constant cannot be observed directly since both protons are equivalent. However, from a study of HD where the observed coupling is 43.7 cps and the knowledge of $\gamma_H / \gamma_D = 6.514$, the proton-proton coupling can be calculated to be 278 cps (27). Ramsey (31) calculated the contact term for HD and found that it contributed about 40 cps to the total coupling constant. The dipolar contribution was about 3 cps ($\mathcal{H}_2$ term) while the orbital terms ($\mathcal{H}_1$) were less than 0.5 cps. Hence, the contact term is the dominant one. The various theoretical estimates of the $H_2$ coupling have been reviewed (27) and will not be considered further.

The theory has now been applied to coupling constants between protons in molecules where there is no <u>direct</u> bond. Ramsey's equations also serve as a starting point for these calculations. These involve both the valence bond and the molecular orbitbal wave functions in the calculation of the term

$$\left\langle O \left| \sum_k \sum_j \delta(\underline{r}_{kN}) \, \delta(\underline{r}_{jN'}) \, \underline{S}_k \cdot \underline{S}_j \right| O \right\rangle$$

in equation ( 2 - 24). Reasonable values of $\Delta$ E must also be obtained. The latter problem is difficult and is often avoided by comparing sets of coupling constants for groups of compounds within which $\Delta$ E is expected to be constant. Then variations in the coupling constants are attributed to minor changes in the ground-state total electronic wave function.

McConnell (38) formulated the molecular orbital treatment within the framework of Ramsey's perturbation results. The wave function is expressed as a product of molecular orbital and spin functions of the electrons. Configuration interaction, i.e. the "mixing in" of excited electronic configurations of the correct symmetry, was not included and hence leads to the result that the coupling constant should always be positive. This conclusion is contrary to experimental results since coupling constants of both signs are measured (27).

Recently Pople and Santry (39) have developed the molecular orbital method without invoking the average energy approximation. They use both ground and excited state wave functions. The contact contribution to the spin-spin coupling constant between nuclei N and N' is given in terms of the atomic orbitals taking part in the bonding process (since molecular orbitals are expressed as a linear combination of atomic orbitals) and the mutual atom-atom-polarizability associated with atoms N and N' (40). Using Pople and Santry's theory the calculated coupling constant can have either sign.

The Pople and Santry theory can explain the effect of electronegative substituents on gem H-H coupling constants (41). It has recently been applied with moderate success to directly bonded $C^{13}$ - H and $C^{13}$ - $C^{13}$ coupling constants (42) and all the $C^{13}$ - H and $C^{13}$ - $C^{13}$ coupling constants in ethane, ethylene and acetylene (43). In the latter paper a positive $J_{gem}$ (H,H) is calculated for ethane whereas experimentally it is negative. Besides this, positive values for $J(C^{13} - C - H)$ over two bonds were calculated for ethane and ethylene

whereas experimentally these are also negative. Hence Pople and Santry (43) claim that their approach tends to over-emphasize the positive contributions to the spin-spin coupling even though molecular orbital theory may also lead to negative coupling constants. More detailed calculations on these molecules were carried out by Fahey et al (44). Both of these groups of workers (43, 44) point out that their calculations do not include contributions to the coupling from the $\pi$-electrons in molecules like ethylene and acetylene due to the neglect of the $\sigma - \pi$ interaction. This is a failure of the molecular orbital theory. Semiempirical methods for estimating $\pi$-electron coupling have been developed by McConnell (36) and Karplus (45).

Ramsey's theory becomes more successful when the ground state wave function is constructed using valence bond methods. This approach was first reported by Karplus et al (35, 45, 46). The ground state electronic wave function $\psi_0$ is represented as a linear sum of the contributing valence bond structures (a canonical set); i.e. $\psi_0 = \sum_i c_i \phi_i$ where each $\phi_i$ is a combination of 2n singly occupied orbitals together with a spin function for the electrons. The system contains 2n electrons, n is the number of bonds and the $c_i$ are coefficients determined by minimizing the energy. This approach has been successful in several predictions (35).

One reason for the success of the valence bond approach will be discussed. Assuming that the Fermi contact term is responsible for most of the coupling, equation (2 - 24) can be applied. For example consider the coupling between two protons in the hydrogen molecule.

The $\gamma_N$ are equal to $\gamma_H$. Summing over $\sum_j \sum_k$ is equivalent to multiplying the integral by 2 since there are two possibilities: (a) electron 1 is associated with nucleus N and electron 2 with nucleus N' and (b) electron 1 is associated with nucleus N' and electron 2 with nucleus N. However these electrons are indistinguishable. Consequently equation (2 - 24) is written as:

$$2\text{-}25 \qquad J_{HH'} = \frac{-4}{3h}\left(\frac{16\pi\beta\hbar}{3}\right)^2 \gamma_H^2 \frac{1}{\Delta E}\left\langle \psi_o \middle| \delta(\underline{r}_{1H})\,\delta(\underline{r}_{2H'})\;\underline{S}_1 \cdot \underline{S}_2 \middle| \psi_o \right\rangle.$$

The total electronic spin $\underline{S}$ may be written as:

$$2\text{-}26 \qquad \underline{S} = \underline{S}_1 + \underline{S}_2.$$

The expectation value for a singlet state is

$$2\text{-}27 \qquad \left\langle \underline{S}^2 \right\rangle = \left\langle \underline{S}_1^2 \right\rangle + \left\langle \underline{S}_2^2 \right\rangle + 2\left\langle \underline{S}_1 \cdot \underline{S}_2 \right\rangle = 0.$$

Hence

$$2\text{-}28 \qquad \left\langle \underline{S}_1 \cdot \underline{S}_2 \right\rangle = \tfrac{1}{2}\left[\left\langle \underline{S}^2 \right\rangle - \left\langle \underline{S}_1^2 \right\rangle - \left\langle \underline{S}_2^2 \right\rangle\right].$$

But

$$2\text{-}29 \qquad \left\langle \underline{S}_1^2 \right\rangle = \left\langle \underline{S}_2^2 \right\rangle = S(S+1).$$

For electrons $S=\frac{1}{2}$. Hence $\left\langle \underline{S}_1 \cdot \underline{S}_2 \right\rangle = -3/4$. In equation (2 - 25) $\psi_o$ is a function of the position and spin coordinates. Substituting the results obtained in equation (2 - 29) into (2 - 25):

$$2\text{-}30 \qquad J_{HH'} = \frac{1}{h\Delta E}\left(\frac{16\pi\beta\hbar}{3}\right)^2 \gamma_H^2 \left\langle \lambda \middle| \delta(\underline{r}_{1H})\;\delta(\underline{r}_{2H'}) \middle| \lambda \right\rangle$$

where the $\lambda$ is the ground state function of position coordinates. In the above equation the integral is the value of the wave function when electron 1 is associated with nucleus H and electron 2 with nucleus H', a situation in which the wave function is nicely described by valence bond theory since this theory overcorrelates the electrons. Another

advantage of this approach is that it offers the possibility of predicting the signs of the spin-spin coupling constants. Depending on whether there are an odd or an even number of bonds separating the coupled nuclei in a saturated chain of carbon atoms, the coupling constant is predicted to be positive or negative. A positive coupling constant is one in which the two coupling nuclei favor an antiparallel arrangement of their nuclear spins. A negative coupling constant is observed when the nuclear spins are coupled in a parallel arrangement.

This prediction is highly simplified and only applies to the case where the coupling mechanism between nuclei is dominated by intra-atomic electronic Hund interactions which may be described in terms of the Dirac vector model (27). When electrons enter degenerate energy levels, available orbitals are singly occupied; until each orbital is so occupied no electron pairing occurs. For a single non degenerate orbital, only two electrons will occupy it with antiparallel spins. On this basis the atomic orbitals for a molecule may be drawn up, the electrons then occupy these orbitals according to Hund's rule and the spin states of the electrons associated with the protons under consideration are thus determined. Since the contact mechanism is so important for protons, the proton spin states will be opposite to those of their neighbouring 1s electrons. In this manner, protons coupled over an even number of bonds are predicted to have negative coupling constants while those coupled over an odd number of bonds should have positive coupling constants.

When a proton-proton coupling is transmitted via a Hund exchange interaction between the electrons, only the bonding electrons take part.

This is a very simplified approach. There are other paths in a molecule and other electrons by which protons may couple which are neglected by the simple Hund exchange interaction. The valence bond treatment incorporates all possible electronic paths which may lead to a transmission of a coupling between protons. However, for coupling over three bonds or more the Hund exchange interaction predominates and hence signs of these coupling constants may be predicted. For example, a simple Hund exchange interaction via the bonding electrons contributes to a positive coupling constant between vicinal (3-bond) protons which should be independent of the orientations of the C-H bonds. Experimentally, vicinal proton coupling constants are positive yet their magnitudes are a function of the dihedral orientations of the C-H bonds. This arises due to contributions from other electronic paths besides the bonding electron path (Hund exchange) which may transmit the coupling. For example, the spin state of one proton will determine the spin of the neighbouring 1s electron via the contact interaction. The spin of this 1s electron may polarize the electron in a hybrid orbital on the carbon atom to which it is <u>not bonded</u>. This interaction may then proceed via the remaining bonding electrons to the 1s electron situated on the second proton. The contact interaction will then determine the spin state of the second proton and thus the coupling path is complete. (When the coupling is transmitted via the Hund exchange interaction, the spin of the first 1s electron will polarize the electron in a hybrid orbital on the carbon atom to which it <u>is bonded</u>.)

There are many of these possible electronic paths by which the

coupling between two protons may be transmitted. Their magnitudes may be large or small. They may make a positive or a negative contribution to the total coupling and hence may augment or decrease the contribution to the coupling constant transmitted via the Hund exchange interaction. All of these possible electronic bonding paths are incorporated into the valence bond treatment which predicts the change of vicinal coupling constants with dihedral angle (35).

An example where the valence bond theory has been unsuccessful is the prediction of the angular dependence of geminal coupling constants (2-bond) by Gutowsky, Karplus and Grant (47). Their theoretical treatment predicts that the coupling constant J (gem) decreases from 32 cps to zero cps for H-C-H angles from 100° to 125°. For angles greater than 125°, J (gem) is predicted to be negative. These results predict a positive value for J (gem) in methane which actually has a value of -12.4 cps. Also, subsequent experimental data have established the opposite trend for hydrocarbons and in molecules with substituents there is little correlation with bond angle. These results are discussed by Pople and Bothner-By (41) and their molecular orbital approach gives a satisfactory interpretation of geminal coupling constants.

Karplus (35) used the valence bond approach successfully to calculate the proton-proton, proton-fluorine and fluorine-fluorine coupling constants in ethanic and ethylenic molecules. The valence bond theory has also been applied in calculating the $\pi$-electron contribution to the total coupling constant in unsaturated molecules and this will be discussed in the next section.

The alternative method to perturbation is the use of the variation principle in calculating coupling constants which has been employed by several workers (48, 49). The principal advantage claimed for this approach is that it avoids the average energy approximation yet the computation of the energy $\triangle$ E in these equations is still also very difficult (27). Hence the variational approach is not used very often in the calculation of coupling constants.

## D. LONG-RANGE PROTON-PROTON COUPLING CONSTANTS

### 1. Introduction

A coupling constant across four or more bonds is known as long-range. The theories of coupling constants between nuclei separated by two bonds (geminal coupling) and three bonds (vicinal coupling) have been reviewed and discussed before (27, 35, 41, 45-47, 50, 51). As well, the theories of long-range proton-proton coupling constants have been reviewed briefly (27) and the experimental results have been compiled (52). These coupling constants have only become available with the great resolution now obtainable by n.m.r. techniques.

### 2. Non-Aromatic Hydrocarbons

Electron-coupled proton-proton spin-spin interactions through four $\sigma$-bonds have been observed in a number of molecules (52, 53). However, no detailed theoretical predictions of their magnitude have been made. Karplus (45) estimates that the $\sigma$-electron contribution to this coupling is of the order of 0.5 cps whereas most of the experimental values lie in the range 0.3 to 1.5 cps (53). Since these coupling constants are strongly stereospecific in saturated hydrocarbons and sometimes appear in those conformations of unsaturated hydrocarbons for which the $\pi$-electron calculations predict a zero contribution to the coupling constant from the $\pi$-electrons, there must be a significant long-range coupling mechanism involving $\sigma$-electrons (27).

Barfield and Grant (27) obtain an expression for the $\sigma$-electron contribution to long-range coupling constants between protons separated

by four $\sigma$ -bonds. They find a strong angular dependence of the coupling constant in which the maximum value arises from the straightest zig-zag path of an all trans conformation.

Long-range coupling constants between protons in unsaturated hydrocarbons are also well known (52, 53) and are much more common. Karplus (45, 54) found that these coupling constants were much larger than could be obtained by the $\sigma$ -electron mechanism and arise from a contribution from the $\pi$ -electrons (55). He has applied the valence bond approach to calculate the $\pi$ -electron contribution to long-range coupling constants $J_{HH'}(\pi)$ which is expressed as (45)

2-31 $$J_{HH'}(\pi) = 2.1 \times 10^{-15} \sum_T \frac{a_H(T)\ a_{H'}(T)}{\Delta\pi(T)} .$$

This semi-empirical relationship was obtained in terms of experimentally determined hyperfine constants from electron spin resonance spectra and triplet state energies, as was done by McConnell (36, 56). The quantities $a_H(T)$ and $a_{H'}(T)$ are the proton hyperfine constants in cps and $\Delta\pi(T)$ is the excitation energy for the $\pi$ -electron in ev. The quantity $a_H(T)$ is a measure of the extent to which the spins of the hydrogen nucleus and an unpaired electron in a carbon 2p $\pi$-orbital are coupled together in the radical fragment T. Karplus lists hyperfine constants for several radical fragments. Since the singlet-triplet transition is forbidden, relatively little is known about the $\pi$ -electron triplet state energies in simple organic molecules. However, using values from theoretical calculations for $\Delta\pi(T)$ for ethylenic and acetylenic compounds as well as experimental $a_H(T)$ values, Karplus calculated

$J_{HH'}$ ($\pi$) for a variety of compounds. The agreement between experimental coupling constants and those calculated (with a small correction for a $\sigma$-bond contribution) is very good. The $\pi$-electrons dominate the coupling in these systems. The success of equation (2 - 31) in conjunction with experimental values of electron spin resonance hyperfine constants is a strong argument for the use of empirical values of integrals based on experimental magnetic resonance data (27).

One feature of long-range coupling constants in unsaturated hydrocarbons is that the magnitude of the coupling is not strongly decreased as the number of bonds between the two coupling protons increases. This is consistent with the mechanism proposed by Karplus (45) which predicts that replacing a proton by a methyl group should only change the sign but not the magnitude of the above coupling constant. This arises because of the relative magnitudes and signs of the hyperfine interaction constant $a_H$ (T) for the radical fragments $H-\dot{C}=C$ and $CH_3-\dot{C}=C$ for example. When the methyl group is freely rotating the values of $a_H$ (T) for these radicals have similar magnitudes but opposite signs.

In summary the theoretical valence bond treatment (45, 54) predicts the following (52):

(a) Cisoid and transoid allylic (H - C = C - C - H) and homoallylic (H - C - C = C - C - H) coupling constants should be of similar magnitude unlike the cis and trans coupling constants in olefins.

(b) The magnitude of the long-range coupling constants should depend on the angle made by the bond joining the proton to the $sp^3$

hybridized carbon stom and the plane of the multiple bond.

(c) Coupling constants for protons separated by an odd number of bonds should be positive and for protons separated by an even number of bonds negative in sign.

(d) Replacement of = C-H by = C-$CH_3$ should alter the sign but not the magnitude of the inter-proton coupling across the intervening π-system.

All these predictions have been verified experimentally (52).

3. Aromatic Hydrocarbons

The coupling constants in substituted benzenes have the following values:

J (ortho) = 6 to 9 cps; J (meta) = 1 to 3 cps and

J (para) = 0 to 1 cps.

All of these coupling constants have a positive sign (50).

Several generalizations have been made regarding the substituent effect on the magnitudes of the ortho and meta coupling constants. The para couplings do not show any pronounced trends (50).

The ortho and meta proton coupling constants are not usually considered as long-range couplings. However, the mechanism for the coupling between the ring protons will be briefly discussed since it also applies to the long-range coupling mechanism between a side-chain and a ring proton to be considered in the next section.

The magnitudes of the ring proton-ring proton coupling constants are determined by both the σ -bond and π -bond coupling mechanism (36).

The coupling $J_{HH'}$ may be written as (36):

2-32 $$J_{HH'} = J_{HH'}(\sigma) + J_{HH'}(\pi)$$

where $J_{HH'}(\sigma)$ is the contribution to the total coupling arising from the spin-spin interaction proceeding via the $\sigma$ -electrons. This quantity is very rapidly attenuated with an increasing number of bonds by as much as a factor of 10 for each additional intervening bond between the coupled protons. The second contribution $J_{HH'}(\pi)$ to the total coupling is that due to the $\pi$ -electron coupling mechanism.

A qualitative picture of this mechanism will be briefly given (36). Proton-proton coupling constants are dominated by the (nuclear spin) - (electron spin) - (electron spin) - (nuclear spin) coupling mechanism. The (electron spin) - (electron spin) link is a strong electrostatic interaction between electrons and is of the Dirac spin exchange type. The (nuclear spin) - (electron spin) interaction is the Fermi contact interaction. This discussion is the same as in the valence bond approach and is given here to show how it is modified to the case where the coupling may be transmitted via the $\sigma$ - $\pi$ electron interaction.

When only $\sigma$ -bonds are involved the coupling mechanism is easy to follow. By a magnetic coupling proton H polarizes the spin of the electron in a hydrogen-like 1s orbital centered on H. This polarized spin, through exchange coupling, polarizes the spin of the electron in a carbon $sp^2$ orbital used to form the aromatic C-H bond.

This polarization mechanism proceeds along the σ -bond electrons and eventually produces an electron spin polarization at some other electron centered on proton H' which then magnetically couples with H'. When dealing with carbon hybrid orbitals Hund's rule must be accounted for. When the π -electrons take part in the coupling mechanism the coupling path may proceed as follows. Proton H again by a magnetic coupling polarizes the spin of the hydrogen 1s electron which in turn couples with the $sp^2$ carbon electron. Then through intra-atomic exchange coupling the polarized spin in the $sp^2$ bond couples with the π -electron spins and this π -electron spin polarization is distributed over the aromatic ring system. This π -electron spin polarization then couples back into the σ -electron system and eventually produces an electron spin polarization at some other proton H'. The magnetic interaction between this electron spin and proton H' completes the coupling path from H to H'. This π -electron contribution is small ( $\sim$ 2 cps) but not so strongly attenuated since it requires the contribution of σ - π electron configuration interaction to the molecular ground-state wave function and this contribution is small.

McConnell has used the molecular orbital (36) and the valence bond (56) approach to calculate the π - electron contribution to the total coupling constant in aromatic systems. He was able to calculate the π -electron contribution directly from the data obtained from the isotropic splittings due to aromatic protons in the electron spin resonance spectra of aromatic π -electron radicals. Since the observed

isotropic hyperfine splittings in these radicals arise from a contact interaction due to a $\sigma$ - $\pi$ configuration interaction, they give a direct measure of the unpaired spin densities at the $\sigma$ -protons. But proton-proton coupling also requires that the $\pi$ -electron have a finite spin density (s - character) at the proton. Therefore, the $\pi$ -electron contribution to proton-proton coupling constants may be calculated from aromatic proton hyperfine splittings (36). The $\sigma$ -electron contributions should be similar to those found for vicinal and other non-aromatic proton couplings which occur via the $\sigma$ -electrons.

McConnell's (36) treatment is as follows. Experimental evidence shows that

2-33 $$a_N = Q_{CH} \rho_N$$

where $a_N$ is the hyperfine splitting due to proton N, $\rho_N$ is the unpaired electron density at carbon atom N bonded to proton N and $Q_{CH}$ is a constant (in gauss). Hence $Q_{CH}$ corresponds to an <u>effective</u> isotropic hyperfine coupling constant arising from the interaction between a $\pi$ -electron in a carbon atomic orbital and the adjacent $\sigma$ -proton. From molecular orbital calculations the contribution of the $\pi$ -electrons to the coupling between protons N and N' is (57).

2-34 $$J_{NN'}(\pi) = \frac{\beta^2 Q_{CH}^2 P_{NN'}^2}{h \Delta E}$$

where $P_{NN'}$ is the mobile bond order between the carbon atoms bonded to the hydrogen atoms, $\Delta E$ is an average excitation energy to triplet states and $\beta$ is the Bohr magneton. $Q_{CH}$ is determined experimentally and is found to depend on the charge (58) and hybridization of the carbon atom (59, 60) and is approximately equal to -24 gauss (61, 62).

For proton-proton coupling constants in alternant aromatic molecules this relationship predicts zero coupling of protons attached to carbon atoms separated by an even number of carbon-carbon bonds.

McConnell's (56) valence bond approach gave more reasonable contributions of π -electrons than his molecular orbital approach. The calculated π -electron contributions to the total coupling constants in benzene using this approach are +0.47, -0.21 and +0.23 (cps) for the ortho, meta and para proton-proton coupling constants respectively.

These results indicate that since the calculated values of $J_{HH'}$ (π) for the ortho and meta proton coupling constants are much smaller than the observed values, the main coupling mechanism in both cases is via the σ -electrons. The π -bond mechanism dominates the para coupling since the calculated value of +0.23 cps agrees with the magnitudes and sign obtained for the para coupling in many substituted toluenes as determined in this study.

The magnitude and positive sign of the meta coupling constant and analogous 1:3 couplings across heterocyclic aromatic rings still remain as an anomaly (63). In the vast majority of non-aromatic molecules proton-proton coupling constants across this number of bonds are negative in agreement with the usual Dirac vector model (38, 64). McConnell showed that the π -electron contribution to this coupling is also negative (56). Hence there is some speculation that the meta coupling mechanism may involve a direct overlap between the small $sp^2$ orbitals of the two meta carbon atoms across the ring (63). Then the effective coupling would be across three bonds. This mechanism has

been suggested to explain four σ -bond coupling constants in saturated systems which can adopt a "tail-to-tail" configuration (65 and references therein). Barfield (65) has studied the angular dependence of four-bond coupling constants using the valence bond approach. He applied his treatment to many saturated and unsaturated systems and estimated the σ -bond contribution to the meta coupling constant to be +1.03 cps.

McConnell (36, 56) has also considered the π -electron contribution to the total coupling in naphthalene where he found that the para and longer-range proton-proton coupling constants are also dominated by the π -electron mechanism and the σ -electron contribution is negligible.

## 4. Long-Range Benzylic Proton-Ring Proton Coupling Constants

### (a) Introduction

Coupling between protons in benzylic methyl and methylene groups and ring protons has been only slightly investigated (52). Hoffman (55) attributed such coupling in mesitylene to hyperconjugation between the π -electron orbitals of the unsaturated molecule and the pseudo π -orbitals of the methyl group. Schaefer and Schneider (66) observed a broadening of the resonances of ring protons ortho to a methyl group in substituted benzenes which was ascribed to a small coupling between the methyl and ortho ring protons. This coupling can be eliminated by a simple double resonance experiment as is done in this study.

Another interpretation had been advanced to explain the multiplicity of the methyl resonance in a related system. The proton magnetic resonance spectrum of 2, 2' - dimethyldiphenylether was studied (67) and the doublet which was obtained for the methyl resonance was said to arise from restricted rotation about the C-O bond. This has since been disproved (68, 69) and the hyperfine structure observed for the methyl resonance was shown to arise from long-range coupling to the ring.

The signs and magnitudes of the long-range coupling constants between ring protons and methyl protons in substituted toluenes are in qualitative agreement with a theory based on $\sigma - \pi$ interactions (36, 45, 55, 56, 70-72). McConnell (36, 56) and Karplus (45), using the hyperfine splitting due to aromatic protons in electron spin resonance experiments, obtained an estimate of the $\sigma - \pi$ electron interaction and thus of the $\pi$ -electron contribution to the spin-spin coupling constant. This contribution is also given by equation (2 - 34).

When the $C_1$-H bond is replaced by $C_1$-$C_2$-H, where $C_1$ is $sp^2$ and $C_2$ is $sp^3$ hybridized, one of the $Q_{CH}$ terms in equation (2 - 33) and (2 - 34) is replaced by $Q_{CCH}$ whose value is about +25 gauss for a freely rotating methyl group (57, 70, 73-76). Consequently when a methyl group is substituted for a proton on the benzene ring the magnitude of the proton coupling constant determined by the $\sigma - \pi$ electron mechanism should remain approximately the same. Only the sign of this coupling should change. This was discussed previously for non-aromatic unsaturated systems and is based on the data that electron spin resonance

spectra reveal couplings due to the methyl group in compounds such as methyl-substituted semiquinones with magnitudes nearly equal to those observed for aromatic protons (73). These results indicate a nice way of testing and determining whether a particular coupling constant between two protons is dominated by the $\sigma$ -$\pi$ electron mechanism. The procedure is to substitute a methyl group for one of the coupling hydrogens and then to compare the magnitudes of the two coupling constants (73). Hoffman and Gronowitz (73) present a nice discussion on the mechanism of coupling involving $\sigma$ - $\pi$ interactions.

The application of McConnell's equation (2 - 34) to methyl-substituted benzenes predicts a negative sign of the coupling constant between the methyl protons and the ring protons in the ortho and para positions. This approach however predicts a zero coupling to the meta ring proton. The more refined valence bond treatment (56) does predict a positive sign for this coupling.

When the valence bond calculation is carried out the equation for the $\pi$ -electron contribution to the total coupling is very similar to equation (2 - 34) except that it contains a term which describes the correlation between the $\pi$ -electron spins on the two carbon atoms N and N' directly bonded to the hydrogen nuclei H and H'.

McConnell's approach (36, 56) has been shown to be correct. Acrivos (70) studied mesitylene and observed the methyl-ortho and methyl-para coupling constants. The magnitudes of these coupling constants were predicted satisfactorily by his calculations which also predicted that these couplings should have negative signs. The signs

of methyl-ring proton coupling constants were also predicted by Hoffman and Gronowitz (73). In 2-hydroxy-3-5-dibromotoluene the long-range coupling constants from the methyl protons to the ortho and para ring protons were shown conclusively to be negative using double resonance techniques (72). In this study we show using one disubstituted toluene that the methyl-meta ring proton coupling constant is positive and confirm the negative sign of the methyl coupling to the ortho and para ring positions. These signs have recently been confirmed in a study of fluorotoluene derivatives by Blears, Danyluk and Schaefer (77).

Several other experimental results are of interest. Cohen and McLauchlan (71) in 2-carbomethoxy-5-6-dimethylbenzofuran found a methyl-ortho ring proton coupling constant of $|0.74 \pm 0.10|$ cps and methyl-meta coupling constant of $|0.37 \pm 0.10|$ cps. The signs were not determined. Dewar and Fahey (57) studied the long-range coupling in acenaphthene and observed long-range ortho and para ring proton coupling to the methylene protons but no coupling from the meta protons. Applying a correction factor to equation (2 - 34) to account for that fact that the methylene group is kept in a rigid cyclic structure and not freely rotating the magnitudes of the observed coupling constants were predicted using this equation. The more sophisticated valence bond approach (56) was not used since it predicts a measureable coupling constant to the meta position (57).

The applicability of equations (2 - 33) and (2 - 34) and their application to $= \dot{C}-H$ and $= \dot{C}-CH_3$ fragments has been further studied by

McConnell and Chesnut (78). They discussed indirect proton hyperfine interactions in $\pi$ -electron radicals in terms of a hypothetical $\dot{C}$-H fragment which holds one unpaired $\pi$ -electron and two $\sigma$ -CH bonding electrons. Molecular orbital and valence bond theories yield almost identical results for the unpaired electron density at the proton due to exchange coupling between the $\pi$ -electron and $\sigma$ -electrons. The unpaired electron spin density at the proton tends to be antiparallel to the average spin of the $\sigma$ -electron which leads to a negative proton hyperfine constant. They then extended the theory of the indirect proton hyperfine interaction in the CH fragment to the case of polyatomic $\pi$ -electron radical systems such as aromatic radicals and equation (2 - 33) was derived under these general conditions. It was found to be valid for these systems assuming that the $\sigma$ - $\pi$ exchange interaction can be treated as a first-order perturbation in $\pi$ -electron systems and that all effective $\sigma$ - $\pi$ excited states have approximately the same excitation energy. These were found to be good approximations in general for polyatomic $\pi$ -electron radicals.

In summary McConnell's molecular orbital (36) and valence bond (56) approach predict a negative long-range coupling constant for a coupling path separated by an even number of bonds and positive coupling constant for a path with an odd number of bonds. Since $a_N$ for a methyl proton is related to the spin density $\rho_N$ on the aromatic carbon atom by the formula of the same type as for a proton directly attached to this carbon atom (equation 2 - 33), the mechanism of the hyperfine interaction in both cases must be the same (74). The hyperfine constant $Q$ for fragment H - $\dot{C}$ = is -24 gauss and for $CH_3$-$\dot{C}$= it is + 25 gauss.

(b) Factors affecting equation (2 - 34) and its application to the calculation of long-range coupling constants in substituted toluenes.

1. Mobile bond order between the carbon atoms bonded to the methyl group and the proton.

Equation (2 - 34) predicts that long-range coupling constants (which are due mainly to the $\sigma$ - $\pi$ electron mechanism) in a given molecule will be proportional to the square of the bond order $P^2_{NN'}$. In fact the magnitudes of long-range ring proton-methyl proton coupling constants have been interpreted in terms of the double bond character (mobile bond order) between the carbon atoms bonded to the methyl group and the proton (52). Rottendorf and Sternhell (79) have measured the methyl proton-ring proton coupling constants in the three isomeric tetrachlorotoluenes as well as in several methyl aromatic compounds where bond localization is expected to occur. Their results indicate that the magnitude of $J^{o}_{H,CH_3}$ appears to be related to the bond order in these compounds as well as in five-membered heterocyclic compounds. In their discussion they assume, however, that the measured $J^{o}_{H,CH_3}$ in 3,4,5,6 -tetrachlorotoluene (0.63 $\pm$ 0.02 cps) represents an ideal or an unperturbed system and postulate that the magnitude of $J^{o}_{H,CH_3}$ in six-membered aromatic and heterocyclic rings where no bond localization can be postulated is approximately equal to this value. An increase or a decrease in this coupling is then ascribed to a corresponding change in the associated bond order. However, the measured $J^{o}_{H,CH_3}$ value does not represent an unperturbed situation since substituents do have an

effect on $Q_{CH}$ and $Q_{CCH}$ and hence on the magnitude of the long-range coupling constants as determined using equation (2 - 34) (discussed in the next section).

The large $J^{o}_{H,CH_3}$ values for 1-methylnaphthalene and 2-methylnaphthalene (0.7 cps) and 2-methylanthracene (0.8 cps) have also been associated (80) with large $C_1 - C_2$ bond order in these compounds. However, the methyl signals were poorly resolved and accurate measurements of other long-range coupling constants could not be determined.

Associated with these compounds, the high resolution spectra of 22 alkyl-substituted phenanthrenes have also been studied and completely analyzed (81). The ortho, meta and para ring proton coupling constants are all positive and their magnitudes confirm that in phenanthrene, as in benzene and naphthalene (36, 56) the $\sigma$ -electron contribution is dominant for ortho and meta couplings but the para coupling is mainly of $\pi$ -electron origin. Long-range coupling constants were also observed between ring protons H (4) and H (10) which corresponds to a coupling over five conjugated bonds in a "zig-zag" (52) path. The long-range coupling constants from the methyl protons to the ring protons were calculated by an application of equation (2 - 34). The excitation energy $\triangle$ E was taken as 4 e.v. and $Q_{CH}$ and $Q_{CCH}$ were -25 and +25 gauss respectively. Using calculated bond orders, the theoretical long-range coupling constants were obtained and found to be proportional to the widths at half height of the methyl resonances.

The increase in $J^{o}_{H,CH_3}$ magnitudes with the introduction of a CHO group ortho to the methyl group in substituted orcinol derivatives

has also been interpreted in terms of increased $\pi$ -bond order (82).

All the available evidence for the relationship between long-range ring proton-methyl proton coupling constants and mobile bond order has recently been reviewed (83) and the dangers of an uncritical application of this relationship pointed out. Working with hydrocarbons for which both calculated bond orders and measured coupling constants are known (propene, acenaphthene, mesitylene, and 9 -methylphenanthrene), a straight line plot is obtained for $J_{H,CH_3}$ as a function of $P^2_{NN'}$ (measured coupling constants are used to avoid errors in values of $Q_{CH}$, $Q_{CCH}$ and $\Delta E$).

Although a straight line plot is obtained, the prediction of bond orders from J values (or the reverse) by direct interpolation is subject to a number of difficulties. These arise from the many factors affecting $Q_{CH}$, $Q_{CCH}$ and $\Delta E$ in equation (2 - 34). In substituted toluenes, $J^{\circ}_{H,CH_3}$ values range from -0.60 to -0.87 cps (83). Such a range could adequately be attributed to a 20% variation in $P^2_{NN'}$. Therefore Blears, Danyluk and Schaefer (83) concluded that variations in coupling constants can be related to variations in bond order provided consideration of the concomitant substituent induced changes in the other parameters of equation (2 - 34) is included. These are now discussed.

2. Charge on the carbon atom.

Colpa and Bolton (58) studied the dependence of hyperfine splittings on charge densities of the carbon atoms. Since in paramagnetic ions of aromatic molecules the carbon atoms have in general

a non-zero excess charge density besides a non-zero spin density, they proposed that McConnell's equation (2 - 33) should have the form (84)

2-35 $$a_k^H = (Q' + K\epsilon_k)\rho_k^\pi$$

This equation has two semiempirical parameters $Q'$ and K. The unpaired $\pi$ -electron spin density on the $k^{th}$ carbon atom is $\rho_k^\pi$ and $\epsilon_k$ is the excess charge density $(1-q_k)$ where $q_k$ is the total $\pi$ -electron charge density on the $k^{th}$ carbon atom. Consequently $Q_{CH}$ is also dependent upon the charge of the carbon atom.

This equation is supported by proton hyperfine splittings obtained for mononegative and monopositive radical-ions of the same molecule (58). Since the spin density functions in both cases are the same, application of equation (2 - 33) leads to equal splittings for both positive and negative ions. This is in disagreement with experiment since the observed splittings are larger in the positive ion. The different magnitudes of the splittings are explained by the different charge densities on the carbon atoms. Equation (2 - 35) has been applied to the proton hyperfine splittings in the benzene positive radical-ion by Carter and Vincow (84) who could thus account for the observed 15% larger splittings in this ion as compared with the benzene negative radical ion.

As well, in aromatic systems the charge on the carbon atom is affected by the substituents on the ring (85, 86). Thus there exists a substituent effect on $Q_{CH}$. A change in $Q_{CH}$ on substitution of up to 10% has been estimated in representative compounds (83).

Similar considerations also apply to $Q_{CCH}$ as shown by Carter

and Vincow (87) in their study of the proton hyperfine splittings of the hexamethylbenzene positive radical ion.

3. Hybridization state of the carbon atom.

The magnitude of $Q_{CH}$ is affected by the hybridization state of the carbon atom in question (59, 60). Theoretical interpretations of $C^{13}$ hyperfine interactions showed $Q_{CH}$ to vary from a $CH_3$ to a $CHC_2$ radical. This is further complicated since substituents on the benzene ring also affect the hybridization state (88).

4. Steric effects.

The methyl and other alkyl proton hyperfine splittings in ortho substituted nitrobenzene anion radicals have been examined (76) for conformational implications. Arising from steric interactions, there is a dependence of the $C_1$ - H proton hyperfine splitting ($C_1$ is $sp^3$ hybridized) and hence of $Q_{CCH}$, on the angle between the $C_2$ - $C_1$ - H plane and the axis of the $\pi$ -orbital on the $C_2$ carbon atom (76) ($C_2$ is $sp^2$ hybridized and forms part of the ring system). Thus bulky ortho substituents will affect $Q_{CCH}$ and consequently the applicability of equation (2 - 34).

A temperature dependence of J ($\pi$) in ortho substituted toluenes is also a possibility. In toluene and some of its para derivatives the rotation of the methyl group is essentially free (83 and references therein). Hence the application of equation (2 - 34) is justified. When dealing with ortho substituted toluenes the three-fold symmetry of the methyl group is reduced since the potential barrier to free rotation is no long zero (89). For example, in a similar system, this has been

observed in 2,6 asymmetrically disubstituted benzotrifluorides. There are two different rotational conformers of the $CF_3$ group (89) with which there is associated a strong temperature dependence of $J^{o}_{F,F}$ ($F\text{-}CF_3$). The magnitude of the potential barrier to internal rotation of the $CF_3$ group was found to be about 1 kcal./mole.

The temperature dependence of the coupling constant in ortho substituted toluenes is further supported by studies carried out on propene and its derivatives. In these systems the potential barrier to internal rotation of the methyl group is between 2.0 and 2.7 kcal./mole (90-92). Thus this effect must be considered when applying equation (2 - 34).

5. Other effects.

The proton hyperfine splittings have been found to be temperature dependent (76, 84, 87), solvent dependent (84) and substituent dependent (76, 93).

In summary, when a comparison is made between the observed long-range coupling constants and those calculated using equation (2 - 34) or when deviations exist in these couplings from molecule to molecule, all interpretations have to be carried out with extreme care since many factors are always present.

(c) Effects of alkyl groups on ring $\pi$ -electron systems.

Many electron spin resonance studies have been carried out on aromatic radical ions to determine the effects of alkyl groups on $\pi$ -electron systems. The electron spin density may be transferred to the

methyl protons via three mechanisms, namely, polarization by the σ framework, hyperconjugation due to the π -orbitals and inductive effects (94-102). The various studies indicate that the last two mechanisms predominate (102) and that the contributions from the spin polarization mechanism account for only about 3 per cent of the observed methyl proton hyperfine splittings in paramagnetic aromatic systems (96).

The substituent effect of the methyl group on the proton chemical shifts in aromatic systems has also been studied (85, 103).

These results together with those described in the previous section confirm the conclusion that any interpretation of long-range coupling constants and the application of equation (2 - 34) must be carried out with extreme care.

5. Long-Range Coupling Constants in Fluorotoluene Derivatives

The signs of the spin-spin coupling constants between the methyl protons and fluorine nuclei in ortho, meta and para fluorotoluene derivatives have also been determined by double resonance techniques (77). $J^{o}_{F,CH_3}$ and $J^{p}_{F,CH_3}$ are positive while $J^{m}_{F,CH_3}$ is negative. This sign sequence is opposite to that of the methyl proton-ring proton couplings determined in this study and arises from the opposite sign of the hyperfine coupling constant $Q_{CF}$ as compared with $Q_{CH}$, i.e. positive. Support for a positive $Q_{CF}$ also comes from a study of fluorine contact interaction shifts (104-105).

The signs of the long-range couplings between the fluorine nucleus and ortho, meta and para ring protons have also been determined

in 2-amino-5-bromobenzotrifluorides (106). The coupling constants $J^{o}_{H,CF_3}$ and $J^{p}_{H,CF_3}$ are negative and $J^{m}_{H,CF_3}$ is positive. The signs are the same as for the corresponding $J_{H,CH_3}$ couplings since $Q_{CCF_3}$ is positive as is $Q_{CCH_3}$ (107).

## E. ABSOLUTE SIGNS OF COUPLING CONSTANTS IN AROMATIC SYSTEMS

The electron-coupled spin-spin interaction or coupling constant in which the preferential orientation of the coupling nuclear spins is antiparallel is defined as a positive coupling (108). The coupling constant is negative when the spins are parallel.

Absolute signs of coupling constants cannot be determined directly from a nuclear magnetic resonance spectrum whose appearance, while depending upon the relative signs of these couplings, is unaffected by a complete sign reversal (109). Two methods have been used which allow the determination of the absolute signs of coupling constants in aromatic systems. In both methods one compares the isotropic electron-coupled spin-spin interaction with the anisotropic dipole-dipole interaction.

The first approach is due to Buckingham and McLauchlan (109). A strong dc electric field is applied to the sample and at the same time the spectrum is recorded. The orienting effect of the electric field induces a small change in the hyperfine splittings in the spectrum from which the sign of the coupling can be obtained. The normal high resolution spectrum exhibits splittings arising from the isotropic coupling constant but the nuclear magnetic dipole-dipole interaction is averaged to zero by molecular tumbling. The application of the electric field, however, produces a partial alignment of the electric dipoles and hence a non-zero nuclear magnetic dipole-dipole interaction results which appears in the spectrum as an additional splitting.

This either adds to or subtracts from that due to the isotropic coupling constant according to the sign of the latter. Using this method the ortho ring coupling constant in para-nitrotoluene was found to be positive (109). However, this induced coupling was found to be absent in the studies carried out by Sears and Hahn (110, 111). Hence an element of doubt is still associated with these results.

A related method is to dissolve the molecule being studied in a nematic liquid crystalline solvent which is partially oriented in the magnetic field. This experiment was first carried out by Saupe and Englert (112, 113) who showed that the signs of the ortho and meta ring proton coupling constants in benzene are positive. In a magnetic resonance experiment, a nematic solvent provides a homogeneous but anisotropic environment for the solute molecules. Tumbling and translational movements of the solute molecules are rapid but all orientations of the molecule with respect to the applied magnetic field are no longer equally likely. Hence the direct intramolecular dipole-dipole interactions do not average to zero as they do in a normal liquid while the intermolecular interactions do average to zero. From the analysis of the spectrum, which contains peaks arising from these intramolecular dipole-dipole interactions, the absolute signs of the coupling constants can be determined.

Once the absolute sign of one coupling constant is known, the signs of the other couplings may be determined with respect to it. The first approach in the determination of relative signs is based on spectral analysis which shows that in substituted benzenes all the ring

proton coupling constants are positive (114-117).

The second approach is the application of double and multiple resonance techniques. These are discussed in the next section. The positive sign of all the ring proton coupling constants has been confirmed in this manner (118). Only one negative ring coupling constant has been observed so far, namely the meta coupling constant $J_{26}$ in 3-acetylpyridine. The result obtained is -0.21 cps (119). The presence of the nitrogen in the ring however, via which this coupling proceeds, has a large effect on the sign.

## F. NUCLEAR MAGNETIC DOUBLE AND MULTIPLE RESONANCE

One of the most powerful tools for handling the interpretation of complex high resolution spectra, the determination of energy level diagrams, and the signs of spin-spin coupling constants is the nuclear magnetic double (or multiple) resonance technique which has been discussed by various authors (118-137). In these experiments the magnetic resonance of one group or nuclei (for example A) is observed by means of a radiofrequency field $H_1$ at a frequency $\omega_1$ while a second group of nuclei (say X) is irradiated with a field $H_2$ at a frequency $\omega_2$. Certain modifications in the spectral group structure of A result from the irradiation of group X if the multiplet structure is caused by spin-spin coupling between the two groups of atoms. Thus strong radiofrequency irradiation represents a well-defined experimental perturbation of the spin system and allows the spectroscopist to modify his spectra in a controlled manner (136).

This technique has been extensively used and has been well reviewed by Baldeschwieler and Randall (127) and Hoffman and Forsen (136). A brief introduction will be given here. The actual procedure for predicting which multiplets will collapse on spin decoupling and which transitions will split into doublets on tickling a "connected" transition are described in the "Experimental Results" section of this chapter in connection with observed spectra. The details are also given in the above references.

In this study the double resonance experiments have been carried

out in the frequency-sweep mode of operation. This procedure requires that the irradiating field $H_2$ at frequency $\omega_2$ and the external field $H_o$ remain constant while the observing frequency $\omega_1$ (and $H_1$) is varied so as to scan the observed part of the spectrum in the region of group A (the frequency $\omega_2$ is applied at a fixed spectral position in the X group).

The intensity of $\omega_1$ is usually kept as small as is compatible with a good signal-to-noise ratio. The strength of $\omega_2$ can be varied and thus determines the type of experiment that is carried out. Two different double resonance experiments were carried out in this study and will be discussed separately.

1. Spin Decoupling (Weakly Coupled Systems)

In this experiment $\gamma H_2 \gtrsim 2\pi J$. This corresponds to a strong perturbation of the multiplet structure and is the condition for the spin decoupling technique. A splitting in the X region is irradiated while the A multiplet is simultaneously observed to see which corresponding doublets collapse into a singlet line. This collapse depends upon the relative signs of the coupling constants involved. This approach is usually applied to weakly coupled spectra. A spin decoupling experiment carried out on intermediate or strongly coupled systems is difficult because it is usually not possible to prevent more than one coupling from being disturbed by the strong irradiation field. When this happens the interpretation of the results is difficult.

Consider a weakly coupled AMX system in which a splitting corresponding to $J_{MX}$ in the X quartet is irradiated and hence decoupled

from the rest of the spectrum. The relative signs of $J_{AM}$ and $J_{AX}$ may be determined since $J_{MX}$ is decoupled in just those molecules of the sample for which nucleus A has one of its possible spin states while not appreciably perturbing molecules for which nucleus A is in the other spin state. The relative signs of $J_{AM}$ and $J_{MX}$ can be determined from the multiplets which collapse when a splitting corresponding to $J_{AX}$ is irradiated. Hence the signs of two of the coupling constants with respect to the third can in principle be obtained. As far as relative signs of coupling constants are concerned, this is all the information that is available from such a spin decoupling experiment. The determination of the relative signs of coupling constants in AMX systems has been illustrated by Freeman (122).

The exact method and procedure for determining relative signs of coupling constants from spin decoupling data is illustrated in this thesis for the molecule 2-bromo-5-chlorotoluene in the "Experimental Results" section. By decoupling the quartets in the ring proton region of the spectrum corresponding to the long-range coupling from the methyl protons to the ring protons and at the same time observing the collapse of the methyl proton multiplet, the relative signs of the long-range coupling constants with respect to the signs of the ring couplings are determined.

The nuclear magnetic double resonance spectra of three spin systems has been discussed by Rao and Baldeschwieler (126). A Hamiltonian is used that is made stationary by transformation to a rotating coordinate system and is diagonalized in the rotating frame. The

energies and relative intensities of the transitions of nucleus A in an AMX system are given for the case where nucleus X is being irradiated. The results of the relative sign determination discussed above are predicted by this analysis.

2. Spin Tickling (Strongly Coupled Systems)

In this case $2\pi J > \gamma H_2 \approx \frac{1}{T_2}$ of the irradiated line. This corresponds to a double resonance with a weak irradiating field. This is the condition for a tickling experiment in which a transition in the X region is irradiated and several transitions in the A region split into a number of components. The tickling experiment consequently may be carried out on a strongly coupled system and gives direct information about the ordering of the energy levels between which the irradiated and the observed transitions occur.

The principle of the tickling experiment is that if two nuclear magnetic resonance transitions have a common energy level, irradiation of one of these single transitions in a spectrum at $\omega_2$ will cause the second transition to split into a doublet. The practical value of this method is that the perturbation of the other lines in the spectrum may be kept small. The theoretical treatment of the effect of weak perturbing fields on strongly coupled systems has been carried out by Freeman and Anderson (125).

Three basic rules for the interpretation of observed double irradiation spectra in terms of the energy level diagram of the system were set down. The first rule shows how any transition which has an energy level in common with a nondegenerate transition excited by a

frequency $\omega_2$ will be split into a doublet. The second rule predicts that these doublets may be either well or poorly resolved depending on the arrangement of the energy levels. Lines corresponding to transitions having an energy level in common are called "connected" transitions which may further be divided into two categories:

a. The energy of the common level "c" is intermediate between those of the two terminal levels - transitions are in a progressive configuration, and

b. The energy of the common level "c" falls outside the interval demarcated by the two other levels - transitions are in a regressive configuration.


In a, the spin quantum numbers of the two connected energy levels r and s differ by two units and in b, the spin quantum numbers are the same. Rule 2 states that the doublet formed on tickling a transition in the progressive configuration will be poorly-resolved while in the regressive configuration it will be well-resolved. The third rule states that the magnitude of the splitting in the well-resolved doublet is proportional both to the strength of the perturbing frequency $\omega_2$ and to the square root of the intensity of the perturbed line.

Freeman and Anderson (125) applied the tickling experiment to various systems and have demonstrated the sensitivity of this method for an ABC system . It was possible to distinguish the optimum setting

of $\omega_2$ for one line as compared to the neighbouring line despite the fact that the two lines are unresolved in the normal spectrum. The two settings of $\omega_2$ differed by only 0.4 cps.

The effect of a weak perturbation on a three spin ABC system is easy to study. An unsymmetrical three-spin system has eight energy levels and twelve strong transitions. The energy level diagram may be represented by a cube where the corners represent the eight energy levels and the three sets of four parallel edges represent the quartets of the transition lines. When this representation is used, the effects to be observed upon double-irradiation can very easily be predicted as is shown in the "Experimental Results" section of this chapter. Tickling experiments, as well as spin decoupling experiments only determine relative signs of coupling constants. Absolute signs cannot be determined. Changing the signs of all the coupling constants merely inverts the energy level diagram as given by the cube model and the same experimental results will be obtained as in a tickling experiment with the reverse sign assignment.

## NATURE OF THE PROBLEM

Since long-range coupling constants between the methyl protons and ring protons in substituted toluenes had been only slightly investigated, the object of this research was to study them further, to compare them with existing theoretical calculations and to determine any substituent or solvent effects.

Applying tickling experiments, the signs of the meta and para ring proton coupling constants are determined with respect to the known positive sign of the ortho proton coupling constant. The signs of the long-range coupling constants from the methyl protons to the three ring protons are determined in 2-bromo-5-chlorotoluene with respect to the signs of the ring proton coupling constants using double resonance techniques. This molecule is also studied in several solvents to determine any solvent effects on the long-range couplings. Various other disubstituted toluenes, a trisubstituted toluene and a side-chain substituted toluene are studied to determine substituent effects on these couplings.

The signs and magnitudes of the long-range methyl proton-ring proton coupling constants are interpreted in terms of McConnell's theory (36, 56) of $\pi$-electron contributions to coupling constants. From the ring proton spectra with the methyl group decoupled the ring proton shifts and coupling constants are determined using an ABC analysis.

The long-range coupling constants agree with the theoretical calculations and are not substituent dependent nor solvent dependent. The magnitudes of the ortho ring proton coupling constants depend on the substituent electronegativities. The methyl proton shifts vary with the sum of Hammett substituent constants.

4.

# EXPERIMENTAL METHODS

## A. COMPOUNDS

The substituted toluenes were obtained from K & K Laboratories, Inc., Crown Zellerbach Chemical Products Division, Columbia Organic Chemicals Co., Inc., Matheson Coleman and Bell, Pfister Chemical Works Inc., Aldrich Chemical Co., Inc., and Eastman Organic Chemicals. Only 2-hydroxy-3-5-dinitrotoluene was recrystallized twice from benzene before being studied. The other substituted toluenes and toluene were studied without further purification. The solvents acetone, benzene and carbon disulfide were spectroquality grade from Matheson Coleman & Bell, dimethylsulfoxide-$d_6$ was obtained from Stohler Isotope Chemicals and benzene-$d_6$ was obtained from Merck, Sharp & Dohme Co. These were all used without further purification. All compounds were studied with about 2 mole % tetramethylsilane (TMS) as internal reference. For most of the measurements $CS_2$ was chosen as the solvent rather than $CCl_4$ since it has a lower viscosity and therefore permits inherently better resolution (138) which was required to observe all the splittings of the methyl group.

## B. PROTON MAGNETIC RESONANCE MEASUREMENTS

All p.m.r. spectra were measured on a Varian DA-60-I spectrometer locked to internal TMS. Calibrations were carried out by reading frequency differences in the frequency sweep mode and subsequent interpolation gave the peak positions with a precision of about 0.05 cps. The solutions were degassed by the freeze-thaw technique. The temperature of the samples was $28.5 \pm 1.0^{\circ}C$ as determined using an ethylene glycol sample and a calibration graph of internal shift versus temperature. This was prepared by Varian Associates, Palo Alto, California. All spectra were run at least four times without and then with the methyl group decoupled.

With two exceptions the toluenes were all disubstituted and belong to the $ABCX_3$ system (1). Since the methyl shift is at least 200 cps from the ring proton shift and the long-range coupling constants from the X (methyl) protons to the three ring protons are all smaller than 1 cps, the magnitudes of the long-range coupling constants were obtained from the ring proton spectra directly using first order rules. They are the average of twenty to thirty values and the errors are all standard deviations from the mean. As a check these values were always used to predict the splittings of the methyl protons. The separations of the methyl protons were also calibrated and standard deviations obtained. The predicted separations for the methyl protons as obtained from the ring proton spectra agreed very well with the observed values and were always well within the standard error limits.

The analysis of the ABC part of the $ABCX_3$ proton spectrum was considerably simplified by decoupling the methyl protons. This allowed an accurate determination of all the ring proton line positions. All decoupling and tickling experiments were performed in the usual manner (120, 121, 125, 127, 129). In the frequency sweep mode of operation the irradiating radiofrequency $\omega_2$ is set on the desired transition or transitions while the whole spectrum is simultaneously examined by sweeping the observing frequency $\omega_1$. For double and triple resonance experiments two Hewlett-Packard 200 CD audio oscillators were used to which sets of reduction gears were attached. The power of the decoupling frequency for the methyl group was kept as low as possible consistent with complete decoupling. The centers of the quartets corresponding to the long-range splittings by the methyl group were always compared with the single line position obtained when the methyl group was decoupled and there was never more than a change of about 0.1 cps on decoupling. Since the methyl and ring proton shift difference is so large, decoupling the methyl protons thus causes only a very small perturbation of the ring proton spectrum. For this reason the Bloch-Siegert shift (139) is small. Therefore the ABC analysis was carried out on the ring proton spectra with the methyl group decoupled.

The analysis of the 3-spin ABC system was carried out following the method of Castellano and Waugh (140) and Cavanaugh (141). The program in Fortran-II for this analysis was obtained from J.R. Cavanaugh (141). It was modified to Fortran-IV by Dr. H.M. Hutton and all the computations were carried out on the IBM-360 Disc Operating System at

the University of Manitoba. The required input data were the centers of the three quartets with respect to the center of the ring proton spectrum, the three common spacings, the position of the lowest field line and the relative line intensities normalized to twelve. The line positions to low field of center by convention were always negative with those to high field being positive. Many solutions for each ABC analysis were always obtained. However, there was no problem in choosing the correct one since only one solution gave positive signs for all three ring proton coupling constants. That both the meta and para ring proton coupling constants are positive if the ortho coupling is positive is demonstrated in this study using tickling techniques.

The assignment of the three quartets associated with the three ring protons was straightforward. In all the disubstituted toluenes that were studied all three ring proton coupling constants, i.e. ortho, meta and para, were always present. For example, any one molecule never had two ortho coupling constants. In such a situation a proton assignment may be much more difficult. Since the magnitudes of the three coupling constants decrease in the order ortho $>$ meta $>$ para, the assignment was not difficult.

The ring proton and methyl proton shifts as well as all the coupling constants are summarized in the next section. The sum of the squared deviations between the calculated and observed intensities are given for the ABC ring proton spectra. These were also calculated by the computer program. The error in the proton shifts is estimated at .005 ppm. This is probably an overestimate but takes account of the

small Bloch-Siegert shift, small variations in temperature and the fact that all spectra were run from low to high field.

There were two exceptions to the $ABCX_3$ system, namely $\alpha$,3,4-trichlorotoluene ($ABCX_2$) and 2-hydroxy-3-5-dinitrotoluene ($ABRX_3$). The analysis of these systems will be discussed in the next section.

# EXPERIMENTAL RESULTS

The substituted toluenes under consideration are divided into four series and these will be considered separately.

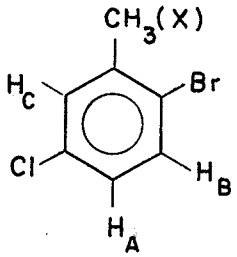
## Series I

In this study several 2,5-disubstituted toluenes were considered in the study of the long range coupling between the methyl protons and the ring protons. The coupling constants are given in Table 2-IA and the chemical shifts in Table 2-IB. The effect of different solvents and concentrations on the long-range coupling constants was studied but none was observed. The change in long-range coupling constants as a function of the substituent in the 2-position was studied while the 5-position substituent (chlorine) remained unchanged. Only the magnitude of $J^{o}_{H,CH_3}$ changes very slightly when the bromine atom is replaced by the amino group (a strong electron donor). This change is within the experimental errors obtained for this coupling constant in these two compounds. The compound 2-nitro-5-chlorotoluene (a strong electron withdrawer is in the 2-position) could not be obtained. However, in the next series, various other nitro-substituted toluenes are studied. Replacement of both the 2- and 5- substituents was studied in the compound 2-thiomethyl-5-hydroxytoluene and again a change in the magnitudes of the long-range coupling constants was not observed.

The signs of the ring-methyl and ring-proton coupling constants were determined using the 10 mole % solution of 2-bromo-5-chlorotoluene in $CS_2$. These will now be discussed in more detail. Several spectra for this solution are also shown and are typical of the many compounds studied.

TABLE 2-IA Series I

Coupling constants of 2,5-disubstituted toluenes in cps.

| Compound | Concentration (mole %) | Solvent | Long-Range Coupling Constants | | | | Ring Proton Coupling Constants[1] | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | $J_{CX}; J^{o}_{H,CH_3}$ | $J_{BX}; J^{m}_{H,CH_3}$ | $J_{AX}; J^{p}_{H,CH_3}$ | $J_{H_B,SCH_3}$ | $J_{AB}; J^{o}_{H,H}$ | $J_{AC}; J^{m}_{H,H}$ | $J_{BC}; J^{p}_{H,H}$ |
|  | 10% | $C_6H_6$ | -0.68±0.03 | +0.35±0.03 | -0.58±0.02 | ——— | +8.53±0.03[2] | +2.60±0.03 | +0.29±0.03 |
| 2-bromo-5-chlorotoluene | 10% | $CS_2$ | -0.67±0.04 | +0.36±0.03 | -0.58±0.03 | ——— | +8.45 | +2.56 | +0.31 |
| 2-bromo-5-chlorotoluene | 10% | $CH_3COCH_3$ | -0.68±0.04 | +0.34±0.03 | -0.59±0.02 | ——— | +8.51 | +2.64 | +0.29 |
| 2-amino-5-chlorotoluene | 5% | $CS_2$ | -0.75±0.03 | +0.32±0.03 | -0.56±0.03 | ——— | +8.39 | +2.47 | +0.32 |
| 2-thiomethyl-5-hydroxytoluene | 5% | $CS_2$ | -0.69±0.03 | +0.34±0.05[3] | -0.57±0.03 | $\sim\|0.15\|$[4] | +8.44 | +2.82 | +0.35 |

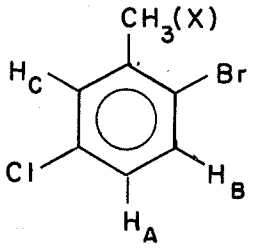
Footnotes to Table 2-IA

1. Determined by an ABC analysis of the spectrum with the methyl group decoupled.
2. The errors are standard deviations. The ABC analysis was carried out on the IBM-360 computer. Maximum and minimum values of the measured common spacings as well as the average values were used as input data in determining the chemical shifts and coupling constants. It was found that the magnitude of the coupling constant increased or decreased by the same amount as the change in the magnitude of the common spacings used as input data. Hence, the standard deviations for the ring proton coupling constants obtained from an ABC analysis are equivalent to the standard deviations obtained experimentally for the common spacings.
3. Determined when the thio-methyl group was decoupled.
4. The coupling between the thio-methyl protons and ring proton $H_B$ is very small and could not be determined exactly. The sign of this coupling with respect to the ring proton coupling constant was not determined. The thio-methyl protons were found to couple only to ring proton $H_B$.

TABLE 2-IB Series I

Chemical shifts of 2,5-disubstituted toluenes in ppm

to low field of internal TMS at 28.5±1°C.

| Compound | Concentration (mole %) | Solvent | $CH_3(X)$ | Ring Proton Shifts (1) $H_A$ | $H_B$ | $H_C$ | Ring Proton Intensity Deviations (2) | $NH_2$ | $S-CH_3$ | OH |
|---|---|---|---|---|---|---|---|---|---|---|
|  | 10% | $C_6H_6$ | 1.951±0.005 | 6.628±0.005 | 7.021±0.005 | 6.795±0.005 | ——— (3) | ——— | ——— | ——— |
| 2-bromo-5-chlorotoluene | 10% | $CS_2$ | 2.313 | 6.920 | 7.317 | 7.097 | 0.0603 | ——— | ——— | ——— |
| 2-bromo-5-chlorotoluene | 10% | $CH_3COCH_3$ | 2.345 | 7.105 | 7.497 | 7.305 | 0.2604 | ——— | ——— | ——— |
| 2-amino-5-chlorotoluene | 5% | $CS_2$ | 2.025 | 6.801 | 6.361 | 6.828 | 0.5500 | 3.404 ±0.005 | ——— | ——— |
| 2-thiomethyl-5-hydroxytoluene | 5% | $CS_2$ | 2.215 | 6.486 | 6.950 | 6.495 | 0.2461 | ——— | 2.277 ±0.005 | 5.702 ±0.005 |

Footnotes to Table 2-IB

1. The ring proton shifts were determined by an ABC analysis of the spectrum with the methyl group decoupled. Only a very small shift of approximately 0.1 cps was observed for the ring proton peak positions on decoupling the methyl group in comparison with the centers of the multiplets of the non-decoupled spectra. This small shift is within the quoted experimental error limits.
2. The sum of the squared deviations in intensities between observed and calculated ABC-ring proton spectra.
3. The sum of the squared deviations in intensities could not be determined since the low field doublet of proton $H_B$ was obscured by the solvent.

Figure 2-1 gives the ring proton spectrum of 2-bromo-5-chlorotoluene using the frequency sweep mode. It is a loosely coupled ABC part of an $ABCX_3$ spectrum. The resonances of the three protons are sufficiently well separated to be assigned by inspection. The fine splittings of all the lines are due to the coupling between the ring protons and the methyl protons. This was confirmed by carrying out a spin-decoupling experiment in which the irradiating frequency was centered on the methyl resonance while the ring proton spectrum was observed. The resulting ABC ring proton spectrum is shown in Figure 2-2b. The calculated spectrum following ABC analysis is shown in Figure 2-2c. In Figure 2-2a, the A,B, and C quartets are labelled and the spin states of the two neighbouring protons during each transition are indicated, assuming all ring couplings positive. All the shifts and coupling constants for this compound as well as the others in Series I are given in Tables 2-IA and 2-IB. Similar spectra were obtained in all cases.

The transitions shown in Figure 2-2b were assigned to the three ring protons in the following manner. The para coupling is the smallest and is under one cps. A splitting of this magnitude is observed between transitions B1 - B2, B3 - B4, C1 - C2, and C3 - C4. An ortho coupling is the largest and approximately 8 cps. A splitting of this magnitude is observed between transitions B1 - B3, B2 - B4, A1 - A3, and A2 - A4. Hence transitions B1 to B4 are assigned to proton $H_B$ which has protons ortho and para to it. The other transitions were assigned to the two remaining protons in the same manner utilizing the experimental observation that meta ring proton coupling constants have magnitudes of approximately 2 cps.

Figure 2-1

Ring proton specturm of a 10 mole % solution of 2-bromo-5-chlorotoluene in $CS_2$ recorded by sweeping the frequency $\omega_1$.

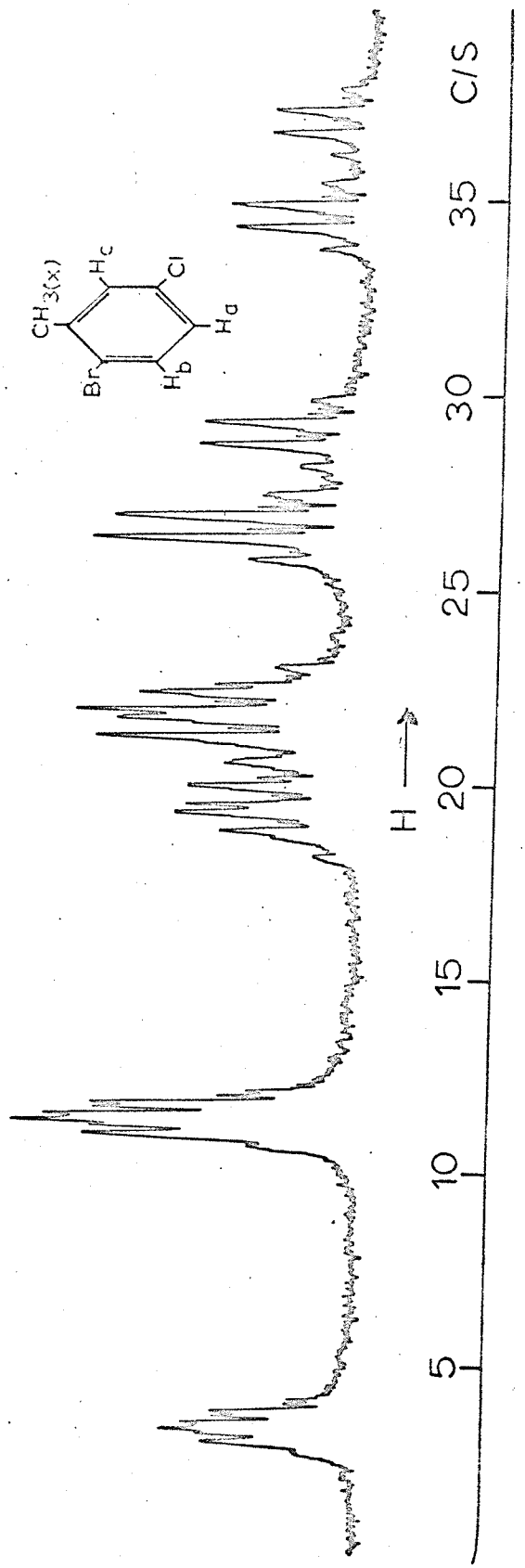

CH3(x)
Hc
Cl
Ha
Br
Hb
H ⟶
5
10
15
20
25
30
35
C/S

Figure 2-2

The ABC (ring proton) part of the spectrum of 2-bromo-5-chlorotoluene in $CS_2$ with the methyl group decoupled (b). In (a), the A, B, and C quartets and their respective transitions are labelled and the spin states of the two neighbouring protons during each transition are indicated. The three ring proton couplings are all positive. The calculated spectrum is shown in (c).

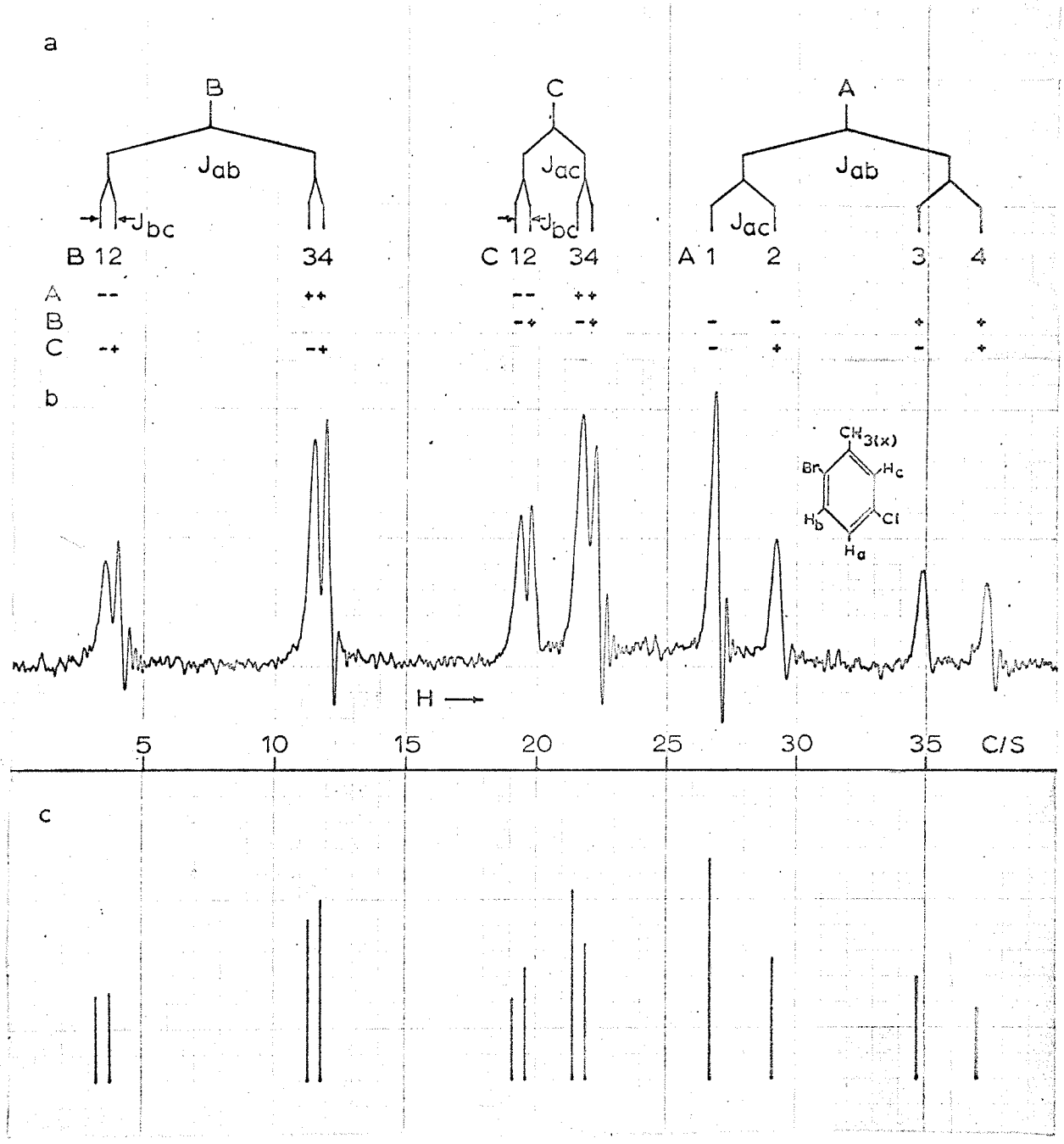

a
B
Jab
Jbc
C
Jac
Jbc
A
Jab
Jac
B 12 34
C 12 34
A 1 2 3 4
A
B
C
b
CH3(x)
Br
Hc
Hb
Cl
Ha
H
5 10 15 20 25 30 35 C/S
c

Figure 2-3

Spectrum obtained by tickling transition B1 of the ring proton spectrum while the methyl group is decoupled, a triple resonance. The spectrum is observed by sweeping the frequency $\omega_1$, the methyl group is decoupled with a second oscillator at its resonant frequency $\omega_2$, while the spin tickling is carried out by a third frequency irradiating transition B1 at its resonant frequency $\omega_3$. B2 is obscured by tickling B1, but there is no doubt that B1 is the tickled transition.

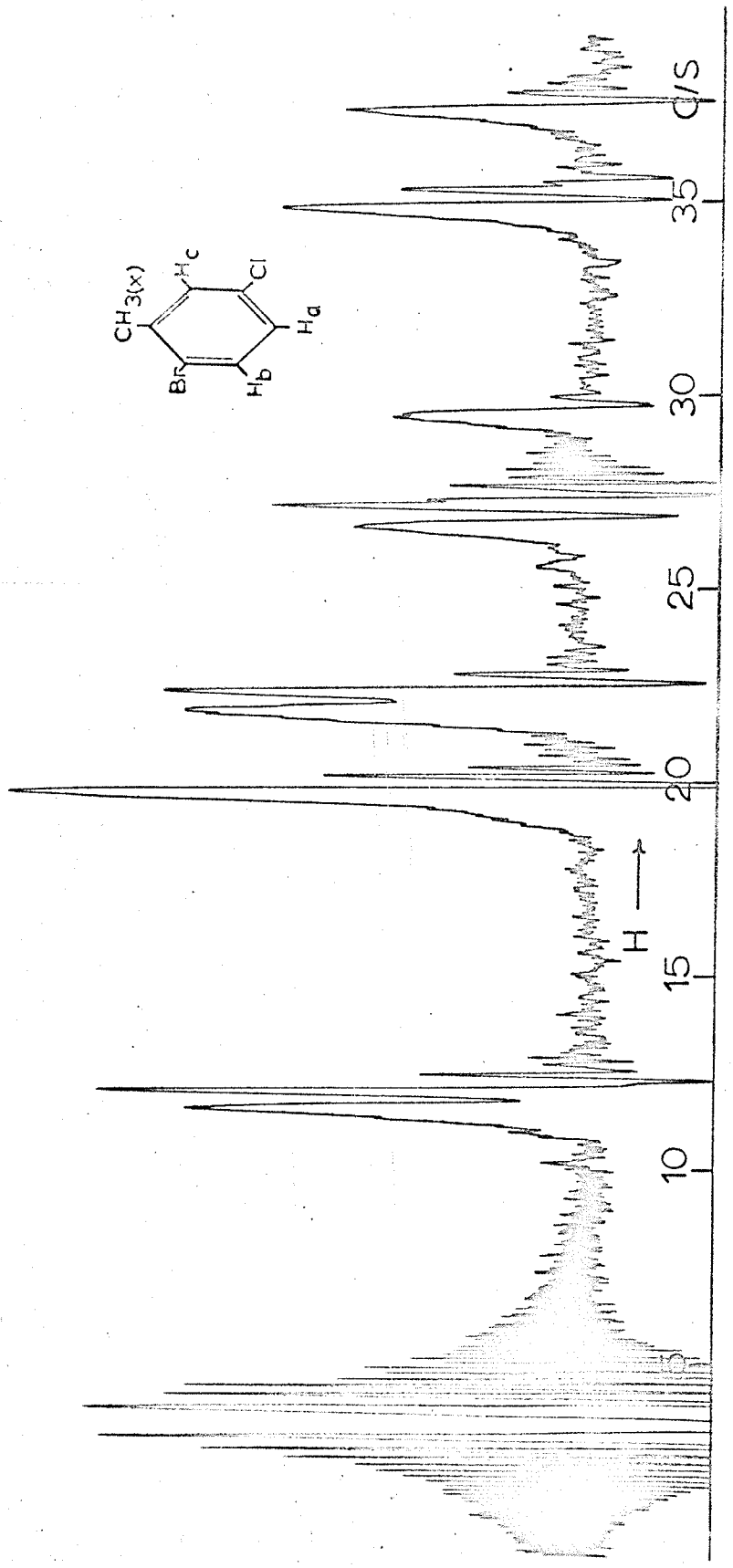

CH3(x)
Hc
Cl
Ha
Br
Hb
C/S
35
30
25
20
H
15
10
5

Figure 2-3 gives the spectrum obtained by tickling transition B1 of the ring proton spectrum while the methyl group is decoupled (triple resonance experiment). The observed spectrum shows that the ring proton coupling constants are all of the same sign. Similar tickling experiments on other transitions served to confirm this result. Hence all the ring proton coupling constants must be positive since the ortho coupling constant is positive.

Freeman and Anderson (125) describe the arguments needed to find the relative signs of the coupling constants using tickling experiments. Their approach will now be applied to our system. Only one experiment will be described, namely the tickling of transition B1. All the experiments that were carried out were analyzed in this manner.

The tickling experiment was carried out by observing the ring proton spectrum with frequency $\omega_1$. At the same time the methyl group was decoupled with a second oscillator at its resonant frequency $\omega_2$ and the spin tickling was carried out by a third frequency irradiating transition B1 at its resonant frequency $\omega_3$.

Freeman and Anderson show that the experimental spectrum obtained from only one tickling experiment will correspond to only one of the four possible arrangements of the relative signs of the meta and para coupling constants with respect to the ortho coupling. Assuming that all three coupling constants are of the same sign, the labelling of the transitions is shown in Figure 2-2a. The energy level diagram of the ABC system assuming all three coupling constants are positive is given in Figure 2-4. From the energy level diagram of the system it is

seen that tickling transition B1 should split transitions C1 and A1 into sharp doublets (regressive configuration of the common energy levels) while C2 and A3 should also be split but not as much (progressive configuration of the energy levels) nor as well as C1 and A1. Relative to the splitting observed for C1 and A1, C2 and A3 should be broadened doublets. From the observed spectrum shown in Figure 2-3 it is seen that transitions A1 and A3 are indeed split. However, only a single peak is obtained for transitions C1 and C2 instead of the expected four. This may be explained by the fact that the separation between C1 and C2 is only 0.5 cps and the four lines cannot be resolved. They all overlap and only a singlet is observed on tickling B1. These results together with several other tickling experiments show that all three ring proton coupling constants are of the same sign.

Figure 2-5a shows the single resonance spectrum of the methyl group of 2-bromo-5-chlorotoluene. The lines are numbered from low to high field. Because of the magnitudes of the ring-methyl couplings there is overlapping of two transitions in two cases, resulting in six instead of eight observed transitions.

The relative signs of the long-range coupling constants between the methyl protons and the ring protons with respect to the known signs of the ring proton coupling constants were determined by spin decoupling. These experiments were carried out by irradiating various quartets arising from the long-range coupling constants in the ABC region with a frequency $\omega_2$ while simultaneously observing the methyl proton resonance with frequency $\omega_1$. The first decoupling experiment was carried out by irradiating

Figure 2-4

The energy level diagram appropriate to 2-bromo-5-chlorotoluene assuming that all three spin coupling constants are positive and $|J_{AB}| > |J_{AC}| > |J_{BC}|$. It is calculated for the case in which the methyl group is decoupled from the rest of the system and the ring protons may be treated as an ABC system. The corners of the cube represent the eight energy levels and the three sets of four parallel edges represent the quartets of the transition lines.

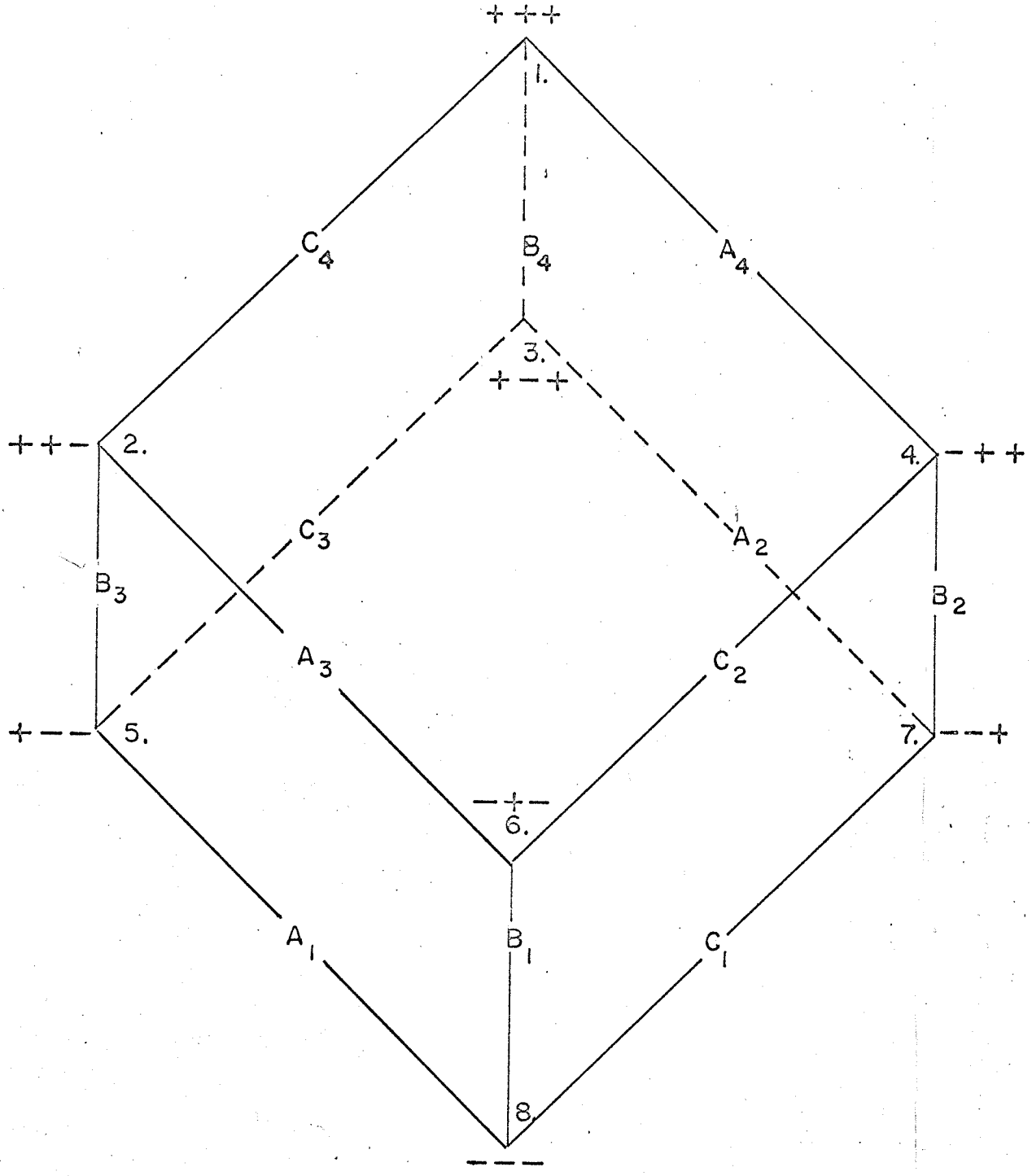
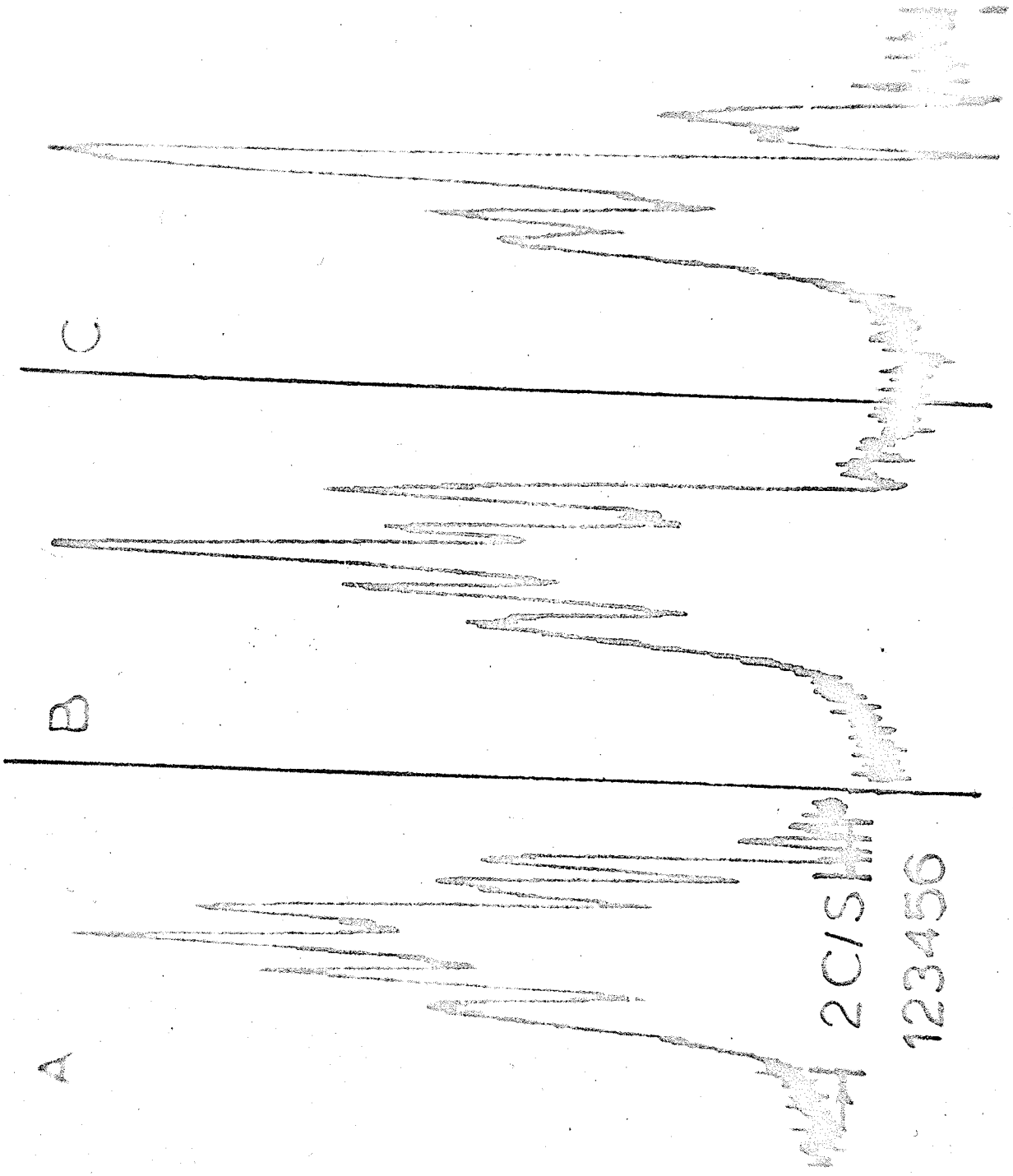

+++
1.
C4
B4
A4
3.
+−+
++−
2.
4.
−++
C3
A2
B3
B2
A3
C2
+−−
5.
7.
−−+
−+−
6.
A1
B1
C1
8.
−−−

Figure 2-5

The methyl group proton spectrum observed by sweeping the frequency $\omega_1$. The lines are numbered from low to high field. (A) Unperturbed spectrum. (B) The methyl group proton spectrum observed when the decoupling frequency $\omega_2$ irradiates the quartet centered on transition B1 which arises from the long-range coupling between the methyl protons and ring proton $H_B$. Transitions 5 and 6 collapse into a singlet. (C) Spectrum observed with the quartet centered on transition A1 decoupled. Transitions 3 and 5 collapse and overlap transition 4.


A
B
C
2 C/SHIFT
123456

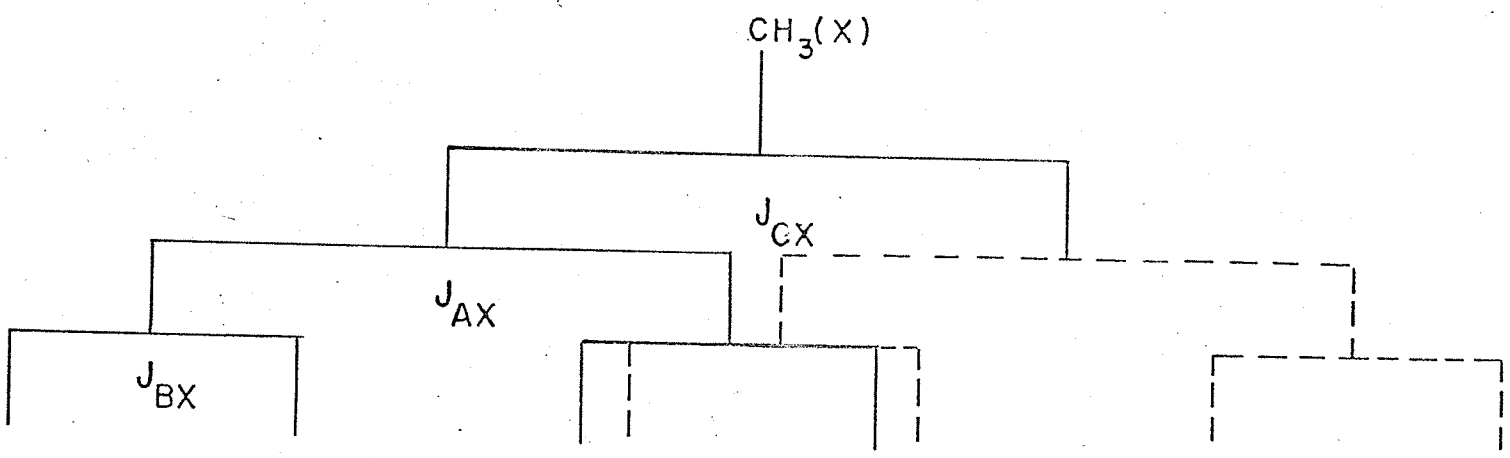
the quartet centered on B1 (Figures 2-1 and 2-2a) arising from the long-range coupling between the methyl protons (X) and proton $H_B$. In Figure 2-1 it is seen that this quartet is not completely observed since it partially overlaps the quartet centered on transition B2. By irradiating the quartet centered on B1, from Figure 2-2a it is seen that the coupling $J_{BX}$ with negative spin states of protons $H_A$ and $H_C$ is erased. In Figure 2-6 the only transitions that have negative spin states of both protons $H_A$ and $H_C$ are 5 and 6 assuming that $J_{CX}$ and $J_{AX}$ are both negative while $J_{BX}$ is positive. The observed spectrum is shown in Figure 2-5b and since transitions 5 and 6 of the methyl resonance collapse to a singlet, this confirms that $J_{CX}$ ($J^{o}_{H,CH_3}$) and $J_{AX}$ ($J^{p}_{H,CH_3}$) are of opposite sign to the ring proton couplings, i.e. negative.

In Figure 2-5c a similar decoupling experiment was performed by decoupling the quartet centered on transition A1. This corresponds to decoupling $J_{AX}$ with negative spin states of protons $H_B$ and $H_C$. From Figure 2-6, this occurs only for transitions 3 and 5 which collapse and overlap transition 4 in the methyl resonance. This will only occur if $J_{CX}$ ($J^{o}_{H,CH_3}$) is of opposite sign, and $J_{BX}$ ($J^{m}_{H,CH_3}$) is of the same sign as the ring proton couplings. Various other confirming experiments were also carried out.

In summary, if $J_{H,H}{}^{o}$ is positive, the other two ring couplings are positive. The couplings between the methyl and the ortho and para ring protons are negative, while the coupling with the meta proton is positive. The signs of these coupling constants will be the same for the various substituted toluenes since it is seen that various ring substituents have almost no effect on the long-range coupling constants.

Figure 2-6

The assignment of the transitions obtained for the methyl proton resonance of 2-bromo-5-chlorotoluene corresponding to the long-range ring proton - methyl proton coupling constants. The spin states of the three ring protons during each transition are indicated and labelled assuming that $J_{CX}$ ($J^{o}_{H,CH_3}$) and $J_{AX}$ ($J^{p}_{H,CH_3}$) are both negative and $J_{BX}$ ($J^{m}_{H,CH_3}$) is positive. The sign convention followed is the same as in Figures 2-2a and 2-4. The diagram corresponds to the experimental spectrum given in Figure 2-5a.




| TRANSITION : | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| RING PROTON | | | | | | |
| A | + | + | − + | − + | − | − |
| B | − | + | − − | + + | − | + |
| C | + | + | + − | + − | − | − |

## Series 2

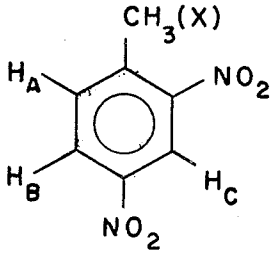
In this series 2,4-disubstituted toluenes were studied. The long-range and ring proton coupling constants are given in Table 2-IIA and the proton chemical shifts are listed in Table 2-IIB.

A study was carried out to see how long-range coupling constants from the methyl protons to ortho and meta ring protons vary with a change in the 2-substituent (ortho to methyl group) while the 4-substituent is the same ($NO_2$ group). The results of this study are illustrated by the first four compounds listed in Table 2-IIA. Only one small trend could be observed, namely that $J_{CX}$ increases as the 2-substituent is respectively iodine, bromine and chlorine. This variation is very small and only slightly outside the error limits of the coupling constants.

A comparison may also be made between the ring-methyl coupling constants observed for the last two compounds in Table 2-IIA. In these compounds, the 2-position substituent is the same (chlorine) while the 4-position has in turn a strong electron withdrawer ($NO_2$ group) and a strong electron donor ($NH_2$ group). The results indicate that the long-range methyl-ortho ring proton and methyl-meta ring proton coupling constants are not affected by the change in the 4-substituent (para to methyl group). In fact, the long-range coupling constants shown in Table 2-IIA are equal within experimental error to the respective values of the coupling constants in Table 2-IA (Series 1). Hence in all the compounds studied in these two series, the various substituents have essentially no effect on the long-range coupling constants.

TABLE 2-IIA Series 2

Coupling constants of 2,4-disubstituted toluenes (cps).

| Compound | Concentration (mole %) | Solvent | Long-Range Coupling Constants | | | Ring Proton Coupling Constants (1) | | |
|---|---|---|---|---|---|---|---|---|
| | | | $J_{AX}; J^{o}_{H,CH_3}$ | $J_{BX}; J^{m}_{H,CH_3}$ | $J_{CX}; J^{m}_{H,CH_3}$ | $J_{AB}$ | $J_{AC}$ | $J_{BC}$ |
|  | Sat'd <5% | $CS_2$ | -0.73±0.03 (2) | +0.33±0.02 | +0.38±0.05 (3) | +8.42±0.03 | +0.39±0.03 | +2.39±0.03 |
| 2-iodo-4-nitrotoluene | Sat'd <5% | $CS_2$ | -0.66±0.03 | +0.36±0.03 | +0.34±0.02 | +8.36 | +0.31 | +2.34 |
| 2-bromo-4-nitrotoluene | 5% | $CS_2$ | -0.70±0.03 | +0.38±0.03 | +0.39±0.03 | +8.38 | +0.33 | +2.36 |
| 2-chloro-4-nitrotoluene | 5% | $CS_2$ | -0.70±0.04 | +0.36±0.03 | +0.42±0.03 | +8.39 | +0.32 | +2.35 |
| 2-chloro-4-aminotoluene | 5% | $CS_2$ | -0.69±0.03 | +0.33±0.02 | +0.37±0.03 | +8.08 | +0.32 | +2.43 |

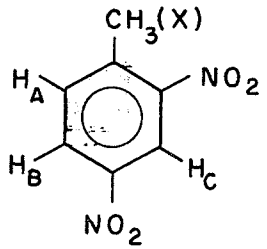
Footnotes to Table 2-IIA Series 2.

1. Obtained from an ABC analysis of the ring proton spectrum with the methyl group decoupled.
2. All the errors in the coupling constants are standard deviations.
3. The peaks corresponding to proton $H_c$ are broadened by the two neighbouring nitro groups. For this reason $J_{CX}$ ($J^{m}_{H,CH_3}$) could not be obtained from the ring proton splittings but was obtained only from the splittings of the methyl group.

TABLE 2-IIB Series 2

Chemical shifts of 2,4-disubstituted toluenes in ppm

to low field of internal TMS at 28.5±1°C.

| Compound | Concentration (mole %) | Solvent | $CH_3(X)$ | Ring Proton Shifts(1) $H_A$ | $H_B$ | $H_C$ | $NH_2$ | Ring Proton Intensity Deviations(2) |
|---|---|---|---|---|---|---|---|---|
|  | < 5% Sat'd | $CS_2$ | 2.724±0.005 | 7.562±0.005 | 8.280±0.005 | 8.669±0.005 | ——— | (3) |
| 2-iodo-4-nitrotoluene | Sat'd < 5% | $CS_2$ | 2.524 | 7.339 | 8.013 | 8.531 | ——— | 0.1357 |
| 2-bromo-4-nitrotoluene | 5% | $CS_2$ | 2.497 | 7.357 | 7.967 | 8.258 | ——— | 0.1506 |
| 2-chloro-4-nitrotoluene | 5% | $CS_2$ | 2.475 | 7.360 | 7.921 | 8.070 | ——— | 0.0574 |
| 2-chloro-4-aminotoluene | 5% | $CS_2$ | 2.164 | 6.811 | 6.278 | 6.454 | 3.406±0.005 | 0.1511 |

Footnotes to Table 2-IIB.

1. The ring proton shifts were determined by an ABC analysis of the spectrum with the methyl group decoupled.
2. The sum of the squared deviations in intensities between observed and calculated ABC-ring proton spectra.
3. The ring proton intensity deviations could not be determined. The quartet corresponding to proton $H_c$ was broadened so that only two broad peaks were observed.

## Series 3

In this series only one compound, 2-hydroxy-3,5-dinitrotoluene was studied. It was recrystallized twice from benzene and then studied in $C_6D_6$ and DMSO-$d_6$.

The proton magnetic resonance spectrum of this compound in $C_6D_6$ is completely first order and hence belongs to the $AMRX_3$ system. However, the OH(R) proton couples only to ring proton $H_A$. The long-range coupling constants $J_{AX}$ and $J_{BX}$ were obtained by simple spacing rules after the OH proton was decoupled to simplify the spectrum of proton $H_A$. The coupling constant $J_{AB}$ was determined by first order rules and coupling $J_{H,OH}(J_{AR})$ was obtained from the spacings of the OH proton doublet. Using the magnitudes of $J_{AX}$ and $J_{BX}$ obtained from the ring proton spectra, the splittings observed for the methyl group were exactly reproduced. The chemical shifts were also very easily determined by simple first order rules. All of these results are tabulated in Table 2-III.

One interesting point must be mentioned about this study and that is the very low-field shift of the OH proton resonance in $C_6D_6$. This is due to an intramolecular hydrogen bond of the phenolic OH proton with the neighbouring oxygen of the nitro group. This will be considered further together with the stereospecific long-range $J_{AR}$ coupling in the "Discussion".

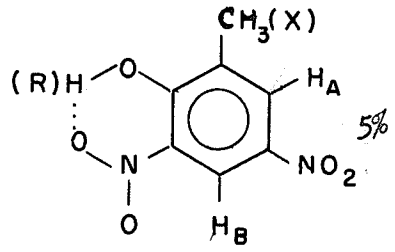
The shifts and coupling constants for this compound studied in DMSO-$d_6$ solution are also given in Table 2-III. Several changes in these spectra are observed. First of all, the OH proton resonance shifts

to high field and no longer couples with any of the ring protons. This is evidence for a broken intramolecular hydrogen bond and will be discussed later. The other protons belong to the $ABX_3$ system since the ring proton spectrum is no longer completely first order. Since the methyl resonance is at least 300 cps removed from the ring proton resonance and the long-range coupling constants are under 1 cps, the long-range couplings $J_{AX}$ and $J_{BX}$ were obtained from the ring proton spectrum by simple spacing rules. The simple AB analysis was carried out on the ring proton spectrum assuming the centres of the four quartets arising from the long-range couplings correspond to the four AB transitions. The methyl proton shift position was taken at the centre of the observed quartet.

TABLE 2-III Series 3

Chemical shifts in ppm to low field of internal TMS and coupling constants (cps)

of 2-hydroxy-3,5-dinitrotoluene at 28.5± 1°C.

| Compound | Concentration (mole %) | Solvent | Coupling Constants | | | | Chemical Shifts | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | $J_{AX};J^{o}_{H,CH_3}$ | $J_{BX};J^{p}_{H,CH_3}$ | $J_{AB};J^{m}_{H,H}$ | $J_{AR};J_{H,OH}$ | $H_A$ | $H_B$ | $CH_3(X)$ | OH(R |
|  | 5% | $C_6D_6$ | -0.87(1) ± 0.02 | -0.61(2) ± 0.03 | +2.78± 0.03 | +0.62(3) ± 0.03 | 7.601 ±0.005 | 8.342 ±0.005 | 1.765(2) ±0.005 | 10.865 ±0.005 |
| 2-hydroxy-3,5-dinitrotoluene | 5% | (4) DMSO-$d_6$ | -0.85± 0.02 | -0.58± 0.02 | +2.89± 0.03 | ——— | 8.340 ±0.005 | 8.558 ±0.005 | 2.344 ±0.005 | 5.921 ±0.005 |

1. The magnitude of this long-range coupling constant was determined while OH proton was decoupled.
2. Decoupling the OH proton has no effect on the spectrum of proton $H_B$ nor on the methyl proton spectrum.
3. The magnitude of this coupling constant was determined from the splitting of the OH proton resonance. The sign is positive as determined by Forsen and Hoffman (142).
4. Dimethylsulfoxide.

## Series 4

The effect of replacing a methyl proton by a chlorine atom on the long-range coupling constants between the $CH_2$ protons and the ring protons was studied in this series. The molecule chosen was 3,4-dichlorobenzylchloride. The spectrum that was obtained was of the $ABCX_2$ type. The long-range coupling constants to the ortho and meta ring protons $J_{AX}$, $J_{BX}$ and $J_{CX}$ were obtained from the ring proton spectrum by simple spacing rules. The magnitudes of these couplings were used to predict the splittings for the $CH_2Cl$ group protons and the agreement was excellent and certainly within the observed experimental errors. The ring proton spectrum was analyzed with the $CH_2$ protons decoupled at their resonant frequency. The ABC analysis was carried out as in series 1 and 2. The errors are all standard deviations from the mean. The results are tabulated in Table 2-IV.

The compound $\alpha$, $\alpha$, 2,6-tetrachlorotoluene was also studied as a 5 mole % solution in $CS_2$ (degassed with internal TMS as reference). Since the commercially obtained sample was impure, it was vacuum distilled before being studied. However, only a very broad peak was obtained for the ring protons and a decoupling experiment on the $CHCl_2$ proton could not be carried out since the shift difference between the $CHCl_2$ multiplet and the ring proton peak is only about 8 cps. As well, the separate peaks of the $CHCl_2$ proton multiplet could hardly be resolved. No further studies were carried out on this compound.

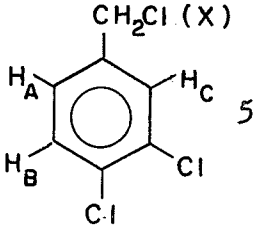
In order that a comparison of the methyl proton shifts in 3,4-dichlorobenzylchloride could be made with the methyl proton shift in

toluene and also the methyl proton shifts in the ring substituted toluenes, a 5 mole % solution of toluene in $CS_2$ was studied. This solution was degassed with internal TMS as reference. The methyl proton shift is 2.284 ± 0.005 ppm to low field of TMS. The methyl resonance consists of many overlapping lines none of which could be properly resolved.

From Table 2-IV it is seen that the long-range coupling constants $J^{o}_{H,CH_2Cl}$ and $J^{m}_{H,CH_2Cl}$ decrease by about 0.2 cps when compared with corresponding long-range coupling constants in toluenes without a non-proton substituent on the methyl carbon as studied in series 1-3. The signs of the long-range coupling constants are the same as were observed before. Since the signs of the long-range couplings depend on the sign of $Q_{CCH_3}$, which is positive, replacing a proton by a chlorine atom will have no effect on the sign of the corresponding $Q$ value since even in the system $C_2 - C_1 - F_3$, $Q_{CCF_3}$ is positive (107).

TABLE 2-IV Series 4

Chemical shifts in ppm to low field of internal TMS and coupling constants (cps) of 3,4-dichlorobenzylchloride in $CS_2$ at 28.5± 1°C.

| Compound | Concentration (mole %) | Solvent | Long-Range Coupling Constants | | | Ring Proton Coupling Constants (1) | | |
|---|---|---|---|---|---|---|---|---|
| | | | $J_{AX}; J^{o}_{H,CH_2Cl}$ | $J_{BX}; J^{m}_{H,CH_2Cl}$ | $J_{CX}; J^{o}_{H,CH_2Cl}$ | $J_{AB}; J^{o}_{H,H}$ | $J_{AC}; J^{m}_{H,H}$ | $J_{BC}; J^{p}_{H,H}$ |
|   | 5 % | $CS_2$ | -0.45±0.04 | +0.20±0.02 | -0.53±0.02 | +8.26± 0.03 | +2.16± 0.03 | +0.31± 0.03 |

| Ring Proton Chemical Shifts (1) | | | Ring Proton Intensity Deviations (2) | $CH_2Cl(X)$ Proton Shift |
|---|---|---|---|---|
| $H_A$ | $H_B$ | $H_C$ | | |
| 7.143± 0.005 | 7.328± 0.005 | 7.382± 0.005 | 0.1037 | 4.437± 0.005 |

(1) Obtained from an ABC analysis of the spectrum with the $CH_2$ protons decoupled.

(2) The sum of the squared deviations in intensities between observed and calculated ABC-ring proton spectra.

# DISCUSSION OF RESULTS

## A. RING PROTON COUPLING CONSTANTS AND METHYL PROTON SHIFTS

Before discussing long-range coupling constants, the ring proton couplings will be analyzed first of all. By an exact analysis of the $^{13}C$-H satellite spectra, Read, Mayo and Goldstein (143) have carried out a precise determination of the proton coupling parameters in benzene. These were found to be $J^{o}_{H,H} = 7.54$, $J^{m}_{H,H} = 1.37$, and $J^{p}_{H,H} = 0.69$ cps. The effects of substituents on the proton-proton coupling constants of monosubstituted benzenes were studied by Castellano and Sun (144). They found that the vicinal coupling constants between the ortho and meta protons (with respect to the substituent; an ortho ring proton coupling constant) increases as the Pauling electronegativity of that atom of the substituents bonded to the benzene ring increases. This was predicted by Cohen and Schaefer (145). Castellano and Sun also found that of the remaining coupling constants only the ones connecting the ortho protons to the other protons in the ring clearly show definite trends with electronegativity. The most important indication of this effect was the increase (with an increase in electronegativity) of the meta ring proton coupling constant between the protons ortho to the substituent. Their experimental results indicate that as far as the magnitudes of the coupling constants are concerned, the perturbation introduced by the substituent attenuates rapidly with distance and is not appreciable beyond the ortho carbons as is expected for an inductive effect. As well, by direct interpolation of the experimental data, all three ring proton coupling constants for benzene were obtained in agreement with the values obtained by Read, Mayo and Goldstein.

Read and Goldstein (146) in their exact analysis of the proton magnetic resonance spectra of the monohalobenzenes found that the effect of the halogen substituents on the ring proton couplings is small. They also found it significant only in the case of an ortho ring proton coupling constant $J_{23}$ (when the substituent is in the one position) where one of the protons is next to the substituent, and the meta ring proton coupling $J_{2,6}$ where the substituent is located on the carbon atom between the two carbon atoms to which the coupling protons are bonded. These coupling constants together with the para couplings and the coupling constants found in benzene are given in Table 2-V. The electronegativities of the substituents are also given (147).

The coupling constants that were determined and are given in Tables 2-I to 2-IV are for molecules that are much more complex. The benzene ring has at least three substituents and consequently correlations between the coupling constants are harder to draw. It is found that in the compounds studied in series 1 and 2 (Tables 2-IA and 2-IIA) in $CS_2$, all the ortho ring proton coupling constants are of magnitude from $8.45 \pm 0.03$ to $8.36 \pm 0.03$ cps, nearly within experimental error limits. The one exception is 2-chloro-4-aminotoluene, with an ortho coupling constant of 8.08 cps.

Electronegativity is the probable explanation for this smaller coupling. In 2-chloro-4-nitrotoluene the ortho coupling is 8.39 cps. The two molecules are identical except that the amino group with an electronegativity of 2.91 (148) is replaced by the nitro group with an electronegativity of 3.70 (149). To show the electronegativity effect, the ortho ring proton coupling constants $J^{2,3}_{H,H}$ of the monosubstituted haloben-

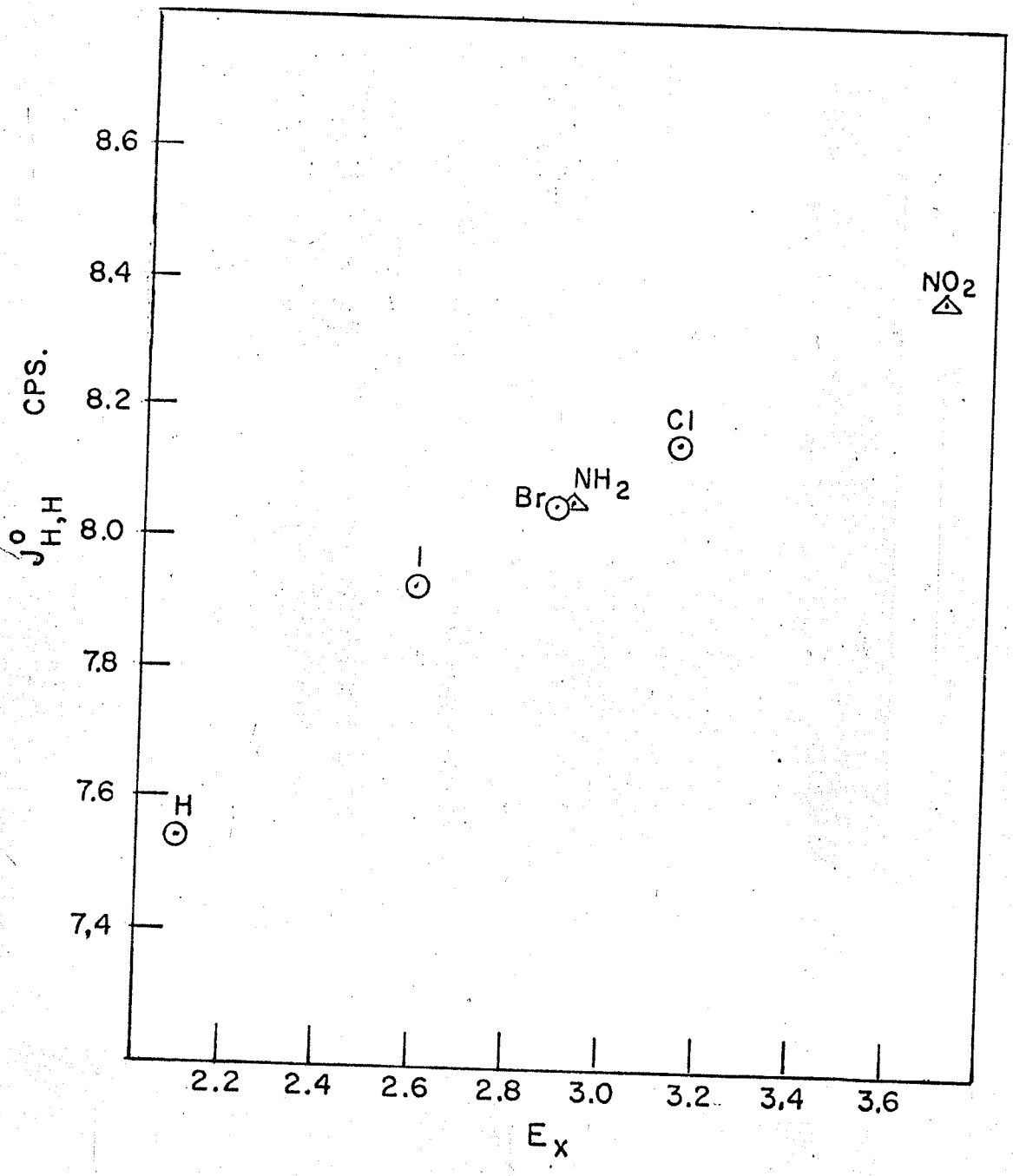
TABLE 2-V

Coupling constants for benzene and monosubstituted benzenes obtained by Read and Goldstein (146). The substituent is in the 1-position.

| Compound | Substituent | Substituent Electronegativity (147) | $J^{2,3}_{H,H}$ | $J^{2,6}_{H,H}$ | $J^{2,5}_{H,H}$ |
|---|---|---|---|---|---|
| benzene | H | 2.10 | 7.54cps | 1.37cps | 0.69cps |
| iodobenzene | I | 2.60 | 7.93 | 1.88 | 0.47 |
| bromobenzene | Br | 2.87 | 8.07 | 2.08 | 0.46 |
| chlorobenzene | Cl | 3.15 | 8.15 | 2.24 | 0.50 |

Figure 2-7

Plot of $J^{2,3}_{H,H}$ ($J^{o}_{H,H}$) given in Table 2-V as a function of the substituent electronegativity. The two points indicated by triangles correspond to the ortho coupling constants observed in the molecules 2-chloro-4-nitrotoluene and 2-chloro-4-aminotoluene.


8.6
8.4
8.2
8.0
7.8
7.6
7,4
CPS.
$J^{o}_{H,H}$
NO2
Cl
NH2
Br
I
H
2.2
2.4
2.6
2.8
3.0
3.2
3,4
3.6
$E_x$

zenes given in Table 2-V are plotted as a function of the substituent electronegativity as shown in Figure 2-7. As well, the ortho coupling constants for the above-mentioned two molecules are plotted in the figure and it is seen that they follow the same trend. This correlation is only approximate. It assumes that only the ortho substituent to one of the coupling hydrogens has the most important effect on the coupling (i.e. amino and nitro groups in the two molecules) and that the methyl group has nearly the same effect as a hydrogen atom.

No correlation is evident for the meta ring proton coupling constants given in Tables 2-I to 2-IV. The results in Table 2-V suggest a correlation with the electronegativity of the substituent on the carbon atom separating the carbon atoms bonded to the coupling protons. Such a relationship was not found in this study, possibly because the molecules are too varied and polysubstituted. For example, in 2-chloro-4-nitrotoluene, the meta coupling is 2.35 cps and the intermediate group is the nitro group. In 2,4-dinitrotoluene this same coupling is 2.39 cps and one of the coupling protons is surrounded by nitro groups. Yet in 2-hydroxy-3,5-dinitrotoluene this same coupling increases to 2.89 cps and is solvent dependent. Hence other effects are important, i.e.: solvents and intramolecular hydrogens bonds.

One minor trend was obtained, however. In series I, comparing molecules 2-amino-5-chlorotoluene and 2-thiomethyl-5-hydroxytoluene, the meta coupling constant increases from 2.47 to 2.82 cps as the intermediate substituent electronegativity increases from 3.15 (Cl) (147) to 3.43 (OH) (148). This is the only example of this trend in the measured meta coupling constants.

Considering now the para ring proton coupling constants, from Table 2-V it is seen that this coupling changes from benzene (0.69 cps) to 0.50 cps in chlorobenzene and is independent of the substituent other than hydrogen. In the polysubstituted toluenes under consideration (series 1-4), this coupling constant has a range of 0.29 to 0.39 cps and is also essentially independent of the ring substituents.

The conclusion arrived at from spin tickling experiments that all of the ring proton coupling constants are of the same sign, presumably positive, agrees with earlier work on substituted benzenes using spectral analysis (114-117) and decoupling techniques (118). The suggestion is that $J^{p}_{H,H}$ arises from a $\sigma - \pi$ mechanism (56, 70) since coupling through the $\sigma$-electrons alone is expected to be negligible (36, 45).

Considering now the methyl proton shifts, an interesting relationship is found between these shifts and Hammett's $\sigma$ constants for the ring substituents. The chemical shifts of the methyl protons in toluenes along with those in acetophenones and thioanisoles have recently been studied and interpreted by the application of Hammett's equation (150). Most of the toluenes studied were meta or para substituted and Hammett $\sigma$ constants for these substituents are readily obtainable (151). Hammett's equation is best applied to these systems. In the polysubstituted toluenes given in Tables 2-I to 2-III, an ortho substituent to the methyl group is always present and hence the situation is much more complicated.

A simpler and more approximate approach than the previous one (150) was therefore used in interpreting the methyl proton shifts in

these toluenes. In Table 2-VI are listed the methyl proton shifts of the poly-substituted toluenes that were studied only in $CS_2$ solution (hence eliminating solvent shifts). These are taken from Tables 2-IB and 2-IIB. All the Hammett substituent constants are also given and were taken from reference (151). Since a generally reliable set of σ (ortho) values is not available (150), σ (para) values were used instead (150). The sums of the Hammett substituent constants are also calculated and given in Table 2-VI.

A plot of the methyl proton shifts as a function of the sum of Hammett's substituent constants is given in Figure 2-8. A straight line may be drawn through seven of the points and there are only two exceptions. The straight line is in the expected direction. As the sum becomes more positive (greater electron withdrawing power of the substituents) the methyl resonance shifts to lower field.

Several approximations have been made in obtaining the above plot and these probably account for the scatter of the points. First, the bulk effect of the ortho group on the methyl proton shift is neglected. It is assumed that all of the substituent effects on the methyl proton shift are transmitted via the electronic system. This is not true and for this reason accurate σ (ortho) Hammett constants are not available. Secondly, it was also assumed that the σ (ortho) values may be replaced by the σ (para) values for the same substituent (150). Finally, the additivity rule does not necessarily hold (152). However, despite these approximations, a trend is illustrated by Figure 2-8 in the expected direction and the surprising fact is that seven out of

nine methyl shifts are linearly correlated. A more precise correlation of these shifts with other substituent constants or a more refined treatment were not attempted since the bulk effect of the ortho group is hard to estimate.

Two methyl shifts were far removed from the straight line, namely for the molecules 2-chloro-4-aminotoluene and for toluene itself. These results cannot be explained.

In summary, the low field shift of the methyl resonances in the polysubstituted toluenes is proportional to an increase in the sum of Hammett's substituent constants. As the electron withdrawing power of the substituents increases, the methyl resonance shifts to lower field. Hence most of the substituent effects are transmitted via the electrons of the molecule and affect the shielding of the methyl protons.

TABLE 2-VI

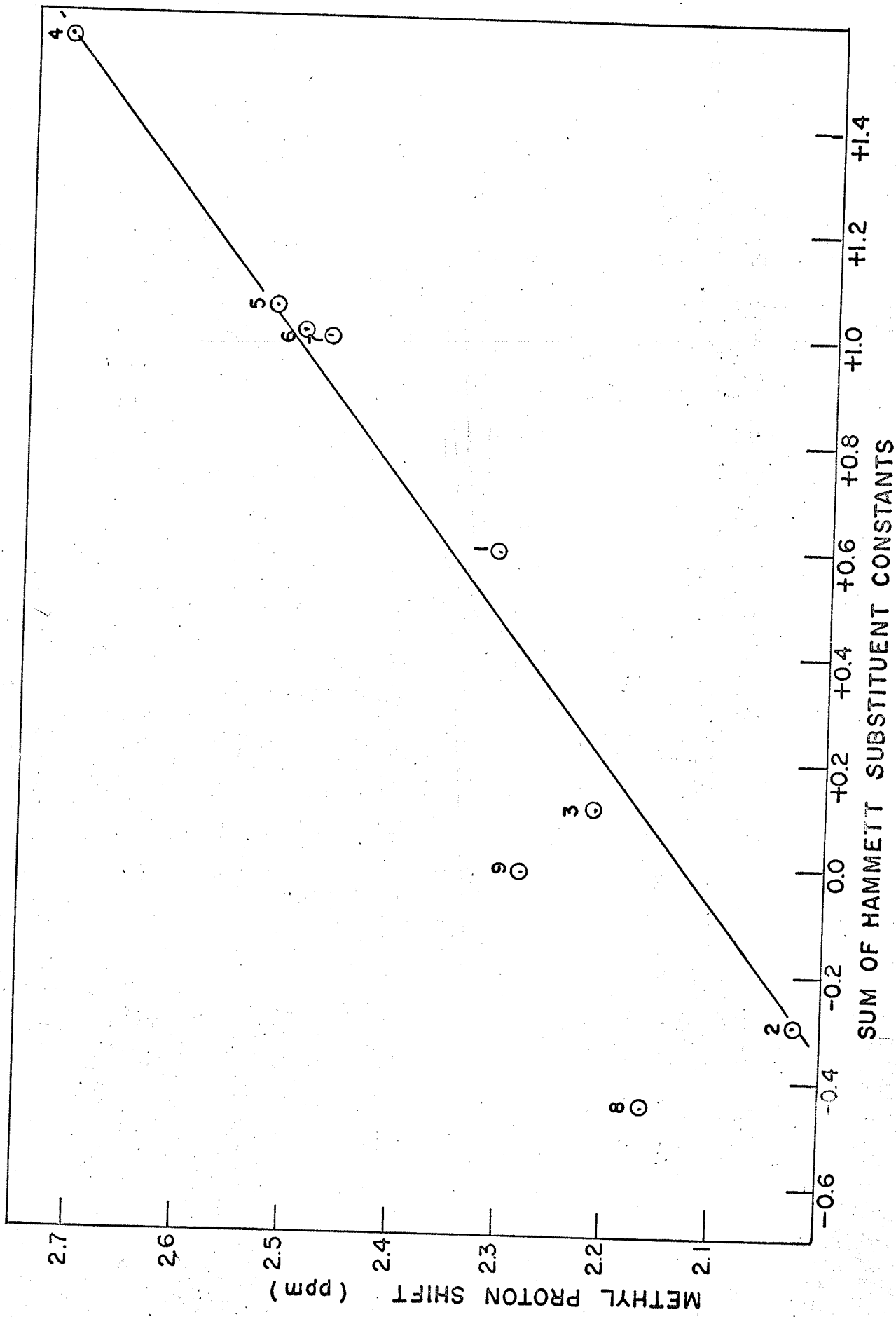
The methyl proton chemical shifts of the polysubstituted toluenes studied in series 1 and 2 (Tables 2-IB and 2-IIB) in $CS_2$ solution are given below. The shifts are in ppm with respect to internal TMS. The Hammett constants for the ring substituents are listed. The sum of these constants for each molecule is also given.

| | Compound | Shift (ppm) | Hammett Substituent Constants* σ (ortho) | σ (meta) | σ (para) | Sum |
|---|---|---|---|---|---|---|
| 1) | 2-bromo-5-chlorotoluene | 2.313± 0.005 | + 0.232 | + 0.373 | ------- | + 0.605 |
| 2) | 2-amino-5-chlorotoluene | 2.025 | - 0.66 | + 0.373 | ------- | - 0.29 |
| 3) | 2-thiomethyl-5-hydroxytoluene | 2.215 | 0.00 | + 0.121 | ------- | + 0.121 |
| 4) | 2,4-dinitro toluene | 2.724 | + 0.778 | ------- | + 0.778 | + 1.556 |
| 5) | 2-iodo-4-nitrotoluene | 2.524 | + 0.276 | ------- | + 0.778 | + 1.054 |
| 6) | 2-bromo-4-nitrotoluene | 2.497 | + 0.232 | ------- | + 0.778 | + 1.010 |
| 7) | 2-chloro-4-nitrotoluene | 2.475 | + 0.227 | ------- | + 0.778 | + 1.005 |
| 8) | 2-chloro-4-aminotoluene | 2.164 | + 0.227 | ------- | - 0.66 | - 0.43 |
| 9) | Toluene | 2.284 | 0.00 | 0.00 | 0.00 | 0.00 |

* Obtained from reference (151). In all cases σ (para) values are used for σ (ortho) for the same substituent (150).

Figure 2-8

A plot of the methyl proton shift of polysubstituted toluenes as a function of the sum of Hammett's substituent constants. The shifts are in ppm to low field of internal TMS and were all determined in $CS_2$ at 28.5 ± 1°C. The data are listed in Table 2-VI.


METHYL PROTON SHIFT (ppm)
2.7
2.6
2.5
2.4
2.3
2.2
2.1
SUM OF HAMMETT SUBSTITUENT CONSTANTS
-0.6
-0.4
-0.2
0.0
+0.2
+0.4
+0.6
+0.8
+1.0
+1.2
+1.4
4
5
6
7
1
3
9
8
2

## B. LONG-RANGE COUPLING CONSTANTS

The signs found for the ring-methyl proton couplings are in agreement with the $\sigma - \pi$ exchange mechanism. The simple molecular orbital calculation (36, 57) of the $\sigma - \pi$ interaction as given by equation (2 - 34) predicts negative values for $J^{o}_{H,CH_3}$ and $J^{p}_{H,CH_3}$ (as was found experimentally) but $J^{m}_{H,CH_3} = 0$. These results are supported by the data on acenaphthene (57). However, the more refined calculations (56, 70) predict $J^{m}_{H,CH_3}$ to be positive. This result is supported by the present results, and those of Gagnaire and Trinh-Huu-Ich (72) and Blears, Danyluk and Schaefer (77).

Cohen and McLauchlan (71) came to a similar conclusion from the proton spectrum of 2-carbomethoxy-5,6-dimethylbenzofuran but their argument was based on the magnitude of $J^{m}_{H,CH_3}$ only. The signs obtained here agree with those found in methylfurans and methylthiophenes (153, 154). The sign reversal of the coupling to the para proton when the methyl group replaces a hydrogen is also in agreement with a valence bond calculation by Karplus (45).

Equations (2 - 33) and (2 - 34) for calculating the magnitudes and signs of the long-range coupling constants are based on e.s.r. hyperfine splittings which in turn depend on the unpaired electron spin density at the proton. In aromatic radicals the unpaired electron occupies a molecular $\pi$ - orbital delocalized over the carbon atom framework of the molecule with a node in the plane of the molecule where the ring hydrogen atoms are situated (3). Hence at first an unpaired electron spin density is unexpected at the proton. It does arise however, due to the spin

polarization of the σ - electrons in the C-H bond by an exchange coupling with the π - electron system (the σ - π exchange mechanism) (3).

Consider an isolated $>\dot{C}$-H bond fragment with one π - electron. It occupies the $2p_z$ carbon orbital, perpendicular to the plane of the three $sp^2$ bonds as shown in Figure 2-9a. The arrows over the bonds indicate the spin states of the electrons while those above the hydrogen nuclei indicate the proton spin states (these arrows are crossed).

For a given spin of the π - electron there are two possible arrangements of the electrons in the C-H σ - bond. In Figure 2-9a these are labelled 1 and 2. In the first case the electron in the carbon $sp^2$ orbital has its spin parallel to the spin of the π - electron and in the second case it is antiparallel. However, according to Hund's rule the first case is slightly preferred over the second because of the favourable σ - π exchange interaction between the two carbon electrons with parallel spins. In this manner the electron spins in the σ - bond are slightly polarized. Hence if the unpaired π - electron has a spin $\alpha$, there will be a slight excess of carbon $sp^2$ electrons in the $\alpha$ spin state and then a slight excess of 1s electrons (centered on the proton) in the $\beta$ spin state (Pauli principle ). These will determine the proton spin state via the Fermi contact interaction. The spin polarization mechanism is thus responsible for the unpaired electron spin density at the proton and hence the observed hyperfine splittings.

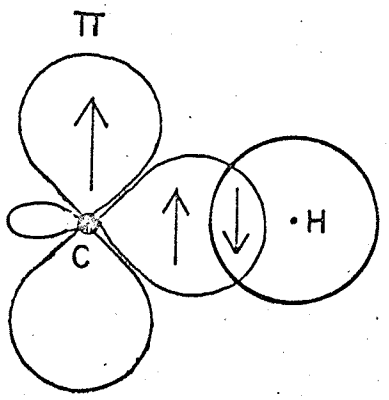
Consider the π - electron contribution to the ring proton coupling constants in benzene arising from the spin-polarization mechanism. This is illustrated in Figure 2-9b. Assuming that the spin state

Figure 2-9

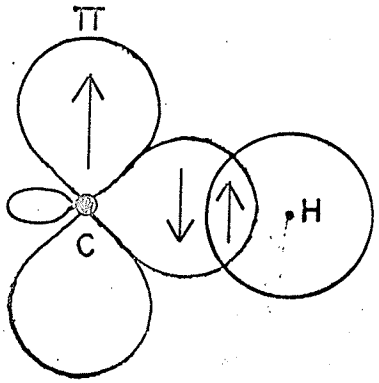
(a) The $\sigma$ - $\pi$ exchange interaction for a C-H bond fragment. (b) The $\pi$ -electron contribution to the ring proton coupling constants in benzene arising from the spin polarization mechanism.

The arrows above the hydrogen nuclei indicate the spin states of the protons (these arrows are crossed) while those above the bonds indicate the spin states of the electrons which take part in the coupling mechanism.

a.

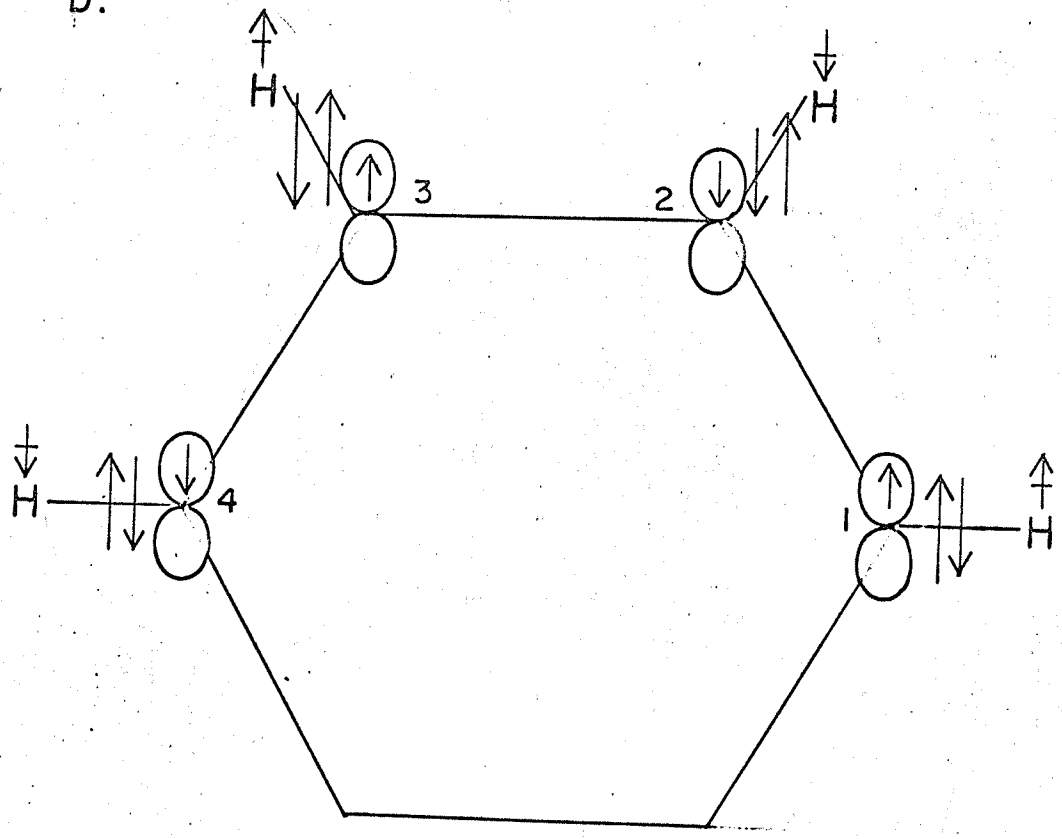



1.




2.

b.



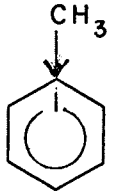
of proton one is as indicated in the Figure by the crossed arrow, the spin state of the neighbouring 1s electron will be antiparallel to it and is transmitted via the Fermi contact interaction. This electron spin polarizes the spin of the second electron in the carbon $sp^2$ orbital used to form the aromatic C-H bond and is antiparallel in accordance with the Pauli principle. Then follows the $\sigma - \pi$ exchange coupling by which the $sp^2$ electron spin couples with the $\pi$ -electron spin centered on the same carbon. At this point in the $\sigma - \pi$ mechanism the $\pi$ -electrons transmit the spin state of proton one all around the ring.

Consider the ortho coupling to proton two. The spin state of $\pi$ -electron one polarizes the spin of $\pi$ -electron two and the latter spin couples back into the $\sigma$ -electron system. The spin state of the $sp^2$ bonding electron on carbon two is thus determined. As before, the electron coupling proceeds along the aromatic C-H bond and finally the spin of the 1s electron centered on proton two determines the spin state of proton two via the Fermi contact interaction. This completes the coupling path between protons one and two. From Figure 2-9b the preferential orientation of the spin states of these two protons is antiparallel. Since a positive coupling constant is one in which the coupling proton spins have a tendency toward this orientation, the $\sigma - \pi$ mechanism thus contributes to a positive coupling constant between the ortho ring protons. As seen in the Figure the $\sigma - \pi$ contribution is negative and positive for the meta and para ring proton coupling constants respectively.

The coupling mechanism via the σ -electrons only is important for the ortho and meta ring proton couplings. However, the para coupling constant is dominated by the σ - π mechanism and the experimentally determined sign of this coupling is in agreement with the above theory.

When the ring proton is replaced by a methyl group the hyperfine splitting arising from the methyl proton spins occurs via three mechanisms namely; spin polarization of the σ -electrons by the unpaired π -electron spin density, hyperconjugation due to the π -orbitals, and inductive effects with the latter two being the most important.

In toluene the inductive effect of the methyl group is a direct electrostatic interaction which modifies the electric potential in the ring (155) since the methyl group has a tendency to release electrons. This is usually designated as




and $C_1$ becomes more electropositive. However, there is assumed to be no actual transfer of charge between the methyl group and the ring.

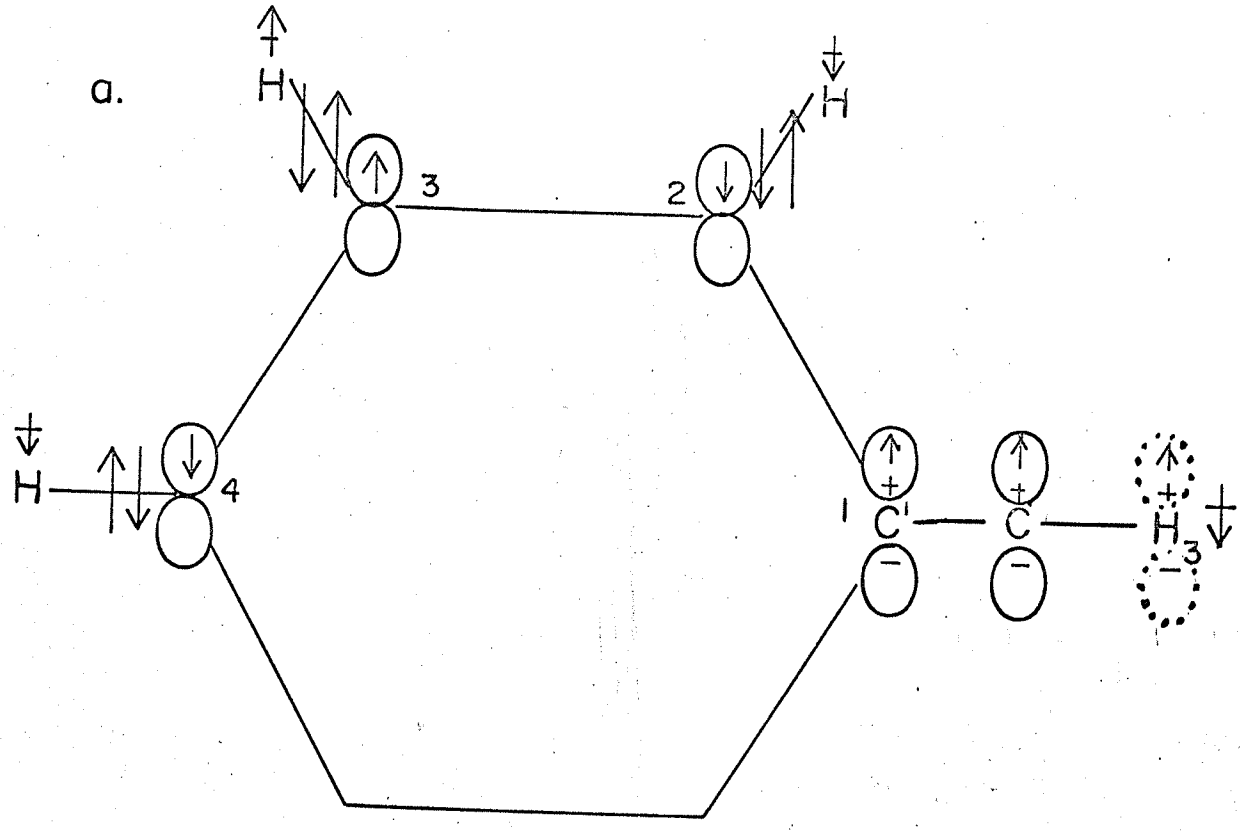
According to the hyperconjugation mechanism the pseudo π -orbitals of the methyl group combine with the ring π -oribtals, hence allowing for a direct flow of electrons from the methyl group to the ring (155). This mechanism is illustrated in Figure 2-10a. The hydrogen orbitals thus are a part of the π -orbital system and the proton spins interact (via the Fermi contact interaction) directly with the unpaired spin polarization. This mechanism predicts the observed signs for the ring-methyl proton coupling constants.

Figure 2-10

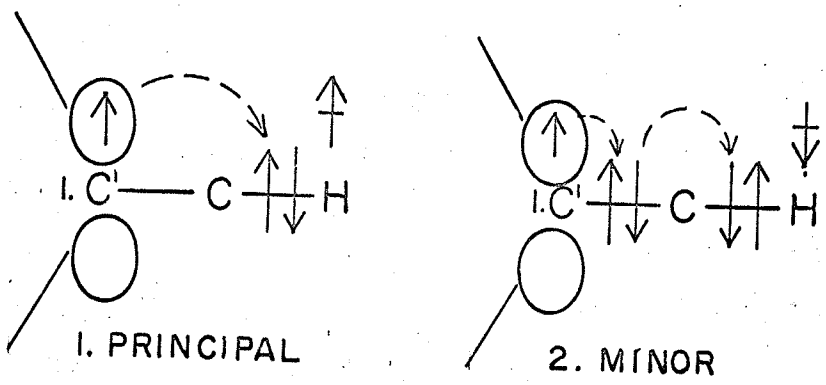
(a) The hyperconjugation mechanism in toluene with a direct overlap of $\pi$ -orbitals permitting the flow of unpaired spin. (b) The spin polarization mechanism of the $>C'-C-H$ group in toluene. The principal mechanism 1 is nearly three times as large but of opposite sign to the minor mechanism 2 (155).

The minor spin polarization mechanism 2 and the hyperconjugation mechanism predict the observed signs of the long-range coupling constants.

a.




b.



There are two possible spin polarization mechanisms between the unpaired electron spin in the aromatic carbon $2p_z$ orbital and the methyl proton spins. These are illustrated in Figure 2-10b. The principal mechanism involves a direct exchange polarization of the methyl C-H bond electrons by the ring electron. The minor mechanism involves a series of two successive exchange polarizations through the C-C bond. Since all four methyl carbon $sp^3$ hybrid electrons are in degenerate energy levels, then according to Hund's rule all will tend to have parallel spins. The minor mechanism will proceed as shown in Figure 2-10b. The magnitude of the principal mechanism is nearly three times that of the minor mechanism and they lead to opposite signs of the hyperfine interactions (155).

By comparing the diagrams in Figure (2-10) it is seen that the minor spin polarization mechanism, as well as hyperconjugation, predict the observed signs of the ring-methyl proton couplings i.e., from the methyl protons to the ortho, meta and para ring protons the long-range coupling constants are negative, positive and negative respectively. The principal spin polarization mechanism predicts opposite signs for these coupling constants.

Colpa and de Boer (96) found on the basis of e.s.r. data that the spin polarization mechanisms account for only about 3% of the observed hyperfine splittings in pyracene positive and negative ions and other aromatic systems. They conclude that the splittings arise mainly by hyperconjugation. However there may be a flaw in their calculations (155). As well, McDowell and Paulus (97) found that the inductive effect

of the methyl group was most effective in predicting the methyl hyperfine splittings in some substituted pyrazine radical anions. Consequently the signs of the long-range ring proton-methyl proton coupling constants in the toluenes under consideration may be determined by a combination of these mechanisms.

From the results shown in Tables 2-IA and 2-IIA, it is seen that the magnitudes of the long-range coupling constants do not depend on the substituents in the various positions in the ring nor on the solvent (156). Equation (2 - 34) depends on many factors, namely, $Q_{CH}$ and $Q_{CCH}$, bond order and the excitation energy to triplet states. Since the substituents have no effect on long-range couplings, this implies that their effect is either negligible or that their effects on the various variables in equation (2 - 34) cancel each other out.

The $J^{o}_{H,CH_3}$ values range from -0.66± 0.03 to -0.75± 0.03 cps, the $J^{m}_{H,CH_3}$ from +0.32± 0.03 to +0.42± 0.03 cps and $J^{p}_{H,CH_3}$ from -0.56± 0.03 to -0.59± 0.03 cps. Rottendorf and Sternhell (79) have studied the long-range coupling constants in the three isomeric tetrachlorotoluenes whose magnitudes are all within the experimental error limits given above.

Only two exceptions to these long-range coupling constants were observed. $J^{o}_{H,CH_3}$ increases in 2-hydroxy-3,5-dinitrotoluene to -0.87± 0.02 cps (in $C_6D_6$) and -0.85± 0.02 cps (in DMSO-$d_6$), (Table 2-III). As well both $J^{o}_{H,CH_2Cl}$ and $J^{m}_{H,CH_2Cl}$ decrease by approximately 0.2 cps from the above values in 3,4-dichlorobenzylchloride (Table 2-IV). These will now be discussed.

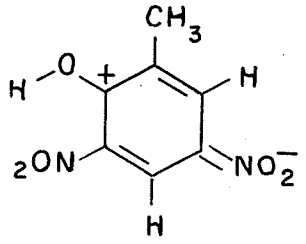
Consider 2-hydroxy-3,5-dinitrotoluene which exhibits several

interesting features. First of all there is a large difference in shift of approximately 5 ppm for the phenolic hydroxyl proton resonance in going from benzene to dimethylsulfoxide as solvent. The low-field shift in benzene indicates that a strong hydrogen bond is present (1) between the hydroxyl proton and the oxygen of the neighbouring nitro group (157). Associated with the low-field resonance is the presence of long-range spin coupling between the hydroxyl proton and ring proton $H_A$. It has been known for some time (118, 142, 157) that substituted phenols capable of forming strong intramolecular hydrogen bonds may display a long-range coupling between the hydroxyl protons and at least one ring proton. These couplings have been mainly observed in phenols with intramolecular hydrogen bonds which stabilize the proton in a rigid configuration and reduce the rate of intermolecular proton exchange (142). The long-range hydroxyl spin couplings are also stereospecific (63, 118, 142, 157) as are the long-range aldehyde couplings in substituted benzaldehydes (63, 157, 158) i.e., the couplings follow the straightest zig-zag path between the coupling protons. This evidence argues for a strong intramolecular hydrogen bond in benzene solution.

In dimethylsulfoxide not only is the hydroxyl proton resonance shifted to higher field, but the long-range coupling with ring proton $H_A$ disappears. This indicates that the intramolecular hydrogen bond is now broken.

The magnitude of $J^{o}_{H,CH_3} = -0.87 \pm 0.02$ cps is the largest yet observed in heteroatom substituted toluenes besides the same magnitude of this coupling observed in the compound 4-chloro-2-fluoro-5nitrotoluene (77). It is tempting to attribute the magnitude of this coupling to an

increase in double bond character (79-82) of the ortho C-C bond induced to a considerable extent by resonance structures of the form



However, as has recently been described by Blears, Danyluk and Schaefer (83) so many other effects enter in equation (2 - 34) that variations in coupling constants can only be related to variations in bond order provided consideration of the substituent induced changes in the other parameters in equation (2 - 34) is included. These include the effects of the methyl group on the $\pi$ -electron systems (94-102) and the various effects on the magnitudes of $Q_{CH}$ and $Q_{CCH}$ as discussed in the Introduction. Hence the large $J^{o}_{H,CH_3}$ in this molecule may arise from many contributions.

In benzene solution this molecule exists as a pseudo-two ring system due to the presence of the intramolecular hydrogen bond. In DMSO solution this bond is broken but the long-range coupling $J^{o}_{H,CH_3}$ remains unchanged. This is evidence in support of the above resonance structure which is present in both solutions. This result therefore supports the conclusion that the magnitude of $J^{o}_{H,CH_3}$ arises from an increase in the mobile bond order.

Considering the molecule 3,4-dichlorobenzylchloride, the decrease of both $J^{o}_{H,CH_2Cl}$ and $J^{m}_{H,CH_2Cl}$ by approximately 0.2 cps from the average values observed for $J_{H,CH_3}$ couplings is hard to account for quantitatively.

Qualitatively however, the presence of the chlorine atom on the methyl carbon in this molecule will have several effects. A comparison will be drawn with toluene and it is assumed that ring substituents have almost no effect on the magnitude of long-range couplings.

1. Steric hindrance to rotation

As discussed in the "Introduction" the barrier height to rotation in toluene is nearly zero as in benzotrifluoride (159). However the magnitude of $J^{o}_{F,CF_3}$ changes with temperature and X-substituent in 2-F, 6-X asymmetrically substituted benzotrifluorides (89, 160). This is explained by the existence of two different rotational conformations of the $CF_3$ group and the ring substituents. Analogous isomers for 2,6 disubstituted toluenes have as yet not been studied (89). For the molecule under consideration, the 6-fold symmetry of the rotational potential function of toluene is reduced and the barrier to hindered rotation increases. The potential barrier is not known. However it may be estimated from a comparison with the values observed for this barrier in propylene and the monosubstituted propylenes (620 - 2671 cal/mole) as summarized by Unland, Weiss and Flygare (92) and the value of 3560 cal/mole in ethyl chloride (161). Steric hindrance to rotation is further supported by the fact that restricted rotation about an $sp^2$ - $sp^3$ C-C bond (no double bond character) has recently been observed (162) in the molecule di-t-butyl, p-methoxyphenyl carbinol in which the substituent group $((CH_3)_3\text{-}C)_2\text{-}\overset{|}{C}\text{-}OH$ is very large.

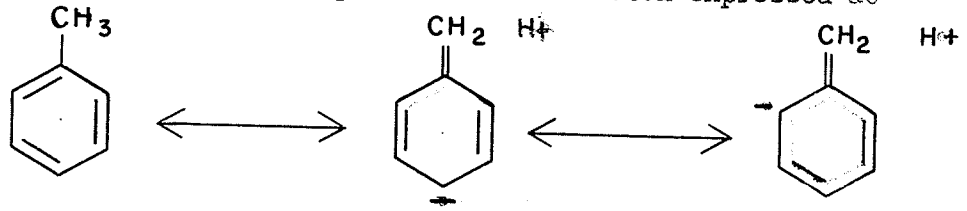
The decrease in the long-range coupling constants in allyl chloride with respect to the magnitude of these constants in propene itself has also been interpreted in terms of different rotamer populations

(163). For propene the long-range coupling constant with the cis protons is -1.7 cps and -1.3 cps with the trans protons (164). In allyl chloride these couplings become -1.38 cps and -0.93 cps respectively (163), a decrease on the average of 0.35 cps.

Hindered rotation will also affect the magnitude of $Q_{CCH}$ in going from the C'-$CH_3$ to the C'-$CH_2$-Cl grouping. $Q_{CCH}$ is a function of the angle $\theta$ between the C'-C-H plane and the axis of the $p_z$ orbital on the trigonal carbon atom C' (76, 165) and will be different in the two molecules.

2. Electronic effects

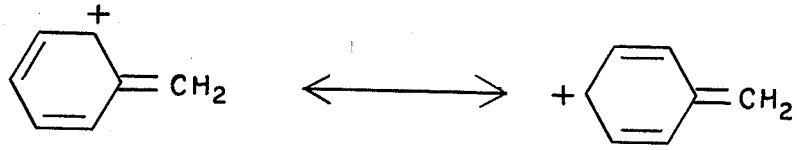
The presence of the chlorine atom on the methyl carbon will have an effect on the three mechanisms by which the unpaired electron spin density is transmitted to the $CH_2Cl$ protons. The hyperconjugative effect of the methyl group in toluene is often expressed as




In benzylchloride the chlorine atom with a greater electronegativity as compared to a hydrogen atom will have an effect on the above mechanism. The amount of overlap between the pseudo $\pi$ -orbitals of the methyl group and the ring $\pi$ -electrons, which determines the extent of hyperconjugation, will now change due to the presence of rotational isomers. The chlorine atom will also tend to counteract the electron releasing inductive effect of the methyl group. The spin polarization mechanism may also be affected.

And, as seen from the rate determining step of the solvolysis of benzylchloride (166)

a positive charge is placed on the methylene carbon atom which is transferred to the ortho and para ring carbon atoms by the resonance structures



All of these effects will influence the unpaired electron spin density at the methylene proton and hence will determine the magnitude of the long-range coupling constants. For example, from the results obtained by Read and Goldstein (146) and tabulated in Table 2-V, $J^{p}_{H,H} = 0.69$ cps in benzene and drops drastically to 0.50 cps in chlorobenzene.

3. Summary

In summary, neglecting ring-substituent effects, the decrease in the long-range coupling constants in the molecule under consideration as compared with the magnitudes of these couplings observed in ring-only substituted toluenes may arise from several effects. The first consideration is steric hindrance to rotation and hence the presence of several rotational conformers. A similar effect has been observed in the long-range couplings in allyl chloride which are about 0.35 cps smaller than those observed in propene. Secondly, the inductive, spin polarization and hyperconjugative effects of the $CH_3$ group, which determine the

magnitudes of the long-range couplings, will be affected in going to the $CH_2Cl$ group. Finally there may be a change in hybridization of the methyl carbon due to the chlorine atom (167). These effects cannot be estimated quantitatively at present.

## C. COMPARISON WITH THE LONG-RANGE COUPLING IN ORTHO-XYLENE

A comparison will now be drawn between the magnitudes of the long-range coupling constants under consideration and those in the molecule ortho-xylene. Very little splitting is observed for the ring protons in this molecule and the ring proton internal shift is very small and nearly zero. The ring proton $\tau$ value of ortho-xylene in $CS_2$ is 3.07 ppm with a peak width at half height of 0.66± 0.02 cps. When the methyl protons are decoupled the peak width decreases to 0.37± 0.02 cps (168). This agrees with the calculated $\pi$ -electron densities which are nearly equivalent at the four carbon atoms bonded to hydrogen (169).

The shift of the ring protons in ortho-xylene must be nearly the same since even at 200 Mc/s the ring proton spectrum is not analyzable as seen from a comparison with the ring proton spectra of toluene and meta-xylene at this frequency (170). The latter two molecules show almost identical shifts for protons ortho and para to the substituents and these shifts are to higher field than the meta shifts. In ortho-xylene those protons which are meta to one methyl are also either ortho or para to the other methyl group so that if ortho or para effects outweigh meta effects sufficiently strongly, the small chemical shift between the ring protons is to be expected. The 0.66 cps width at half-height of the ring proton resonance at 60 Mc is no doubt a combination of a small chemical shift together with extra broadening due to coupling with the methyl protons. The long-range splitting from the methyl protons to the ring protons corresponds to $\frac{J^{o}_{H,CH_3} + J^{m}_{H,CH_3}}{2}$ which is very small because of the opposite signs of these coupling constants.

## D. OTHER CONSIDERATIONS

In conclusion, several points remain that were not answered in the above discussion. First, the simple molecular orbital approach (36) predicts that $J^{m}_{H,CH_3}$ should be zero but it is present in all the molecules that were studied. Therefore, a more sophisticated approach (56) should be applied. Second, $J^{p}_{H,H}$ drops from benzene to a monosubstituted benzene from 0.69 to 0.50 cps and ranges from 0.29 to 0.39 cps in the polysubstituted toluenes that have been analyzed in this study. However, in these same toluenes the $J^{p}_{H,CH_3}$ values range from -0.56 to -0.59 cps. If the only effect of the $CH_3$ group were to replace the proton and change the sign of the long-range coupling, then $J^{p}_{H,H}$ should have a larger magnitude. Hence the larger value of $J^{p}_{H,CH_3}$ as compared with $J^{p}_{H,H}$ cannot be readily explained but probably arises from the many other effects of the methyl group and the other substituents present in the substituted benzenes and toluenes and their effect on the parameters present in equation (2 - 34), as discussed in the "Introduction". Finally a spin polarization mechanism (minor) plus a hyperconjugative effect may be important in determining the magnitudes of long-range couplings since they both operate in the same direction.

7.

# SUMMARY AND CONCLUSIONS

Tickling and decoupling techniques show that $J^{o}_{H,H'}$, $J^{m}_{H,H}$ and $J^{p}_{H,H}$ have the same sign in 2-bromo-5-chlorotoluene and are positive since $J^{o}_{H,H}$ is known to be positive. Decoupling experiments also show that $J^{o}_{H,CH_3}$ and $J^{p}_{H,CH_3}$ are negative and that $J^{m}_{H,CH_3}$ is positive. The signs of the long-range couplings and $J^{p}_{H,H}$ are in agreement with the $\sigma - \pi$ exchange mechanism and the theoretical basis developed by McConnell (36, 56). Various other polysubstituted toluenes were studied and it was found that substituents have a very small effect on the magnitudes of the long-range coupling constants. They are also independent of the solvent. The $J^{o}_{H,CH_3}$ values range from $-0.66\pm$ 0.03 to $-0.75\pm$ 0.03 cps, the $J^{m}_{H,CH_3}$ from $+0.32\pm$ 0.03 to $+0.42\pm$ 0.03 cps and $J^{p}_{H,CH_3}$ from $-0.56\pm$ 0.03 to $-0.59\pm$0.03 cps.

In the molecule 2-hydroxy-3,5-dinitrotoluene the observed coupling $J^{o}_{H,CH_3}$ is $-0.86\pm$ 0.02 cps. It is independent of the solvent. The large magnitude of this coupling may be attributed to an increase in the mobile bond order of the ortho C-C bond induced by a quinoid resonance structure.

In the molecule 3,4-dichlorobenzylchloride the magnitudes of $J^{o}_{H,CH_2Cl}$ and $J^{m}_{H,CH_2Cl}$ decrease by about 0.2 cps from the values given above. A quantitative estimate of this effect was not obtained. Qualitatively however, steric hindrance to rotation and consequently the presence of several rotational conformers will have an effect. A comparison may be drawn with the decrease of about 0.35 cps in the long-range couplings in allyl chloride as compared with propene. As well, the inductive, spin polarization and hyperconjugative mechanisms of transferring unpaired electron spin density to the methyl protons change

in going from the $CH_3$ to the $CH_2Cl$ group. The hybridization state of the methyl carbon will probably also vary.

The ortho ring proton coupling constants $J^{o}_{H,H}$ of the substituted toluenes range from +8.08± 0.03 to +8.53± 0.03 cps. They correlate with the electronegativities of the heteroatoms substituted ortho to one of the coupling protons. The $J^{m}_{H,H}$ values range from +2.16± 0.03 to +2.89± 0.03 cps, and $J^{p}_{H,H}$ from +0.29± 0.03 to 0.39± 0.03 cps and show no trends with substituent effects. As well a rough correlation is observed between the methyl proton shifts and the sum of Hammett's constants for the ring substituents.

8.

# RECOMMENDATIONS FOR FUTURE RESEARCH

The signs of the long-range coupling constants have now been determined between the methyl protons and ring protons in substituted toluenes, between the methyl protons and fluorine nuclei in fluorotoluene derivatives, between the side chain fluorine nuclei and ring protons, in benzotrifluorides. To complete the series, the signs of the couplings must still be determined between the side-chain fluorine nuclei and the ring-substituted fluorine nuclei in fluorobenzotrifluorides. These signs are predicted to be the same as observed between the methyl protons and ring fluorine nuclei in fluorotoluene derivatives.

The long-range coupling constants between the methyl protons and ring protons should also be studied in naphthalene derivatives such as 2-methyl-1-nitronaphthalene, 4-bromo-1-methylnaphthalene and others. The effect of substituents could be studied. As well, the magnitudes and signs of these coupling constants could be compared with those calculated by McConnell (56) for naphthalene. It would be interesting to compare the two sets of data.

The work of Dewar and Fahey (57) on acenaphthene should be repeated. It was carried out in 1963 and since then better stability and resolution has been obtained for n.m.r. spectrometers. Maybe now $J^{m}_{H,CH_2}$ can be resolved. This would add further support to McConnell's (56) valence bond treatment of the $\pi$ contribution to coupling constants.

The long-range couplings in the molecule 2-hydroxy-5-nitrotoluene, which does not form an intramolecular hydrogen bond, should be determined and compared with the corresponding values in 2-hydroxy-3, 5-dinitrotoluene. As well, methyl-substituted benzoquinones and other methyl-substituted compounds with a contributing quinoid structure should

be studied to see how well the long-range couplings correlate with the mobile bond order. This can be extended to determine the effect of a nitrogen nucleus on long-range coupling constants in methyl-substituted pyridines and quinolines.

Finally, systems similar to the above but with a phosphorus atom present should be studied and the signs of the coupling with the phosphorus nucleus determined. This may prove to be important in biological compounds where phosphorus linkages are very important.

Recently Ohtsuru, Tori and Watanabe (171) have discussed a connection between the methyl substituent effect upon the chemical shifts of ortho-protons and the $\pi$ -bond orders in 22 aromatic systems. The long-range couplings were not studied but all the $\pi$ -bond orders were calculated. Since various aromatic systems were considered, it would be interesting to study some of the molecules further to supplement the data on correlations between long-range couplings and bond orders.

When long-range coupling constants are determined, the solutions that are studied must always be degassed. This was not always done in the early work and consequently broadened peaks instead of fine splittings were often obtained due to the broadening effect of the paramagnetic oxygen molecules. For highest precision, degassing is a must.

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# CHAPTER III

## A PROTON MAGNETIC RESONANCE STUDY OF THE INTRAMOLECULAR HYDROGEN BOND, OF PROTON EXCHANGE REACTIONS, AND OF THE ASSOCIATED ACTIVATION PARAMETERS IN 3,5-DICHLOROSALICYLALDEHYDE IN BENZENE SOLUTION

1.

# INTRODUCTION

Proton magnetic resonance techniques have been used extensively in the study of chemical rate processes in solution. These include proton exchange reactions, hindered internal rotation and conformational studies.

The research project under consideration is concerned with the application of p.m.r. to the study of the intramolecular hydrogen bond and proton exchange reactions in 3,5-dichlorosalicylaldehyde in benzene solutions. This system was chosen because the ring proton spectrum was simplified by the presence of two chloro substituents, because of the presence of the long-range splitting $J_{OH-H_4}$ ($J_{OH-H_B}$) and because proton exchange occurred in this solvent. The results of studies in other solvents are also indicated. This system is especially interesting since very few studies have been carried out on proton exchange reactions involving intramolecularly hydrogen-bonded protons.

The theoretical basis of rate studies based on the p.m.r. technique is discussed first, followed by the various methods by which the rate constants may be derived from the analysis of the spectra. The approach chosen in this study involves the measurement of the relative heights of peaks that are associated with an exchanging proton with respect to peak heights involving non-exchanging protons. This method was used when it was discovered that the stereospecific long-range splitting $J_{OH-H_4}$ ($J_{OH-H_B}$) became smaller and disappeared as the temperature of the solution was raised. The two chloro substituents simplify the ring proton spectrum and allow line-shape measurements to be carried out.

The relationships between the proton exchange rate constants and the associated activation parameters are obtained by an application

of the Arrhenius equation and the theory of absolute reaction rates. These parameters are determined and the effects of statistical and systematic errors are considered. The activation parameters, rate constants, the mechanism of proton exchange together with the nature of the transition state are discussed in terms of the intramolecular hydrogen bond strength, solvent effects and barriers to hindered internal rotation of the CHO and OH groups. Solvent effects on the proton chemical shifts are interpreted in terms of a weak solute-solvent interaction.

2.

## THEORETICAL DISCUSSION

## A. SPIN-LATTICE RELAXATION TIME

### 1. Introduction

For an assembly of nuclei of spin $\frac{1}{2}$ in thermal equibibrium at temperature T in a magnetic field $H_o$ there are two energy levels, the lower one being more populated. Transitions between these levels occur by the absorption of energy from a radiation field. The energy is given by

3-1 $$\Delta E = h\nu = 2\mu H_o$$

where $\Delta E$ is the separation between the two energy levels, h is Planck's constant, $\nu$ is the frequency of the radiation, $H_o$ is the external magnetic field and $\mu$ is the maximum observable component of the nuclear magnetic moment. The Boltzmann distribution between the two energy levels is

3-2 $$\frac{N_2}{N_1} = \exp\left(\frac{-2\mu H_o}{kT}\right) \cong 1 - \frac{2\mu H_o}{kT}$$

where $N_2$ and $N_1$ are the number of nuclei in the high and the low energy levels respectively, k is the Boltzmann constant and T is the absolute temperature. The excess population of hydrogen nuclei in a field $H_o$ of 10,000 gauss is $7 \times 10^{-6}$ (1, 2).

The rate at which nuclei reach thermal equilibrium in a magnetic field must also be considered. For an n.m.r. absorption to occur there must be an excess of nuclear spins in the lower state. Consequently the processes by which the spins return to the lower level after excitation and thus maintain the equilibrium Boltzmann distribution are very important and will now be discussed.

The probability of spontaneous emission is negligible (3).

Another mechanism depends on the downward transitions stimulated by magnetic fields oscillating at the Larmor frequency. This is known as the spin-lattice relaxation process and is characterized by a spin-lattice relaxation time $T_1$.

Let $W_1$ and $W_2$ represent the upward and downward transition probabilities. At equilibrium the total number of upward transitions per unit time are equal to the corresponding number of downward transitions so that

3-3 $$W_1 N_1 = W_2 N_2 .$$

Hence

3-4 $$\frac{W_1}{W_2} = \frac{N_2}{N_1} = \exp \frac{(-2\mu H_o)}{kT} .$$

Writing W for the mean of $W_1$ and $W_2$, N for the number of nuclei per unit volume in excess in the lower energy state at any time t, and $N_{eq}$ for the value of N at thermal equilibrium, it may be shown that (1)

3-5 $$N - Neq = (N - Neq)_o \, e^{-2Wt}$$

where $(N-Neq)_o$ is the initial value of (N-Neq). The time $T_1$ is defined by

3-6 $$T_1 = \frac{1}{2W} .$$

Hence the difference between the excess population and its equilibrium value is reduced by a factor e after time $T_1$. This is the spin-lattice relaxation time, a measure of the rate at which the spin system comes into thermal equilibrium with the other degrees of freedom of the lattice.

## 2. Mechanisms of Spin-Lattice Relaxation

The spin-lattice relaxation mechanism can be thought of in terms very similar to those of the radiation-induced transitions forming the basis of n.m.r. spectroscopy. A fluctuating magnetic field induces transitions between spin states when the field has an appreciable component of frequency $\nu_o$, the Larmor precession frequency. Thus the extent of spin-lattice interaction depends upon the magnitude of local fields and the rates of fluctuation of these fields (1).

The most universal mechanism for spin-lattice relaxation involves the direct interaction of neighbouring magnetic dipoles (1). As the nuclear spins move relative to one another in the lattice fluctuating magnetic fields are produced which may, depending on the frequency, induce transitions of the spins in the molecule. On this basis energy can be transferred to the spin system from the translational and rotational degrees of freedom of the "lattice". The theory for this mechanism has been developed by Bloembergen, Purcell and Pound (4) who considered the influence of rotational, translational and vibrational motions of molecules in a liquid upon relaxation times.

Several other important mechanisms have been discussed (1) and can be summarized. Paramagnetic impurities in solution cause a decrease in relaxation times due to the interaction of the nuclear and unpaired electron spins. Secondly, in molecules where the chemical shielding is not isotropic, the secondary magnetic field arising from electronic currents will not generally be parallel to the applied field. A component of this field will therefore be present in the perpendicular direction which due to molecular rotation will oscillate

and may cause transitions to occur. This relaxation mechanism is dependent on the magnitude of $H_o$. Finally for nuclei with $I > \frac{1}{2}$, interactions between quadrupole moments and fluctuating electric field gradients will also decrease $T_1$.

## B. SPIN-SPIN RELAXATION TIME

When magnetic nuclei are placed in an external magnetic field $\underline{H}_o$ (normally chosen in the Z direction) the angular momentum vectors ($\underline{I}\hbar$) precess about this direction. The resonance condition is given by

3-7 $$\omega_o = \gamma \underline{H}_o$$

where $\omega_o$ is the angular frequency of precession (in radians per second) and $\gamma$ is the magnetogyric ratio. In this manner the field $\underline{H}_o$ produces a polarization of the nuclear magnetism along the Z direction.

For protons with two possible spin states the axis of precession is either in the positive or negative Z direction. Arising from the unequal distribution of spins among these two states a resultant macroscopic magnetic moment per unit volume is produced in the direction of $\underline{H}_o$. For all the spinning nuclei the phase of the rotating vectors in the x-y plane will be random in the absence of a rotating magnetic field at the Larmor frequency. Thus the resultant magnetization in this plane is zero. A radiofrequency, applied perpendicular to $\underline{H}_o$ at the resonance frequency $\omega_o$, aligns the individual vectors and thus produces a resultant magnetization in the x-y plane (5).

Any process causing the interruption of phase coherence of the x-y magnetization is associated with a characteristic exponent $(\frac{1}{T_2})$ where $T_2$ is the spin-spin relaxation time (1, 5). This is the second process of nuclear magnetic relaxation and arises from inhomogeneous magnetic fields, local field variations in the sample due to the other nuclear magnetic dipoles nearby, and exchange processes (5).

## C. FACTORS AFFECTING LINE WIDTHS OF NMR SIGNALS

Equation (3 - 1) predicts absorption only at the resonance frequency $\nu$ . Experimentally this would correspond to an infinitely sharp absorption peak. However, in practice resonance occurs over a range of frequencies and the lines are broadened. For this reason a line-shape function $g(\nu)$ has been introduced (1).

The number of nuclei with a resonance frequency between $\nu$ and $\nu + d\nu$ is given by

3-8 $$dN = N_o\, g(\nu)\, d\nu$$

where $N_o$ is the total number of nuclei and the function $g(\nu)$, which is proportional to the absorption at frequency $\nu$, is such that

3-9 $$\int_o^\infty g(\nu)\, d\nu = 1$$

It is a normalized function and has a finite value over a range of frequencies.

Some of the factors causing line broadening and hence affecting $g(\nu)$ are now considered (1).

1) Natural line width due to spontaneous emission.

The natural line width of any transition is determined by the finite lifetime of the nucleus in the upper state. Purcell (3) has shown that the probability of spontaneous emission is negligible and is not effective in bringing a spin system into thermal equilibrium with the lattice. Hence it has little effect on line widths of n.m.r. signals.

2) Line widths due to spin-lattice relaxation.

The spin-lattice relaxation process determines the lifetimes of both spin states of a nucleus. Line broadening occurs as a natural consequence of the uncertainty principle

3-10 $$\Delta E \; \Delta t \cong \hbar$$

where $\Delta E = h\Delta\nu$ . The uncertainty in the frequency of absorption is $\frac{1}{2\pi\Delta t}$ . Hence the line width, measured on a frequency scale in the absence of other broadening mechanisms is of the order of $\frac{1}{T_1}$.

For nuclei with $I > \frac{1}{2}$ electric quadrupole effects lead to smaller $T_1$ values than, for example, the $T_1$ observed for protons in a liquid.

3) Line broadening due to spin-spin relaxation.

In solids and highly viscous liquids the interaction of magnetic dipoles leads to a greater broadening than that given by the spin-lattice mechanism. Each nucleus feels the effect of a variety of local magnetic fields due to these neighbouring magnetic dipoles and consequently $T_2$ is very small. For this reason n.m.r. signals of solids are much broader than those of liquids and gases where rapid molecular motions tend to average local fields to zero.

Since $g(\nu)$ is a normalized function its maximum value is an inverse measure of its width. Hence $T_2$ is defined as

3-11 $$T_2 = \tfrac{1}{2}\left[\; g(\nu)\right]_{max.}$$

and decreases as spin-spin interactions increase. $T_2$ is important for solid state studies but in liquids and gases $T_1$ and $T_2$ are nearly equal.

4) Broadening due to magnetic field inhomogeneity.

When a sample is placed in an inhomogeneous magnetic field, molecules in different parts of the sample see different values of the main magnetic field. Thus this instrumental limitation leads to line broadening.

5) Proton exchange reactions and hindered rotation.

Proton exchange reactions occurring in solution and conformational equilibria affect line widths and the relaxation times. These will be discussed in Section E.

## D. THE BLOCH FORMULATION

Bloch (6) has studied the resultant macroscopic magnetic moment of the nuclei within a sample under investigation. It is a change of orientation of this macroscopic moment with time due to the radiofrequency field $\underline{H}_1$ which causes the observed n.m.r. signal. Bloch used a set of macroscopic or phenomenological equations to describe this motion (1, 6).

Assume that thermal equilibrium between the nuclear moments and their surrounding atoms has been established in an external magnetic field $\underline{H}_o$. Then

3-12 $$\underline{M} = \chi \underline{H}_o$$

where $\underline{M}$ is the resultant magnetic moment per unit volume of an assembly of identical nuclei in the field direction and $\chi$ is the nuclear paramagnetic susceptibility. It is given by the relationship

3-13 $$\chi = \frac{n \mu^2 (I + 1)}{3IkT}$$

where n is the number of nuclei per unit volume, T is the equilibrium temperature and I is the nuclear spin. Equation (3 - 13) has been previously derived (2).

The equations of interest give the time-variation of $\underline{M}$. These are obtained from the classical equations of motion of a single magnetic moment $\mu$ in a field $\underline{H}_o$ by summing them over the whole assembly of nuclei.

A magnetic moment in the field $\underline{H}_o$ experiences a couple ($\underline{\mu} \times \underline{H}_o$) equal to the rate of change of angular momentum $\underline{P}$

3-14 $$\frac{d\underline{P}}{dt} = \underline{\mu} \times \underline{H}_o$$

But

3-15 $$\underline{P} = \frac{\underline{\mu}.\underline{1}}{\gamma}$$

Hence

3-16 $$\frac{d\underline{\mu}}{dt} = \gamma (\underline{\mu} \times \underline{H}_o).$$

This result is extended to bulk material by summing equation (3 - 16) over all the nuclei per unit volume so that

3-17 $$\frac{d\underline{M}}{dt} = \gamma (\underline{M} \times \underline{H}_o)$$

where

3-18 $$\underline{M} = (M_x, M_y, M_z).$$

In the n.m.r. experiment a radiofrequency field $\underline{H}_1$ is applied perpendicularly to $\underline{H}_o$ and rotates with an angular frequency - $\omega$ with components.

3-19 $$H_x = H_1 \cos \omega t$$

3-20 $$H_y = -H_1 \sin \omega t$$

For equation (3 - 17) to be valid all the external magnetic fields acting on the nuclei must be included in the cross product. Hence the components of the external field in the x and y directions are given by the above two equations. Since the steady magnetic field $\underline{H}_o$ is chosen in the Z direction

3-21 $$H_z = H_o$$

Expanding equation (3 - 17)

3-22 $$\frac{d\underline{M}}{dt} = \gamma \begin{vmatrix} \underline{i} & \underline{j} & \underline{k} \\ M_x & M_y & M_z \\ H_x & H_y & H_z \end{vmatrix}$$

so that

3-23 $$\frac{dM_x}{dt} = \gamma (M_y H_z - M_z H_y)$$

3-24 $$\frac{dM_y}{dt} = -\gamma (M_x H_z - M_z H_x)$$

3-25 $$\frac{dM_z}{dt} = \gamma (M_x H_y - M_y H_x)$$

In the absence of $\underline{H}_1$, these equations reduce to ($H_x = H_y = 0$)

3-26 $$\frac{dM_x}{dt} = \omega_o M_y$$

3-27 $$\frac{dM_y}{dt} = -\omega_o M_x$$

3-28 $$\frac{dM_z}{dt} = 0$$

where $\omega_o = \gamma H_z$ is the angular frequency of Larmor precession (resonance condition). The solution of these equations predicts that the total moment $\underline{M}$ will precess about the Z direction with the Larmor frequency (1).

Equations (3 - 23) to (3 - 25) do not allow for relaxation effects. It is known (6) that $M_z$ approaches an equilibrium value $M_o$ due to spin-lattice relaxation. The equation for this process is (6)

3-29 $$\frac{dM_z}{dt} = -\frac{(M_z - M_o)}{T_1}$$

with the stationary solution $M_z = M_o$. Bloch refers to $T_1$ as the <u>longitudinal relaxation time</u> since it measures the rate of change of the component of magnetization along the direction of the main magnetic field $\underline{H}_o$.

The $M_x$ and $M_y$ components of $\underline{M}$ also decay to zero but due to

spin-spin interactions. Bloch calls the time constant $T_2$ for this decay process the transverse relaxation time since it governs the time dependence of the transverse magnetization components $M_x$ and $M_y$ so that

3-30 $$\frac{dM_x}{dt} = - \frac{M_x}{T_2}$$

and

3-31 $$\frac{dM_y}{dt} = - \frac{M_y}{T_2} .$$

Hence, substituting equations (3-19) and (3-20) and allowing for relaxation effects in the Bloch equations (3-23) to (3-25), the complete Bloch equations are

3-32 $$\frac{dM_x}{dt} = \gamma(M_y H_z + M_z H_1 \sin \omega t) - \frac{M_x}{T_2} .$$

3-33 $$\frac{dM_y}{dt} = \gamma (M_z H_1 \cos \omega t - M_x H_z) - \frac{M_y}{T_2}$$

3-34 $$\frac{dM_z}{dt} = \gamma (-M_x H_1 \sin \omega t - M_y H_1 \cos \omega t) - \frac{M_z - M_o}{T_1} .$$

These differential equations are simplified by transforming them to a set of axes rotating with angular velocity $-\omega$ about the Z axis. As well, Bloch replaces $M_x$ and $M_y$ by u and v defined as

3-35 $$u = M_x \cos \omega t - M_y \sin \omega t$$

3-36 $$v = -M_x \sin \omega t - M_y \cos \omega t$$

The Bloch equations, in terms of u, v and $M_z$, and referred to the rotating axes become (1)

3-37 $$\frac{du}{dt} + \frac{u}{T_2} + (\omega_o - \omega) v = 0$$

3-38 $$\frac{dv}{dt} + \frac{v}{T_2} - (\omega_o - \omega)\, u + \gamma H_1 M_z = 0$$

3-39 $$\frac{dM_z}{dt} + \frac{M_z - M_o}{T_1} - \gamma H_1 v = 0$$

The term $\Delta\omega = \omega_o - \omega$ corresponds to the separation between the irradiation frequency $\omega$ (also the angular velocity of the rotating frame of reference) and the resonance frequency $\omega_o$.

The steady state solutions are obtained by setting all time derivatives equal to zero since the equilibrium magnetizations u, v and $M_z$ remain constant in the rotating frame. The solutions are given by Bloch (6) and have been summarized (1). A line-shape function from these solutions may also be obtained which confirms the equivalence of the two definitions of $T_2$.

## E. EFFECT OF EXCHANGE UPON SIGNAL LINE WIDTHS

### 1. Introduction

N.M.R. spectra may be modified if the nuclei take part in various rate processes such as proton exchange, intramolecular rearrangement and internal rotation. Coalescence of separate signals occurs when exchange rates reach a critical value. Since the rate of the process is inversely proportional to the decrease in separation between the signals that are collapsing, n.m.r. techniques can be used to study chemical exchange reactions with exchange rates of the order of 1 to $10^4$ $sec.^{-1}$. The beauty and power of this technique in measuring fast exchange reactions arises from the fact that it gives data on the chemical kinetics while the measured system is in chemical equilibrium and indicates directly the species that are exchanging.

One basic requirement must be met before n.m.r. can be used to study exchange reactions: the exchanging nuclei must have different magnetic environments and consequently different Larmor precession frequencies. Hence if no exchange is observed between these nuclei or if the process is slow, separate signals are observed. When the process is accelerated, by raising the temperature for example, then eventually the rate of exchange becomes sufficiently rapid so that a single resonance line appears at an intermediate position. This applies to chemical shifts as well as to the averaging of spin-spin multiplets.

Exchange can be considered to be a transverse relaxation process since the exchanged nuclei will be out of phase with the other nuclei in the same environment. It thus decreases the transverse relaxation time and consequently increases the width of the signals arising from the exchanging nuclei. Exchange between nuclei in the same environments has

no effect upon the signal width because the nuclei have the same precessional frequencies before and after exchange.

Consider the exchange process between nuclei in two non-equivalent sites with no coupling between them. For slow exchange rates the line widths of the two peaks first broaden. As the rate increases the signals broaden further and move closer together until they collapse to a single peak which becomes sharper for fast exchange rates. Hence for slow rates of exchange the increase in line width is directly proportional to the rate whereas in the fast exchange region the signal width is inversely proportional to the rate. This is a consequence of the uncertainty principle as given by equation (3 - 10).

The literature dealing with the study of time dependent factors influencing signal shape, namely, exchange reactions, hindered internal rotation, chemical equilibria and conformational studies is enormous and has been discussed and summarized in several monographs (7, 8) and review articles (5, 9-11).

## 2. Theoretical Formulations

The first evaluation of a quantitative relation between reversible chemical exchange reactions and resonance lineshapes is based on the treatment suggested by Gutowsky, McCall and Slichter (12-14), known as the GMS approach. These authors modified the Bloch equations to account for chemical exchange between two sites A and B with different Larmor frequencies between which a nucleus X of spin $\frac{1}{2}$ could exchange. A simpler approach was suggested by McConnell (15) and will be followed here.

Consider the simplest rate process which can be studied by n.m.r., namely the collapse of a doublet into a singlet due to the exchange of two uncoupled protons in two nonequivalent environments. This involves the chemical shift difference between these two protons. McConnell modified the Bloch equations and his approach is valid assuming the exchange process meets the following requirements (5):

(a) A nucleus in site A or B changes its site in a very short time compared to its lifetime in state A or state B; i.e. $\tau_A$ or $\tau_B$.

(b) The relaxation times $T_1$ and $T_2$ for nuclei in sites A and B are independent of the lifetimes $\tau_A$ and $\tau_B$.

(c) $\tau_A$ and $\tau_B$ are pseudo first-order lifetimes and hence correspond to the reciprocals of the first order rate constants for transfer out of the respective sites. This arises since McConnell's equations require that the X nuclear magnitizations of the A and B systems relax independently of one another, except for the chemical exchange effects.

McConnell's modified Bloch equations are not given here. They are given in his original paper (15) and the above-mentioned monographs and reviews (5, 7-10). Only the solutions of these equations are considered. First of all however, an important definition is made for the purposes of this thesis. There is little uniformity in the definition of the exchange lifetime parameter $2\tau$ in the literature. It is here defined as

3-40
$$\frac{1}{\tau} = \frac{1}{\tau_A} + \frac{1}{\tau_B}$$

so that

3-41 $$\tau = \frac{\tau_A \tau_B}{\tau_A + \tau_B} .$$

For a simple two-site exchange, $\frac{1}{\tau_A}$ is the probability per unit time of the nucleus jumping to site B. Then the relative populations of the sites are

3-42 $$p_A = \frac{\tau_A}{\tau_A + \tau_B} ; \qquad p_B = \frac{\tau_B}{\tau_A + \tau_B}$$

where $p_B = 1 - p_A$.

For an equal population case

3-43 $$2\tau = \tau_A = \tau_B$$

and corresponds to the average lifetime of a nucleus in either site. In other words, $2\tau$ is the average lifetime between exchanges of any one nucleus. This definition of $2\tau$ is that given by Gutowsky and Holm (14) and corresponds to the $\tau$ as defined by GMS (12), McConnell (15) and Takeda and Stejskal (16). Allerhand et al (17) list the various literature references and their definitions of $2\tau$.

The solutions of the modified Bloch equations for different exchange rates and under slow passage conditions are now discussed following reference (7).

A) Slow exchange limit:-

If lifetimes $\tau_A$ and $\tau_B$ are sufficiently long compared to the inverse of the separation between the two sites, then two signals are observed. Hence the variation in line widths of separated resonances can be studied. Experimentally the variable which is most conveniently measured is the signal width at half height (18). By an application of

the line-shape equation, the line width at half height (in cps) $\Delta\nu_{1/2}$ is equal to (18)

3-44 $$\Delta\nu_{\frac{1}{2}} = \frac{1}{\pi T_2}$$

so that

3-45 $$\pi \Delta\nu_{\frac{1}{2}} = \frac{1}{T_2} = \frac{1}{\tau_A} + \frac{1}{T_{2A}} .$$

$T_{2A}$ is the value of the spin-spin relaxation time in site A which may be obtained from the line widths of the exchanging peak at low temperatures (very slow exchange rate) or from a sharp signal arising from a standard reference (5). Since an <u>actual</u> line width is limited by magnet inhomogeneities, this equation is valid only if the signal has Lorentzian line shape and will be applicable when the resolution is good and $H_1$ is small (no saturation).

B) <u>Intermediate exchange rates</u>:-

This is the region of $2\tau$ values where the peaks overlap and coalesce. Three main methods exist for treating spectral data to obtain the lifetimes in this region (5). The lineshape function may be generated and compared with experiment (14). This procedure adapts itself readily to computer techniques. The second approach is also due to Gutowsky and Holm (14) who studied the decrease in the separation between the two peaks and compared it with the shift in the absence of exchange. Under the conditions of equal populations and lifetimes ($p_A = p_B = \frac{1}{2}$; $\tau_A = \tau_B = 2\tau$) and large transverse relaxation times ($\frac{1}{T_{2A}} = \frac{1}{T_{2B}} = 0$) the rate of collapse of a doublet as a result of exchange is approximately given by (7, 14)

3-46 Separation of peaks

Separation of peaks for large $\tau_A = \tau_B$ $= \left[1 - \frac{1}{2\pi^2\tau^2 (\nu_A - \nu_B)^2}\right]^{\frac{1}{2}}$.

This equation applies to the case where the signal widths in the absence of exchange are small compared with their separation. The critical lifetime ($2\tau$) at coalescence is

3-47 $$2\tau = \frac{\sqrt{2}}{\pi (\nu_A - \nu_B)}$$

where $(\nu_A - \nu_B)$ is the frequency difference (cps) between the A and B sites.

When $T_{2A}$ and $T_{2B}$ must be accounted for, then these two equations are not applicable and detailed equations must be applied (14, 16). Finally, the third approach consists of measuring the exact intensity ratio between two maxima and the intermediate minimum before collapse as applied by Rogers and Woodbrey (19). This method is very sensitive to non-ideal spectrometer conditions. The most accurate method in this region is the generation of the line shape and direct comparison with experiment (5).

C) Fast exchange limit:-

When $\tau_A$ and $\tau_B$ are small the single averaged resonance, broadened by exchange, decreases in half-width until the value $\Delta\nu_{\frac{1}{2}}$ given by equation (3-45) is reached in the limit of fast exchange. For very short lifetimes the signal is centered on a mean frequency

3-48 $$\omega_{mean} = p_A \omega_A + p_B \omega_B.$$

In the region where significant lifetime broadening occurs the linewidth can be used to measure the rates of exchange as has been done by Meiboom et al (20, 21).

## 3. Collapse of Spin-Spin Multiplets

The above results can easily be extended to include the collapse of spin multiplets arising from the interruption of spin-spin coupling between two nuclei by a chemical exchange reaction or hindered internal rotation. The important requirement is that the n.m.r. spectrum must be first order, i.e.: $J_{AB} \ll \delta_{AB}$ (10). Arnold (22) showed that in pure dry ethanol the -OH proton was split into a triplet by spin-spin interaction with the methylene group. This corresponds to the slow exchange limit and the resonance was shown to collapse into a singlet corresponding to fast exchange on addition of acid. By comparing theoretically derived line shapes calculated using an a priori value of the mean lifetime of a proton involved in the exchange reaction with experimental line shapes, a value of the exchange rate was derived.

The collapse of spin multiplets due to proton exchange has been used by Berger, Loewenstein and Meiboom (23) and by Takeda and Stejskal (16) to study the rate of protolysis of N-methylacetamide in aqueous solutions of various pH. The latter authors developed a theoretical treatment for analyzing the effect of exchange on a spin-spin doublet. Based on the work of Gutowsky, McCall and Slichter (12) they evaluate the mean lifetime $2\tau$ of a proton involved in an exchange reaction. From their equations, $2\tau$ is related to the frequency separation $\delta\omega_e$ between the two peaks in a spin-spin doublet produced by the exchanging proton for slow rates, to the width of the observed signal at half maximum $\delta\omega_{\frac{1}{2}}$ under conditions of fairly rapid exchange where a broad doublet is observed and, under rapid exchange conditions, to the ratio $I/I_o$, where I

is the maximum amplitude of the observed singlet and $I_o$ the expected maximum amplitude for $\tau = 0$.

All of these equations have been developed in full detail from the Bloch equations by Blears (24). Two possible processes must be distinguished. The first includes hindered rotation and conformational studies in which every rotation is effective in collapsing the multiplets. The second involves a chemical exchange reaction associated with a bond-breaking-bond-making process. In this case, for example for a proton exchange process between two equally populated sites, any exchange has a 50% chance of changing the environment of the nucleus since an incoming proton has equal probability of being in the same spin state or in the opposite spin state as the outgoing proton on the same site. Hence

3-49 $$k_{\text{chem. exchange}} = 2k_{\text{rotation}} = 2k$$

where k, the pseudo first-order rate constant is

3-50 $$k = \frac{1}{(2\tau)} = \frac{1}{\tau_A} = \frac{1}{\tau_B} \quad (\text{sec}^{-1})$$

for $\tau_A = \tau_B = 2\tau$.

In practice $k_{\text{rotation}}$ is calculated, from which $k_{\text{chem. exchange}}$ can easily be obtained for those cases involving a proton chemical exchange rather than internal rotation. The solutions of the modified Bloch equations for different rates as discussed earlier and by Takeda and Stejskal (16) and Blears (24) are in terms of $k_{\text{rotation}}$. This procedure will also be followed in this thesis. Taking this into account, the equation for fast rates of rotation involving the ratio $I/I_o$ is (16, 24)

3-51 $$\frac{I}{I_o} = \frac{\left(\frac{2}{t} + \frac{1}{Q}\right)}{\left(\frac{2}{t} + \frac{1}{Q} + \frac{Q}{4}\right)}$$

where

3-52 $$Q = T_2 \delta\omega = 2\pi T_2 J$$

3-53 $$t = \frac{\delta\omega}{k} = \frac{2\pi J}{k} .$$

$T_2$ is the spin-spin relaxation time of the nuclei under observation; $\delta\omega$ is the magnitude of the spin-spin interaction (or chemical shift) in angular frequency units in the absence of exchange; and J is the magnitude of this coupling in cps.

To obtain k for a fast exchange reaction using equation (3 - 51) it is necessary to know $T_2$ and J. $T_2$ is obtained using equation (3 - 44) by measuring peak width at half height when $2\tau = 0$ or from some unaffected portion of the spectrum. J is obtained from the spectrum when $2\tau = \infty$ (no exchange). I is measured at the various temperatures under consideration and compared with $I_o$ which is obtained either from the spectrum when $2\tau = 0$ or from another peak unaffected by exchange having an intensity simply related to $I_o$.

The GMS equations have also been extended to the exchange broadening of a quadruplet (25) and a triplet (26). Tables of calculated lineshapes of exchange broadened n.m.r. multiplets as a function of the exchange rate of the interacting nuclei have been compiled (27) and a comparison with the experimental lineshapes yields approximate rate constants.

## 4. Applications and Other Methods of Measuring Exchange Rates

Proton magnetic resonance has been used by various workers to study exchange reactions based on the above principles. A summary of the literature dealing with exchange reactions in aqueous and alcoholic

solutions up until 1964 is given by Reynolds and Schaefer (28). They studied proton exchange reactions of substituted anilines in trifluoroacetic acid by measuring the acid proton signal width. Blears (24) obtained theoretical values of the rate constant k using the various equations relating k to the line shapes based on two-site exchange with equal populations. From his computerized calculations k can be evaluated for a given set of conditions using any of the above methods.

Most of the work on exchange reactions has been discussed in the two most recent review articles (5, 9). Some more recent studies include the application of the coupling $J_{N^{15}-H}$ (29), a study of the protolysis kinetics of glycine (30), and a study of proton exchange involving ion pairs of ammonium salts in t-butyl alcohol (31-33). N.M.R. has shown that the hydroxyl proton exchange rate in methanol is enhanced appreciably by the presence of oxygen (34). The ammonia-amide proton exchange kinetics in liquid ammonia have also been studied (35). Recent papers on internal rotation and conformation studies include a consecutive inversion process at two nitrogens (36), the ring inversion in cyclohexane-$d_{11}$ (37) and rates of internal rotation around carbonyl-to-nitrogen bonds in various benzamides (38).

There have been other approaches to the exchange problem. Piette and Anderson (39) obtained a general equation for exchange between many sites. Quantum mechanical treatments, fast passage, spin-echo, and double resonance methods have now been used by many workers (5, 9).

## F. DETERMINATION OF RATE CONSTANTS AND ACTIVATION PARAMETERS

The pseudo first order rate constant k for an exchange reaction is given by equation (3 - 50)

3-50 $$k = \frac{1}{2\tau} (\sec^{-1}).$$

The activation energy $E_A$ for the reaction is obtained from the Arrhenius equation (40)

3-54 $$k = A\exp\left(\frac{-E_A}{RT}\right)$$

where A is the frequency factor. $E_A$ is therefore obtained from a plot of log k versus $\frac{1}{T}$. The slope of the line is equal to $\frac{-E_A}{2.303R}$ and the intercept is log A.

Enthalpies of activation $\Delta H^{\neq}$ at any temperature T are obtained from $E_A$ values. The two thermodynamic variables are related by

3-55 $$E_A = \Delta H_T^{\neq} + RT$$

The free energy of activation $\Delta G^{\neq}$ is calculated from the theory of absolute reaction rates (40)

3-56 $$k = \kappa \frac{k_b T}{h} \exp\left(\frac{-\Delta G_T^{\neq}}{RT}\right)$$

so that

3-57 $$\Delta G_T^{\neq} = 2.303RT \log\left(\frac{\kappa k_b T}{kh}\right)$$

or

3-58 $$\Delta G_T^{\neq} = 2.303RT\,(10.32 + \log \frac{T}{k}).$$

The transmission coefficient $\kappa$ is taken as one and represents the probability that the activated complex formed between reactants will decompose to form products rather than reactants. $k_B$ is the Boltzmann constant and h is Planck's constant.

The entropy of activation $\Delta S^{\neq}$ is obtained from

3-59 $$\Delta G_T^{\neq} = \Delta H_T^{\neq} - T\Delta S^{\neq}.$$

From these equations all the activation parameters can in principle be obtained once the rate constant k is determined from the line-shape equations of the n.m.r. spectrum. The reliability of these parameters depends on the accuracy of the measured k at various temperatures.

The quantitative measurements of rates and their temperature dependence are subject to systematic errors (9). First of all the line-shape theories assume that the parameters which describe a spectrum in the slow exchange limit can be used to calculate spectra for any exchange rate. However, these parameters often do change with concentration and temperature. The second shortcoming is the narrow temperature range over which the rates usually occur.

Recently (17) the systematic errors which arise in the measurement of exchange rates were analyzed. They were classified into two groups; mathematical and experimental. Mathematical problems arise when the actual system studied is treated in terms of an oversimplified theoretical model or when the model is adequate but a simplified equation is used beyond its region of accuracy (when various approximations do not hold). The experimental errors arise from instrumental instabilities, calibration errors and other spectral distortions. These include temperature drifts, frequency changes, magnetic field drifts, and variations in spinning rates.

The presence of systematic errors and the fact that several of the kinetic methods are applicable only over small temperature ranges is most

evident in the enthalpy and entropy of activation obtained from the temperature dependence of a rate process. For example, values of 7 to 24 kcal/mole have been obtained for the barrier to the hindered internal rotation of N,N - dimethylformamide (17). The rate constants and therefore the free energies of activation agree quite well. On the basis of their analysis Allerhand et al (17) find that the desirable method of determining exchange rates from n.m.r. spectra is by using computerized, complete line-shape fitting methods which do not neglect spectral complications unless their effects are less than other inaccuracies in the rates.

Another system which has been widely studied is the ring inversion of cyclohexane. The agreement between the $\Delta G^{\neq}$ values obtained by carrying out different n.m.r. kinetic experiments is good. However the $\Delta H^{\neq}$ values range from 9.0 to 11.5 kcal/mole and $\Delta S^{\neq}$ from -6.5 to +4.9 e.u. (37). Working with cyclohexane-$d_{11}$ and decoupling the deuterium nuclei, Anet and Bourn (37) obtained kinetic parameters for this process using both line-shape analysis and double resonance techniques. Agreement between both methods was very good. The magnitude of $\Delta G^{\neq}$ (10.22 kcal/mole) is in agreement with previous determinations but the values of $\Delta H^{\neq}$ (10.8 kcal/mole) and $\Delta S^{\neq}$ (2.8 e.u.), while agreeing with other high resolution work, did not agree with spin-echo measurements (41). These authors therefore conclude that since two methods give the same set of kinetic parameters, systematic errors must be responsible for the measurements using spin-echo techniques. From their results the advantages of line-shape analysis and the application of more than one method of obtaining

rate constants are seen. The error in $\Delta E$ is decreased since measurements over a larger temperature range are now possible.

Activation parameters obtained by line-shape measurements were recently compared (38) and agree with those determined by equilibration methods in the study of internal rotation around carbonyl-to-nitrogen bonds.

Allerhand et al (17) did not study the systematic errors involved in determining the rate constant k as a function of the ratio $\frac{I}{I_o}$ in equation (3 - 51). Blears (24) did and found that immediately after coalescence and as the rapid limit is approached, the rate constants assume limiting values and are most reliable in the intermediate region. In this equation the magnitude of the doublet splitting J observed at low temperatures should always equal the splitting at infinitely slow exchange. This may not be true when there is overlap between the two peaks or when the observed "infinitely slow exchange" separation is not the true value (24). Blears found that overlap effects and the incorrect selection of the splitting are not too important. This was also found in the system under consideration and will be discussed in the "Discussion of Results" section.

## G. THE INTRAMOLECULAR HYDROGEN BOND IN 3,5-DICHLOROSALICYLALDEHYDE

### 1. Hydrogen Bonding

Under certain conditions an atom of hydrogen is attracted by rather strong forces to two atoms instead of only to one. It thus acts as a bond between them. This bond is called the hydrogen bond (42). These atoms may be located on the same or on different molecules. In the former case the hydrogen bond is intramolecular while in the latter it is an intermolecular hydrogen bond.

A detailed treatment of the general subject of hydrogen bonds is given in the book by Pimentel and McClellan (43). Pauling (42) gives a general treatment. A Symposium (44) has been held on this subject and Jaffe (45) discusses the differences in energies between intra- and intermolecular hydrogen bonds.

Hydrogen bonds have been studied and detected using many techniques (43) with proton magnetic resonance (p.m.r.) and infrared spectroscopy best suited for carrying out these studies. A shift is observed in the vibrational spectra arising from hydrogen bond formation as measured in the infrared region (43). In proton magnetic resonance a low-field shift is observed for a proton between the unassociated and associated states, the only exceptions being connected with association with aromatic molecules (46). The p.m.r. studies of the hydrogen bond have been reviewed (46-48).

There are two main interpretations of the low-field p.m.r. shift on hydrogen bond (XH...Y) formation (46, 49-51):

1. A contribution to the proton screening (always negative) arises from

the distortion of the electronic structure of the chemical bond X-H in which the proton participates.

2. A negative (or positive) contribution to the proton screening will arise due to any magnetic anisotropy of the molecule Y to which the proton is hydrogen bonded. The first effect is predominant (46).

Reliable values of the thermodynamic functions of hydrogen bonds are derived from the equilibrium constant K (since an hydrogen bond is formed in an equilibrium reaction, the thermodynamic equations are applicable) and its variation with temperature (52). Of the various experimental techniques of determining K, the infrared method is probably the most useful (52). A tabulation of $\Delta$ H and $\Delta$ S values on hydrogen bond formation is given in Appendix B of reference (43). The data indicate that the enthalpies of formation of the O-H....O intermolecular hydrogen bonds in binary solutions range mostly from -3.5 to -5.0 kcal. per mole of hydrogen bond, with the largest number lying between -4.0 and -4.5 kcal. per mole (52). This does not include carboxylic acids which have enthalpies ranging from -6.5 to -7.5 kcal. per mole of hydrogen bond.

Employing infrared, p.m.r. and electronic spectroscopy, hydrogen bonding between various donors and acceptors has recently been investigated (53). The relations between $\Delta$ H, $\Delta$G, the OH stretching frequency shifts upon complexation $\Delta\nu_{OH}$, and other parameters were discussed. The above limits on O-H....O bond strengths were extended and the effects of acidity of the acceptor and the basicity of the donor on the thermodynamics of hydrogen bonding were investigated.

In p.m.r. the difference in the shift between a non-associated and

an associated state, or the hydrogen-bonded shift, is taken as a measure of the hydrogen bond energy (46). For intermolecularly hydrogen-bonded substances, dilution or an increase in the temperature decrease this shift difference. This has been interpreted in terms of the dissociation of the hydrogen bonds (46). However calculations (54) have shown that a large part of the observed temperature variation of the hydrogen-bonded shift may result from changes in the effective length of the H...O bond. These in turn arise from the anharmonicity and low frequency of the hydrogen bond stretching vibration. Hence temperature variations of the shift may not arise exclusively from hydrogen bond breaking (54).

In the infrared the OH stretching frequency shift upon complex formation $\Delta\nu_{OH}$ is also related to the strengths of the hydrogen bond (43). A linear relationship was established (55) between the enthalpy $\Delta H$ of the hydrogen-bond interaction of phenol with a series of bases and $\Delta\nu_{OH}$. The existence of such a relationship has now been verified theoretically (56). A similar relationship between the phenolic OH p.m.r. shift and $\Delta H$ has also been observed (57) for phenol-base systems under conditions of complete association in methylene chloride solvent. The phenol-base hydrogen-bonding interactions have $-\Delta H$ magnitudes ranging from 3 to 10 kcal. per mole of hydrogen bond.

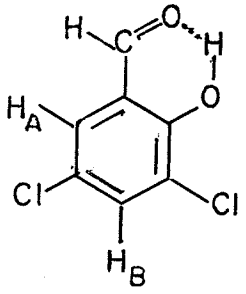
## 2. The Intramolecular Hydrogen Bond

Pimentel and McClellan (58) distinguish between intra- and intermolecular hydrogen bonds. The former form only under specific stringent spatial conditions and their formation does not create molecular association.

For intermolecular hydrogen bond formation, there are no spatial restrictions and most of the changes in physical properties are a direct result of association. The intramolecular hydrogen bonds generally occur in 5-, 6-, or 7-atom rings.

The compound under consideration in this thesis is 3,5-dichloro-salicylaldehyde (A).

A.




Most of the literature is concerned with the hydrogen bond in salicyl-aldehyde and related ortho-substituted phenols. The molecule under consideration was chosen because the two chloro substituents greatly simplify the ring-proton spectrum. This allows an accurate determination of relative peak heights which are required when the exchange rates are computed using equation ( 3 - 51). The intramolecular hydrogen bond in salicylaldehyde will first be considered, compared with the hydrogen bond in other ortho-substituted phenols, and then the effect of the two chloro substituents will be discussed.

The existence of the strong, intramolecular hydrogen bond in salicylaldehyde is confirmed by evidence from many sources, many of which are summarized in reference (58). It melts at 266°K whereas parahydroxy-benzaldehyde (with an intermolecular hydrogen bond) melts at 388°K. A frequency shift in the ultraviolet and infrared regions, an increase in the rates of several reactions, a low-field p.m.r. hydroxyl proton shift, a decrease in the viscosity, all with respect to parahydroxybenzaldehyde,

support the presence of this bond (58, and references therein). Several recent studies of this bond besides p.m.r. and infrared spectroscopy include dipole measurements in benzene, para xylene and dioxane (59-61). The results indicate that the hydroxyl group in salicylaldehyde is still strongly intramolecularly hydrogen bonded even when these solvents are present in solution. This results in spite of the fact that the hydroxyl proton is capable of forming an intermolecular bond with dioxane and with the $\pi$ -electron cloud of the aromatic ring. Infrared data for methyl salicylate (intramolecularly hydrogen bonded) in dioxane and carbon tetrachloride confirmed that the intramolecular hydrogen bonds are sufficiently strong to resist fission in dioxane (59). Dipole moment measurements (62) on salicylaldehyde in benzene are consistent with the intramolecular hydrogen bond as are photoreactions in benzene solution (63).

Most of the evidence is obtained using p.m.r. and infrared techniques and the results from both methods are very often correlated. As well, the intramolecular hydrogen bonds in salicylaldehyde and related ortho-substituted phenols, especially ortho-halophenols are very often compared. These studies have been carried out by many workers (42, 43, 50, 64-95).

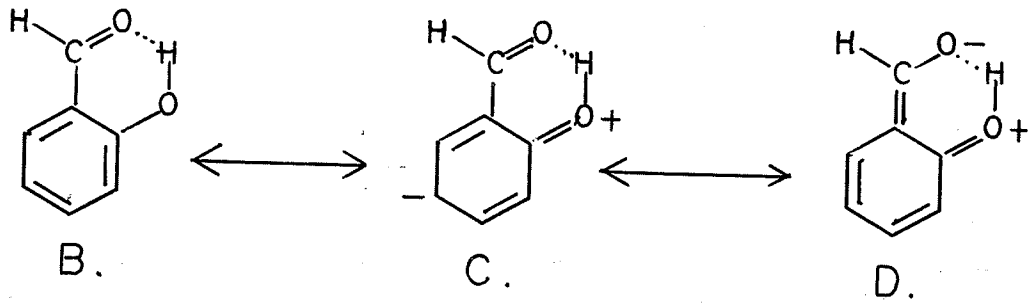
Pauling (42) summarizes spectroscopic evidence showing that the bond in salicylaldehyde is strong and compares it with the hydrogen bond in orthochlorophenol. In carbon tetrachloride solution the latter molecules are present in both the cis and trans configurations of the hydroxyl group with respect to the chlorine substituent. The cis form outnumbers the trans because of the stabilizing influence of the weak intramolecular OH....Cl interaction. In salicylaldehyde only the cis configuration is present.

The C = O bond stretching frequency $\nu_{CO}$ in the infrared decreases from 1709 $cm^{-1}$ in benzaldehyde to 1669 $cm^{-1}$ in salicylaldehyde (in carbon tetrachloride solution) (70) due to the formation of the intramolecular bond. Similarly the OH stretching frequency $\nu_{OH}$ decreases from 3611 $cm^{-1}$ in phenol (monomer) (66, 74, 90) to 3150 $cm^{-1}$ in salicylaldehyde (70, 80). The $\nu_{OH}$ frequencies are approximate since these bands are very broad. However, there is some disagreement over the $\nu_{OH}$ frequency in salicylaldehyde (3255 $cm^{-1}$ in carbon tetrachloride) (90).

The p.m.r. shift of the phenolic proton in the latter molecule, due to the deshielding effect of the C = O group, occurs at very low field - approximately 10.9 p.p.m. to low field of TMS (also in carbon tetrachloride) (80, 87). As well, substituted phenols capable of forming strong intramolecular hydrogen bonds may exhibit a long-range coupling between the hydroxyl and one ring proton (94 and references therein). The hydrogen bond is required in order to reduce the rate of intermolecular proton exchange (94) but mainly to hold the proton in the correct steric configuration since the long-range hydroxyl spin couplings are stereospecific and follow the "straightest zig-zag path" (96). The same stereospecificity is observed in the long-range aldehyde couplings in substituted benzaldehydes (79, 93, 96, 97). In salicylaldehyde, with the -CHO group in the 1-position, the -CHO proton couples to the ring proton in the 3-position, whereas the -OH proton couples with the ring proton in the 4-position. These stereospecific long-range couplings occur over five bonds and are positive (93, 94).

The hydrogen bond in salicylaldehyde (B) is stabilized by resonance structures of the form (C) and (D) (84). All of these form a sterically

favourable 6- membered ring.



B. C. D.

The effect of the chlorine atoms on the hydrogen bond strength in 3,5-dichlorosalicylaldehyde will now be considered. Nagakura (98) found that for intermolecular reactions of phenol and ortho-, meta- and parachlorophenol with methyl acetate in n-heptane, substitution of a chlorine atom for a hydrogen atom increases the proton-donating power of phenol (exception - orthochlorophenol) due to the inductive effect of the chlorine atom. Based on the acid dissociation constants of the isomeric chlorosalicylaldehydes in water, the intramolecular bond was weakened least by chlorine substitution in the 3-position and most in the 5-position (88). This was supported by the hydroxyl proton shifts (88). However Nyquist (84) studied the OH out of plane deformation fundamental $\gamma_{OH}$ and the OH stretching frequency $\nu_{OH}$ in the infrared of 5-chlorosalicylaldehyde and salicylaldehyde. Both of these frequencies are related to the strength of the intramolecular hydrogen bond. However, the $\nu_{OH}$ values indicate a slight increase in this bond strength going from salicylaldehyde to 5-chlorosalicylaldehyde whereas the $\gamma_{OH}$ frequencies indicate a small decrease (84). These results indicate that a 5-chloro-substituent does have an effect on the hydrogen bond strength but that it must be small.

This is substantiated by the study of the substituent effects on

the intramolecular hydrogen bond in 2-hydroxyacetophenone. In this molecule the hydrogen bond is stronger than in salicylaldehyde as seen by the low frequencies $\nu_{OH}$ (3025 $cm^{-1}$) and $\nu_{CO}$ (1646 $cm^{-1}$) in carbon tetrachloride solution (70). This assumes that the decrease in these stretching frequencies with respect to those observed in salicylaldehyde corresponds to an increase in bond strength, possibly due to the electron releasing properties of the methyl group as compared to a hydrogen atom. The $\gamma_{OH}$ frequency also supports the increased bond strength (84).

Considering now a substituent effect, Yoshida and Haruta (99, 100) find that in 5-substituted-2-hydroxyacetophenones, the strength of the hydrogen bond increases with an increase in the electron withdrawing properties of the substituent. However the $\gamma_{OH}$ frequency indicates that the bond strength decreases slightly in going to 5-chloro-2-hydroxyacetophenone (84).

The strength of the hydrogen bond has not been determined in 3,5-dichlorosalicylaldehyde. From the above evidence it is difficult to say whether the bond strength will increase or decrease relative to that of salicylaldehyde by the addition of two chloro substituents. However, their effect is expected to be small.

### 3. Intermolecular Proton Exchange

Forsen and Hoffman (101) have applied the techniques of nuclear magnetic double resonance to the study of proton exchange rates in a mixture of salicylaldehyde and 2-hydroxyacetophenone (5.65: 1 ratio) in $CS_2$, catalyzing the exchange with a trace of acetic acid. The lifetimes of the protons in these two molecules are 11.53 and 2.17 seconds res-

pectively. This was an exploratory study to test the principles of the above method, so that these lifetimes are subject to error.

Before an intramolecularly-bonded proton may exchange with a site on another molecule, the hydrogen bond must first be broken. Again consider salicylaldehyde. This may occur by twisting either the -OH group, or the -CHO group, or both out of the plane of the benzene ring. Studies of benzaldehyde have revealed evidence of a barrier to internal rotation about the C-CHO bond, presumably because it has partial double bond character (102). This also supports evidence in favour of a planar benzaldehyde molecule. Anet and Ahmad (102) have determined the free energy of activation $\Delta G^{\neq}$ for this hindered rotation to be 7.9 kcal/mole (at -123°C). Various para-substituted benzaldehydes have also been studied (102, 103). The internal rotation of the -OH group about the C-O bond in phenol is also hindered because of conjugation effects with the ring $\pi$ -electrons and the consequent partial double bond character of the C-O bond. Evans (104) has estimated the 2-fold barrier to rotation by infrared to be 3.4 kcal/mole whereas microwave data indicates it is 3.3 kcal/mole (105).

## NATURE OF THE PROBLEM

In the study of the long-range coupling constant between the phenolic proton and ring proton $H_4$ (hereafter referred to as $H_B$) in 3,5-dichlorosalicylaldehyde, it was found that by increasing the temperature of a solution of this compound the magnitude of the splitting decreased. By increasing the temperature still further, this splitting could be eliminated altogether.

Since the long-range coupling is associated with the intramolecular hydrogen bond and will disappear when this bond is broken, temperature studies were therefore carried out to study this hydrogen bond and associated proton exchange reactions further. From the data, proton exchange rate constants and thermodynamic activation parameters were obtained.

# EXPERIMENTAL METHODS

## A. COMPOUNDS

The compound 3,5-dichlorosalicylaldehyde was obtained from Frinton Laboratories and was recrystallized from benzene before use. For some confirmatory experiments it was also recrystallized from carbon tetrachloride and ether. 5-chlorosalicylaldehyde was obtained from Eastman Organic Chemicals and was recrystallized twice from benzene. The compound 3,5-dibromosalicylaldehyde, from Aldrich Chemical Co., was used without further purification.

The solvents acetone, acetonitrile, benzene, carbon disulfide, carbon tetrachloride, cyclohexane and methylene chloride were spectro-quality grade from Matheson, Coleman and Bell. The other solvents used were: benzene-$d_6$ and chloroform-d from Merck, Sharp and Dohme Co. of Canada Ltd., hexafluorobenzene from Pierce Chemical Co., dimethylsulfoxide from Aldrich Chemical Co., and tetramethylsilane from Nuclear Magnetic Resonance Specialties. Carbon tetrachloride was purified and dried by passing it through Linde molecular sieve 4A which was heated to 400°C before use. Dimethylsulfoxide was dried over calcium hydride and fractionally distilled at atmospheric pressure. The fraction taken distilled at 189-190°C (106). All other solvents were used without further purification. Several experiments were carried out in highly purified acetone but these will be discussed in the "Experimental Results" chapter.

## B. PROTON MAGNETIC RESONANCE MEASUREMENTS

All compounds in solution were studied with 1 - 2 mole % tetramethylsilane (TMS) as internal reference using the previously described experimental procedures. All solutions were degassed by the freeze-pump-thaw technique before the spectra were obtained.

The ring proton spectrum of 3,5-dichlorosalicylaldehyde belongs to the AB system. Since in most solvents at room temperature proton $H_B$ also couples with the phenolic proton, the two resonances corresponding to $H_B$ were split into doublets. A doublet was also observed for the phenolic proton resonance in these solvents. However, it was always slightly broader than the two ring proton doublets.

The analysis of the spectrum was straightforward. The long-range coupling constant $J_{OH-H_B}$ was obtained by simple spacing rules from the ring proton and the phenolic proton spectra. The ring proton coupling $J_{AB}$ and the $H_A$ and $H_B$ proton shifts were obtained by an AB analysis. The phenolic and aldehydic proton shifts were obtained by first order rules. The aldehydic proton resonance was a sharp singlet. The same procedure was applied in the analysis of the spectrum of 3,5-dibromosalicylaldehyde.

The molecule 5-chlorosalicylaldehyde exhibits two long-range coupling constants. The aldehydic proton couples with the ring proton in the 3-position with a coupling $J_{CHO-H_3}$. The phenolic proton couples with the ring proton in the 4-position, as in 3,5-dichlorosalicylaldehyde, with a coupling $J_{OH-H_B}$. The magnitudes of these two long-range couplings, as well as the phenolic and aldehydic proton shifts were determined by first order rules. The ring proton couplings and shifts were obtained by an ABC analysis.

The $H_B$ proton shift of 3,5-dichlorosalicylaldehyde in most solvents occurred to low field of the $H_A$ proton shift. However in $C_6F_6$ the two doublets corresponding to proton $H_B$ occurred to high field. The question arose: is this a solvent shift or does the zig-zag long-range coupling constant rule break down in this solvent and is a coupling $J_{OH-H_A}$ present? This problem was resolved by studying the spectra of 3,5-dichlorosalicylaldehyde in $CS_2$ - $C_6F_6$ solutions. As well, spectra of this compound were studied in $CS_2$ - Acetone solutions.

All spectra were recorded and calibrated at least four times. The shifts are reported with an accuracy of $\pm$ 0.005 ppm. Several phenolic proton shifts were exceptions where these resonances were very broad and hence the shifts were harder to measure. These are indicated in the experimental data. The errors in the coupling constants are standard deviations from the mean.

Temperature studies on 3,5-dichlorosalicylaldehyde solutions were also carried out. These will now be considered. When the temperature of the benzene - $d_6$ solution was raised above room temperature, the magnitude of the long-range coupling decreased until at the coalescence temperature the two doublets corresponding to proton $H_B$ collapsed into two broadened singlets. As the temperature was raised above the coalescence point these peaks became sharper until finally they were nearly identical in height and width at half height with the peaks corresponding to proton $H_A$. The latter proton and the corresponding resonances were not affected by the temperature. Hence this was an ideal system for studying proton chemical exchange reaction rates by means of

equation (3-51), which applies above the coalescence temperature. By applying this equation to the experimental data, the first order rate constant k for proton exchange is easily obtained. The relative peak heights $I/I_o$ are straightforward to measure since the exchanging and the non-exchanging proton resonances are close together in the spectrum. $T_2$ at every temperature is obtained in the absence of exchange from the line widths at half height $\Delta\nu_{\frac{1}{2}}$, of the $H_A$ proton peaks.

The experimental procedure was as follows. Several solutions of 3,5-dichlorosalicylaldehyde at different concentrations in benzene-$d_6$ were prepared with TMS as internal reference and were then degassed. Each sample was warmed in an oil bath to about 120-130°C to check whether the tubes could withstand the added pressure. The proton spectra were then determined every 2 or 3 degrees until the coalescence temperature was reached. At least an hour was allowed for the solution to come to equilibrium at each temperature before the spectra were recorded. Longer equilibration times had no effect.

Above the coalescence temperature a systematic analysis of the spectra was carried out every 5 to 10 degrees. The resoltuion was always at an optimum and was checked by the appearance of the ring proton $H_A$ peaks, or the aldehydic proton peak. Saturation effects were always checked for and eliminated by observing the spectra at low r.f. intensities. All spectra were recorded with the same sweep times. However, confirmatory experiments were carried out with different sweep times to check for slow passage conditions.

At least 8 measurements of the relative heights $I/I_o$ were obtained, two from each calibration of the spectrum at each temperature. The base line of each spectrum was extended after the resonances were recorded and

peak height measurements were determined with respect to it with a ruler. The peak widths at half height corresponding to the non-exchanging proton $H_A$ were determined at each temperature. At least 8 measurements were always obtained. The errors quoted for the relative heights and peak widths at half height correspond to standard deviations from the mean. All the solutions were studied in the above manner.

Before k can be calculated from equation (3 - 51), the magnitude of the long-range coupling $J_{OH-H_B}$ in the absence of exchange must be known. This was determined by studying a weak solution (1 mole %) at the lowest possible temperature, 9.3°C, where exchange effects are expected to be nearly zero. Studies at a lower temperature in benzene-$d_6$ could not be carried out due to the poor resolution at temperatures near the freezing point of benzene. Spectra above 110°C were also hard to obtain due to the bumping of the solution above the benzene boiling point.

All temperatures were determined before and after each calibration using an ethylene glycol or a methanol sample and a calibration graph of internal shift versus temperature. This was prepared by Varian Associates, Palo Alto, California. The temperature never changed by more than one degree from the beginning of the spectral calibrations until the end. This corresponds to a time interval of about two to three hours in which temperature equilibration was attained, resolution adjusted, a saturation check carried out, and at least four ring proton, phenolic and aldehydic proton calibrations carried out. The precision in measuring the temperature is estimated at $\pm 0.5$°C.

The rate constants for proton exchange could not be determined

by studying the phenolic proton doublet. These peaks were always slightly broader at room temperature than the corresponding $H_B$ proton doublets. As the temperature was increased they collapsed and further broadened. Hence several processes are thought to affect the phenolic proton resonance line widths. The aldehydic proton resonances were always sharp and these line widths at half height were temperature independent.

The rate constant k for proton exchange was calculated for all the solutions using equation (3 - 51). Since the rates change with the concentration of 3,5-dichlorosalicylaldehyde, an intermolecular exchange process must take place and the actual $k_{exchange}$ magnitudes are twice the measured k. The least squares analyses of the data were carried out on the IBM-360 computer at the University of Manitoba. The regression analysis program was obtained from E.T. van der Kouwe. As well, several of these analyses were carried out on a desk calculator.

## C. INFRARED MEASUREMENTS

The infrared spectra were obtained at room temperature using a Perkin-Elmer 337 Grating Spectrophotometer. The C=O stretching frequencies were calibrated on a 10 inch strip-chart Honeywell recorder with calibration bands obtained from an indene reference. A 0.025 mm. cell was used.

# EXPERIMENTAL RESULTS

All of the proton chemical shifts determined in this study are in ppm to low field of internal TMS and all the coupling constants are in cps.

The proton chemical shifts and coupling constants of 3,5-dichlorosalicylaldehyde (A) in various solvents are given in Table 3-I. The $J_{OH-H_B}$ values are the average of the ring proton and the phenolic proton splittings. Both coupling constants $J_{AB}$ and $J_{OH-H_B}$ are positive (94).

The $H_B$ ring-proton shift was assigned to low field with respect to the $H_A$ ring proton shift on the basis of the zig-zag long-range coupling rule in those solvents where the long-range coupling was observed. An exception was $C_6F_6$ in which the $H_B$ proton resonance occurred to high field. This was shown to arise from a solvent shift and not from a breakdown of the zig-zag rule by studying 3,5-dichlorosalicylaldehyde in $C_6F_6$ - $CS_2$ solutions. The proton shifts are given in Table 3-II and Figure 3-1 from which it is seen that increasing the concentration of $C_6F_6$ in solution shifts the $H_A$ proton resonance to low field, below that of the $H_B$ proton resonance.

Table 3-I

Proton chemical shifts[1] and coupling constants [2] for 3,5-dichlorosalicylaldehyde in various solvents at 30°C.

| Solvent | Concentration (mole %) | $\tau_B$ ( $\tau_4$) | $\tau_A$ ( $\tau_6$) | $\tau_{CHO}$ | $\tau_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ |
|---|---|---|---|---|---|---|---|
| $C_6H_{12}$ | < 2.5 | 7.479 | 7.282 | 9.710 | 11.283 | 2.52±0.03 | 0.59±0.03 |
| $CCl_4$ [3] | < 5 | 7.555 | 7.409 | 9.823 | 11.239 | 2.49±0.05 | 0.55±0.04 |
| $C_6H_6$ | 5 | ——[4] | 6.424 | 8.740 | 11.410 | 2.55±0.03 | —— |
| $C_6D_6$ | 5 | 7.047 | 6.418 | 8.734 | 11.413 | 2.54±0.03 | 0.55±0.03 |
| $C_6F_6$ | < 5 | 7.478 | 7.526 | 9.943 | 11.264 | 2.52±0.03 | 0.46±0.03 |
| $CS_2$ | < 5 | 7.494 | 7.392 | 9.806 | 11.234 | 2.52±0.03 | 0.54±0.03 |
| $CDCl_3$ | 5 | 7.581 | 7.470 | 9.841 | 11.333 | 2.51±0.03 | 0.57±0.03 |
| $CH_2Cl_2$ | 5 | 7.586[5] | 7.497 | 9.835 | 11.336[5] | 2.51±0.03 | ——[5] |
| $(CH_3)_2CO$ | 5 | 7.708 | 7.807 | 10.034 | 11.363 | 2.57±0.03 | —— |
| $CH_3CN$ | < 5 | 7.646 | 7.646 | 9.859 | 11.271 | —— | —— |
| DMSO[3,6] | 5 | 7.702 | 7.814 | 10.143 | ——[7] | 2.65±0.03 | —— |

Footnotes to Table 3-I.

1. All proton chemical shifts are in ppm to low field of internal TMS.
2. All coupling constants are in cps.
3. Purified as described under "Experimental Methods".
4. Under solvent peak.
5. The peaks were broadened but definite splittings were hard to calibrate.
6. Dimethylsulfoxide.
7. Not observed.

Table 3-II

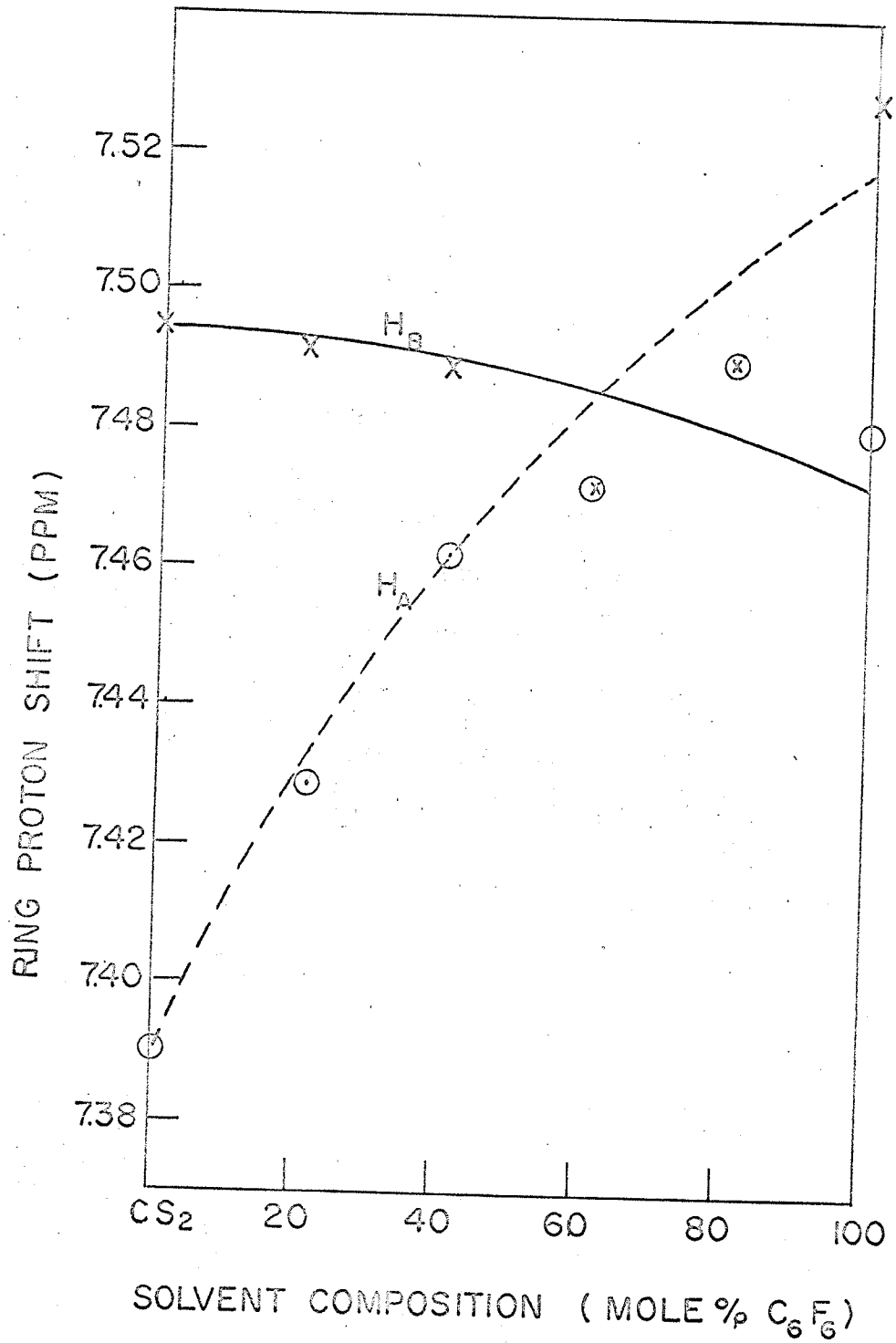
Proton chemical shifts and coupling constants for 3,5-dichlorosalicylaldehyde[1] in $C_6F_6$ - $CS_2$ solutions at 30°C.

| Solvent Composition (mole% $C_6F_6$) | | Low-field proton shift | High-field proton shift | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ |
|---|---|---|---|---|---|---|---|
| 0 | ($CS_2$) | 7.494[2] | 7.392 | 9.806 | 11.234 | 2.52±0.03 | 0.54±0.03 |
| 20 | | 7.491[3] | 7.428 | 9.830 | 11.232 | 2.50±0.04 | ----- |
| 40 | | 7.488[2] | 7.460 | 9.863 | 11.233 | 2.59±0.04 | 0.34±0.03 |
| 60 | | 7.471 | 7.471 | 9.873 | 11.238 | ----- | ----- |
| 80 | | 7.488 | 7.488 | 9.907 | 11.248 | ----- | ----- |
| 100 | ($C_6F_6$) | 7.526 | 7.478[2] | 9.943 | 11.264 | 2.52±0.03 | 0.46±0.03 |

1. Present in all solutions in concentrations $< 5$ mole %.
2. Coupled to the phenolic proton.
3. Coupling to phenolic proton difficult to resolve.

Figure 3-1

The ring proton chemical shifts of 3,5-dichlorosalicylaldehyde in $C_6F_6$ - $CS_2$ solutions at 30°C as a function of solvent composition. The shifts are in ppm to low field of internal TMS. The x indicates the low-field proton shift whereas the O indicates the high-field proton shift.


7.52
7.50
7.48
7.46
7.44
7.42
7.40
7.38
RING PROTON SHIFT (PPM)
$H_B$
$H_A$
$CS_2$
20
40
60
80
100
SOLVENT COMPOSITION ( MOLE % $C_6F_6$ )

When the preliminary experiments in this study were carried out, a 5 mole % solution of 3,5-dichlorosalicylaldehyde in acetone was prepared. Both were used as obtained commercially without special purification procedures. The acetone was spectroquality grade. The solution was degassed with TMS as an internal reference.

When the p.m.r. spectrum of this solution was obtained, the two high-field ring proton lines of the AB spectrum were considerably broader than the two low-field lines. This suggested that the high-field ring proton couples with the phenolic proton. Therefore the acetone solution was studied at several low temperatures and a $J_{OH-H_B}$ splitting of 0.47 cps was observed at -7.3°C. The solution was then studied over a temperature range from -7.3°C to +68.5°C and the ring, phenolic and aldehydic proton shifts were determined. The coalescence temperature was approximately 29°C. Above this temperature the relative heights $I/I_o$ were measured together with the line widths at half height of the low-field AB doublet. The proton chemical exchange rate constants were calculated using equation (3 - 51).

A complete study of 3,5-dichlorosalicylaldehyde in acetone solutions was then planned. Several solutions were prepared. However the long-range coupling between the ring proton and the phenolic proton could never again be observed. Many experiments were tried. The compound was used without further purification, after being recrystallized from $CCl_4$, from acetone or from ether. Another sample of this compound was obtained from Frinton Laboratories and tried. Acetone was purified in many ways. It was refluxed for several hours with $KMnO_4$, then consecutively distilled,

dried over $CaCl_2$ and redistilled. It was kept over alumina. Acetone from several manufacturers was tried. After these purification processes were carried out, many solutions were prepared, many in a dry box and all were degassed. The vacuum line was flamed out before each preparation. Solutions were tried with and without internal TMS.

Solution preparations were also carried out on the vacuum line. The compound was recrystallized from acetone, placed in an n.m.r. tube, attached to the vacuum line, warmed slightly and degassed. Acetone, purified by the $KMnO_4$ process, was placed over $CaH_2$, degassed on the vacuum line and vacuum distilled into the n.m.r. tube. Irrespective of the conditions under which the solutions were prepared, the ring proton spectrum always consisted of a symmetrical AB quartet with no evidence of a long-range coupling, evan at -15°C.

Finally, B. Richardson prepared a 5 mole % solution as he normally would for obtaining an n.m.r. spectrum, with the same result. Consequently no further temperature studies were carried out on acetone solutions.

One interesting result emerged from this study however, which showed that in acetone, as in $C_6F_6$, the $H_B$ ring proton shift is to high field with respect to the $H_A$ proton shift. This was confirmed by studying the spectra of 3,5-dichlorosalicylaldehyde in acetone -$CS_2$ solutions. The results, in Table 3-III and Figure 3-2, show the acetone solvent shift on the $H_A$ proton. The phenolic proton resonance was very broad ( $\sim$30 cps at half height) in solutions with low acetone concentrations and became sharper as the acetone concentration increased. The reason for this is not known.

Table 3-III

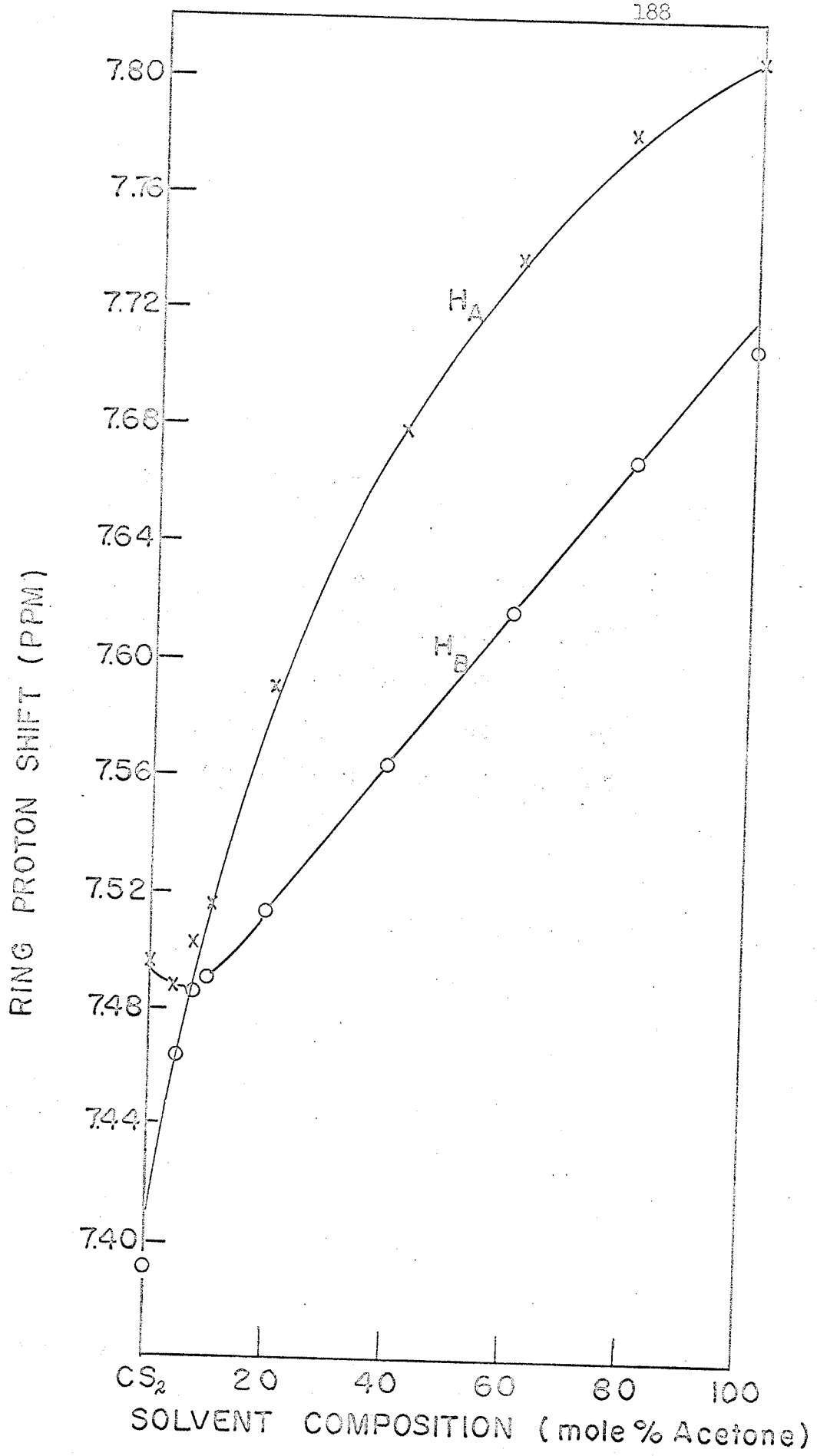
Proton chemical shifts and coupling constants for 3,5-dichlorosalicylaldehyde (A) in Acetone -$CS_2$ solution at 30°C.

| Conc. A. (mole %) | Solvent composition (mole % acetone) | Low-field proton shift | High-field proton shift | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ |
|---|---|---|---|---|---|---|
| < 5 | 0 ($CS_2$) | 7.494(1) | 7.392 | 9.806 | 11.234±0.05 | 2.52±0.03 |
| < 5 | 5 | 7.488 | 7.465 | 9.839 | 11.20 ±0.05 | 2.50 |
| < 5 | 8 | 7.506 | 7.487 | 9.856 | 11.20 ±0.05 | 2.51 |
| < 5 | 10 | 7.515 | 7.490 | 9.861 | 11.23 ±0.03 | 2.51 |
| 5 | 20 | 7.588 | 7.514 | 9.901 | 11.27 ±0.03 | 2.53 |
| 5 | 40 | 7.678 | 7.563 | 9.953 | 11.30, ±0.01 | 2.53 |
| 5 | 60 | 7.737 | 7.617 | 9.989 | 11.33 ±0.01 | 2.55 |
| 5 | 80 | 7.779 | 7.668 | 10.016 | 11.347±0.005 | 2.55 |
| 5 | 100 | 7.807 | 7.708 | 10.034 | 11.363±0.005 | 2.57 |

1. Coupled to the phenolic proton

Figure 3-2

The ring proton chemical shifts of 3,5-dichlorosalicylaldehyde in Acetone - $CS_2$ solutions at $30^{\circ}C$ as a function of solvent composition. The shifts are in ppm to low field of internal TMS. The x indicates the low-field proton shift whereas the o indicates the high-field proton shift.


7.80
7.76
7.72
7.68
7.64
7.60
7.56
7.52
7.48
7.44
7.40
RING PROTON SHIFT (PPM)
$H_A$
$H_B$
$CS_2$
20
40
60
80
100
SOLVENT COMPOSITION (mole % Acetone)

In Table 3-I the $H_B$ ring proton shift in DMSO was assigned to higher field than the $H_A$ proton shift, in analogy with the acetone spectrum.

The assignment of the $H_B$ proton resonance to low field with respect to the $H_A$ proton resonance in most solvents is supported by other evidence. The molecule 3,5-dibromosalicylaldehyde was studied in $CS_2$ (Table 3-IV). If the $H_B$ proton resonance occurs at low field in the dichloro compound, it should occur at even lower field in the dibromo compound relative to the $H_A$ proton resonance. And it does. The internal shift is 0.213 ppm whereas in the dichloro compound it is 0.102 ppm. This is in agreement with the larger ortho $Q$ effect of the bromine atom as compared with the chlorine atom (107).

Conclusive evidence for the above proton assignment comes from a study of 5-chlorosalicylaldehyde in $C_6D_6$ since the replacement of a chlorine atom by a hydrogen atom in the aromatic nucleus should have little effect on the $H_B$ proton shift. This is based on the nearly equal ortho $Q$ effect of these two atoms (107). Also an unequivocal assignment of the p.m.r. spectrum of this molecule may be made since 3 ring protons are present and the 3 ring proton coupling constants are all different. The spectrum is given in Figure 3-3 from which it is seen that the $H_B$ proton resonance occurs to lowest field and exhibits the long-range coupling with the phenolic proton. The aldehydic proton couples according to the zig-zag rule with the $H_C$ ring proton.

Decoupling experiments were carried out on both the phenolic and the aldehydic protons to confirm the assignment of the long-range coupling constants. The ABC analysis was carried out on the decoupled spectra.

Table 3-IV

Proton chemical shifts and coupling constants for 3,5-dibromosalicylaldehyde in $CS_2$ (5 mole %) at 30°C.

$\nu_B$ = 7.778 ppm.
$\nu_A$ = 7.565 ppm.
$\nu_{CHO}$ = 9.757 ppm.
$\nu_{OH}$ = 11.351 ppm.

$J_{OH-H_B}$ = 0.47±0.03 cps.
$J_{AB}$ = 2.35±0.04 cps.

Table 3-V

Proton chemical shifts and coupling constants for 5-chlorosalicylaldehyde in $C_6D_6$ (5 mole %).

a. At 30°C.

$\nu_A$ ( $\nu_6$) = 6.674 ppm.
$\nu_B$ ( $\nu_4$) = 6.866 ppm.
$\nu_C$ ( $\nu_3$) = 6.507 ppm.
$\nu_{CHO}$ = 8.931 ppm.
$\nu_{OH}$ = 11.094 ppm.

$J_{AB}$ = 2.67±0.03 cps.
$J_{BC}$ = 8.91±0.03 cps.
$J_{AC}$ = 0.43±0.03 cps.
$J_{OH-H_B}$ = 0.46±0.01 cps.
$J_{CHO-H_C}$ = 0.63±0.01 cps.

The sum of squared deviations in intensities between calculated and observed ring proton ABC spectra = 0.0198

b. At 95°C.

$\nu_{CHO}$ = 9.111 ppm.

*$J_{CHO-H_C}$ = 0.64±0.02 cps

The splitting due to $J_{OH-H_B}$ has nearly disappeared.

* Also observed at 115°C.

Figure 3-3

The proton magnetic resonance spectrum of a 5 mole % solution of 5-chlorosalicylaldehyde in $C_6D_6$ at 30°C.

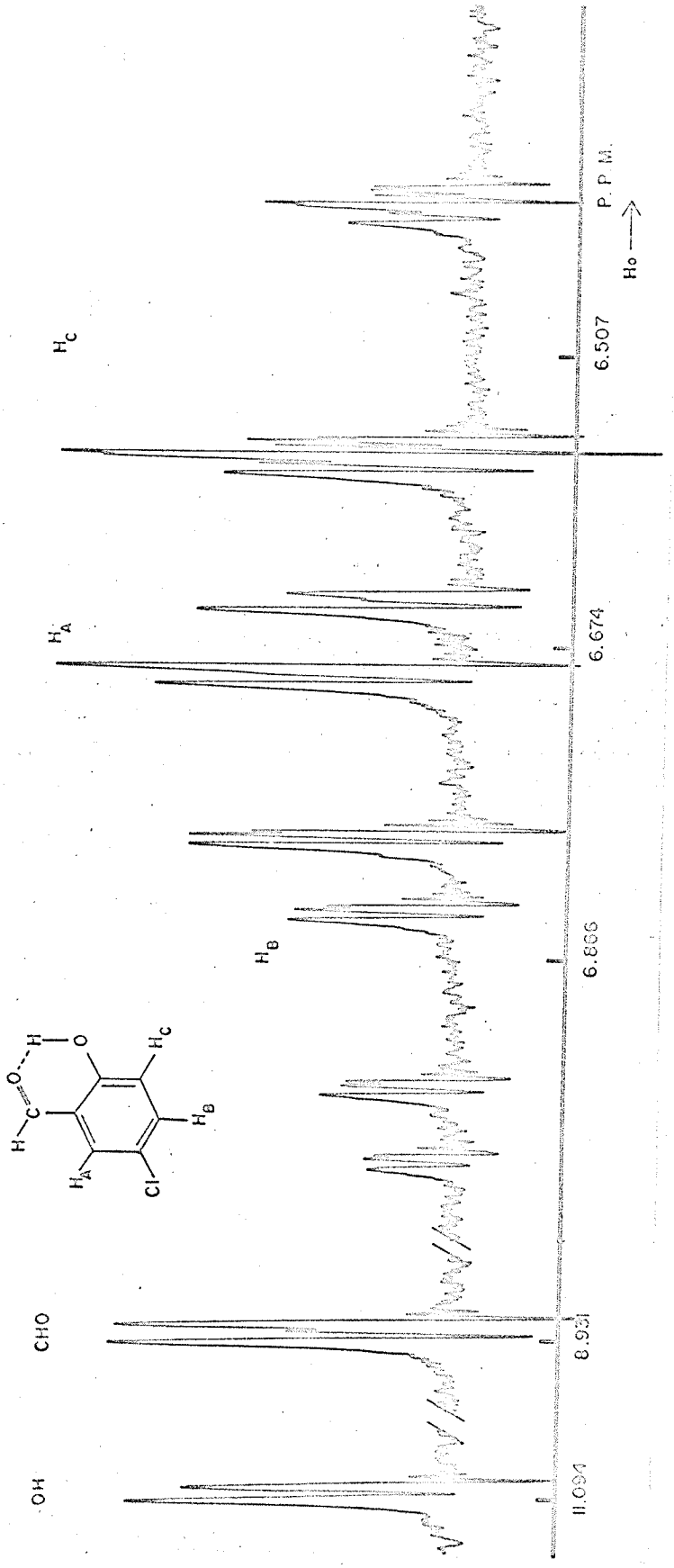

OH
CHO
$H_B$
$H_A$
$H_C$
11.094
8.931
6.866
6.674
6.507
P.P.M.
Ho
O
H
C
Cl

Table 3-V gives the proton chemical shifts and coupling constants for this molecule.

Once the proton assignments of 3,5-dichlorosalicylaldehyde were complete, temperature studies were carried out on solutions of this molecule. Studies of the $CS_2$, $C_6H_{12}$ and $CCl_4$ solutions showed that the exchange rates were sufficiently slow in these solvents so that a complete coalescence of the splittings arising from the coupling $J_{OH-H_B}$ could not be observed, even at temperatures of $\sim$ 110°C. In $C_6D_6$ the proton exchange rates were sufficiently rapid so that the coalescence temperature was well below the boiling point of the solvent and a sufficiently large temperature range was available over which the relative heights $I/I_o$ could be measured. Therefore there is a solvent effect on proton exchange rates.

The proton magnetic resonance spectrum of a 5 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$ at magnet temperatures (30°C) is given in Figure 3-4. The results of the temperature studies of $C_6D_6$ solutions are tabulated in Tables 3-VI to 3-XI. The widths at half height $\Delta\nu_{\frac{1}{2}}$ of the peaks corresponding to the non-exchanging proton ($H_A$) are in cps. The heights (I) of the exchanging proton ($H_B$) peaks with respect to the heights ($I_o$) of the non-exchanging proton peaks are absolute numbers.

The results of a temperature study of a saturated solution of 3,5-dichlorosalicylaldehyde in $CCl_4$ ( $<$ 5 mole %) are given in Table 3-XII, even though proton exchange studies could not be carried out on this solution. This solution was also studied with cyclohexane instead of TMS as an internal reference but this data is not included in Table 3-XII. This enabled temperatures of $\sim$ 120°C to be reached but the rate of proton exchange was still to slow to be measured.

Figure 3-4

The proton magnetic resonance spectrum of a 5 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$ at 30°C.

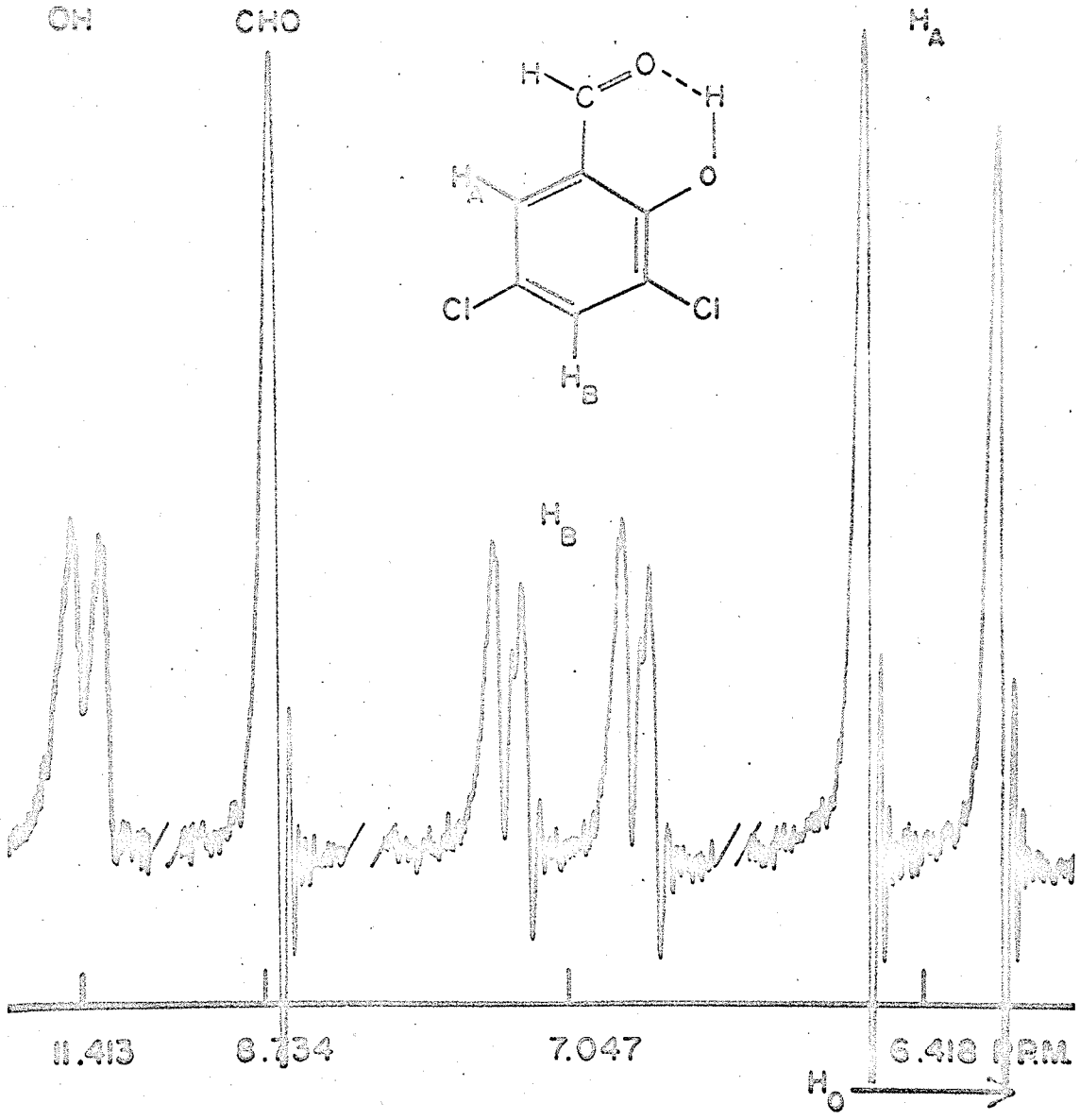

OH
CHO
$H_A$
H
C
O
O
H
$H_A$
Cl
Cl
$H_B$
$H_B$
11.413
8.734
7.047
6.418 P.P.M.
$H_O$

Table 3-VI

Temperature calibration of the 1 mole % solution[1] of 3,5-dichlorosalicylaldehyde in $C_6D_6$.

| Temperature °C | $\nu_B$ | $\nu_A$ | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ |
|---|---|---|---|---|---|---|
| 9.3 | 6.991 | 6.292 | 8.598 | 11.505 | 2.52±0.04 | 0.61±0.03 |
| 30.0 | 7.034 | 6.369 | 8.671 | 11.436 | 2.53±0.03 | 0.56±0.03 |

1. A complete temperature study of this solution could not be carried out since the intensity of the coalescing peaks was too small. Hence saturation effects were difficult to eliminate.

Table 3-VII

Temperature calibration of the 2.5 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$.

| Temperature °C | $\nu_B$ | $\nu_A$ | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ | $\Delta\nu_{\frac{1}{2}}(H_A)$(cps) | $I/I_o$ |
|---|---|---|---|---|---|---|---|---|
| 8.5 | 7.000 | 6.321 | 8.635 | 11.495 | 2.55±0.03 | 0.61±0.02 | ---------- | ------- |
| 30.0 | 7.040 | 6.396 | 8.707 | 11.427 | 2.53±0.02 | 0.55±0.02 | ---------- | ------- |
| 74.3 | 7.121 | 6.551 | 8.864 | 11.251 | 2.51±0.04 | ------- | 0.29±0.01 | 0.40±0.01 |
| 83.3 | 7.134 | 6.578 | 8.894 | 11.214 | 2.49±0.04 | ------- | 0.28±0.02 | 0.48±0.03 |
| 95.0 | 7.149 | 6.609 | 8.930 | 11.171 | 2.53±0.04 | ------- | 0.26±0.02 | 0.53±0.02 |
| 104.8 | 7.164 | 6.641 | 8.966 | 11.122 | 2.53±0.02 | ------- | 0.24±0.03 | 0.63±0.02 |
| 116.0 | 7.179 | 6.674 | 8.998 | 11.071 | 2.51±0.03 | ------- | 0.27±0.03 | 0.68±0.01 |

Table 3-VIII

Temperature calibration of the 5 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$.

| Temperature °C | $\nu_B$ | $\nu_A$ | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ | $\Delta\nu_{\frac{1}{2}}(H_A)$(cps) | $I/I_o$ |
|---|---|---|---|---|---|---|---|---|
| 17.8 | 7.027 | 6.382 | 8.700 | 11.448 | 2.49±0.03 | 0.56±0.03 | ---------- | ---------- |
| 30.0 | 7.047 | 6.418 | 8.734 | 11.413 | 2.54 | 0.55±0.02 | ---------- | ---------- |
| 58.0 | 7.101 | 6.522 | 8.837 | 11.305 | 2.52 | 0.36±0.03 | ---------- | ---------- |
| 68.6 | 7.120 | 6.557 | 8.874 | 11.262 | 2.53 | ---------- | 0.31±0.01 | 0.40±0.03 |
| 76.8 | 7.132 | 6.582 | 8.903 | 11.227 | 2.51 | ---------- | 0.29±0.01 | 0.45±0.02 |
| 81.5 | 7.139 | 6.597 | 8.917 | 11.208 | 2.50 | ---------- | 0.28±0.01 | 0.49±0.03 |
| 88.0 | 7.148 | 6.614 | 8.936 | 11.186 | 2.50 | ---------- | 0.31±0.01 | 0.60±0.04 |
| 96.5 | 7.161 | 6.641 | 8.965 | 11.149 | 2.51 | ---------- | 0.24±0.03 | 0.69±0.04 |
| 106.3 | 7.174 | 6.668 | 8.995 | 11.106 | 2.52 | ---------- | 0.23±0.01 | 0.74±0.05 |
| 111.7 | 7.179 | 6.680 | 9.010 | 11.083 | 2.50 | ---------- | 0.28±0.03 | 0.81±0.03 |

Table 3-IX

Temperature calibration of the 6 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$.

| Temperature °C | $\gamma_B$ | $\gamma_A$ | $\gamma_{CHO}$ | $\gamma_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ | $\Delta\gamma_{\frac{1}{2}}(H_A)$(cps) | $I/I_o$ |
|---|---|---|---|---|---|---|---|---|
| 28.7 | 7.051 | 6.432 | 8.746 | 11.411 | 2.52±0.03 | 0.50±0.03 | ---------- | ---------- |
| 53.6 | 7.099 | 6.519 | 8.835 | 11.319 | 2.50 | ---------- | 0.30±0.01 | 0.44±0.02 |
| 58.7 | 7.106 | 6.536 | 8.854 | 11.298 | 2.50 | ---------- | 0.29±0.02 | 0.49±0.03 |
| 62.0 | 7.111 | 6.545 | ------ | ------- | 2.50 | ---------- | 0.28±0.01 | 0.51±0.03 |
| 67.5 | 7.121 | 6.562 | 8.881 | 11.265 | 2.51 | ---------- | 0.30±0.01 | 0.66±0.04 |
| 75.3 | 7.131 | 6.584 | 8.904 | 11.236 | 2.51 | ---------- | 0.25±0.01 | 0.69±0.03 |
| 82.5 | 7.141 | 6.606 | 8.927 | 11.208 | 2.50 | ---------- | 0.28±0.02 | 0.76±0.03 |
| 91.5 | 7.155 | 6.631 | 8.955 | 11.169 | 2.50 | ---------- | 0.27±0.03 | 0.79±0.04 |
| 95.2 | 7.159 | 6.642 | ------ | ------- | 2.50 | ---------- | 0.30±0.01 | 0.86±0.03 |

Table 3-X

Temperature calibration of the 7.5 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$.

| Temperature °C | $\nu_B$ | $\nu_A$ | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ | $\Delta\nu_{\frac{1}{2}}(H_A)$(cps) | $I/I_o$ |
|---|---|---|---|---|---|---|---|---|
| 28.0 | 7.053 | 6.445 | 8.769 | 11.403 | 2.51±0.03 | 0.52±0.02 | ---- | ---- |
| 48.5 | 7.096 | 6.524 | 8.845 | 11.327 | 2.51 | ---- | 0.29±0.01 | 0.45±0.02 |
| 59.0 | 7.114 | 6.558 | 8.881 | 11.287 | 2.52 | ---- | 0.27±0.02 | 0.60±0.02 |
| 68.7 | 7.128 | 6.587 | 8.911 | 11.250 | 2.50 | ---- | 0.28±0.02 | 0.70±0.02 |
| 73.5 | 7.135 | 6.600 | ---- | ---- | 2.50 | ---- | 0.29±0.02 | 0.79±0.03 |
| 79.3 | 7.143 | 6.619 | 8.944 | 11.208 | 2.51 | ---- | 0.28±0.02 | 0.79±0.05 |
| 86.5 | 7.155 | 6.640 | 8.967 | 11.181 | 2.51 | ---- | 0.29±0.02 | 0.85±0.04 |
| 91.7 | 7.160 | 6.652 | 8.979 | 11.160 | 2.50 | ---- | 0.25±0.03 | 0.89±0.04 |

Table 3-XI

Temperature calibration of the 10 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$.

| Temperature °C | $\nu_B$ | $\nu_A$ | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ | $\Delta\nu_{\frac{1}{2}}(H_A)$(cps) | $I/I_o$ |
|---|---|---|---|---|---|---|---|---|
| 9.3(1) | 7.022 | 6.385 | 8.709 | 11.467 | 2.54±0.03 | 0.58±0.03 | ---- | ---- |
| 30.0 | 7.065 | 6.483 | 8.815 | 11.389 | 2.50 | 0.50±0.03 | ---- | ---- |
| 45.0 | 7.097 | 6.539 | 8.866 | 11.332 | 2.53 | ---- | 0.31±0.01 | 0.44±0.02 |
| 56.3 | 7.115 | 6.573 | 8.899 | 11.295 | 2.50 | ---- | 0.31±0.01 | 0.57±0.04 |
| 64.8 | 7.127 | 6.598 | 8.925 | 11.260 | 2.55 | ---- | 0.27±0.01 | 0.62±0.04 |
| 84.7 | 7.155 | 6.653 | 8.982 | 11.184 | 2.51 | ---- | 0.28±0.01 | 0.79±0.03 |
| 94.7 | 7.169 | 6.682 | 9.014 | 11.140 | 2.50 | ---- | 0.28±0.01 | 0.89±0.03 |

(1) Some solute precipitated out of solution.

Table 3-XII

Temperature calibration of a saturated solution ( < 5 mole %) of 3,5-dichlorosalicylaldehyde in $CCl_4$.(1)

| Temperature °C | $\nu_B$ | $\nu_A$ | $\nu_{CHO}$ | $\nu_{OH}$ | $J_{AB}$ | $J_{OH-H_B}$ |
|---|---|---|---|---|---|---|
| 13.7 | 7.563 | 7.421 | 9.830 | 11.274 | 2.52±0.05 | 0.57±0.03 |
| 30.0 | 7.555 | 7.409 | 9.823 | 11.239 | 2.49±0.05 | 0.55±0.04 |
| 82.5 | 7.543 | 7.381 | 9.816 | 11.103 | 2.51±0.03 | ---------- |
| 89.0 | 7.541 | 7.376 | 9.816 | 11.084 | 2.50±0.05 | ---------- |
| 97.8 | 7.539 | 7.375 | 9.816 | 11.057 | 2.47±0.03 | ---------- |
| 106.8 | 7.536 | 7.371 | 9.815 | 11.027 | 2.50±0.03 | ---------- |
| 114.0 | 7.535 | 7.369 | 9.815 | 11.005 | 2.49±0.02 | ---------- |

(1) Purified as described in the "Experimental Methods" section.

The results of the infrared studies are as follows. The C=O stretching frequency of a saturated ( < 5 mole %) solution of 3, 5-dichlorosalicylaldehyde in $CCl_4$ is 1672 $\pm$ 1 $cm.^{-1}$ When solutions of this compound were prepared in $C_6D_6$ for the p.m.r. measurements, infrared spectra of these were also obtained. For four solutions (0.25, 2.5, 5.0 and 10.0 mole %), the C=O stretching frequencies all ranged between 1670 and 1671 $cm^{-1}$. Hence a 40 - fold change in solute concentration had no measureable effect on the C=O stretching frequency.

## DISCUSSION OF RESULTS

## A. CALCULATION OF THE PROTON EXCHANGE RATES FOR 3,5-DICHLOROSALICYLALDEHYDE IN $C_6D_6$ SOLUTIONS

Using the $I/I_o$ and $\Delta\nu_{\frac{1}{2}}$ values given in Tables 3-VII to 3-XI, the pseudo-first order rate constants for proton chemical exchange, defined by equation (3 - 50), were calculated using equations (3 - 51), (3 - 52) and (3 - 53) for $C_6D_6$ solutions of 3,5-dichlorosalicylaldehyde. The true rates for proton chemical exchange were obtained by multiplying the measured rates by a factor of 2, as defined by equation (3 - 49). The relaxation time $T_2$ for the protons in the absence of exchange was calculated from the $\Delta\nu_{\frac{1}{2}}$ values using equation (3 - 44). The magnitude of $J_{OH-H_B}$ used in these calculations was +0.61 cps, obtained for the 1 mole % solution at 9.3°C where all exchange effects are expected to be small. This value was also obtained for the 2.5 mole % solution at 8.5°C. The results of these calculations are tabulated in Tables 3-XIII to 3-XVII. In order that the activation parameters may be calculated for the proton exchange process, a linear relationship was assumed between log k and 1/T as given by a linear regression (least squares) analysis. These results are also given in the above Tables.

A regression analysis was carried out by standard statistical procedures (108, 109). The presence of a linear relationship between log k and 1/T is evident from the magnitudes of the multiple correlation coefficients. A typical graph of log k versus 1/T is given in Figure 3-5 for the 7.5 mole % solution.

Table 3-XIII

Proton chemical exchange rate constants for the 7.5 mole % $C_6D_6$ solution.

| $T(^{o}K)$ | $\frac{1}{T} \times 10^3$ $(^{o}K^{-1})$ | $k = \frac{1}{(2\tau)}$ $(sec.^{-1})$ | $(2\tau)$ (sec.) | log k $(sec.^{-1})$ |
|---|---|---|---|---|
| 321.7±0.5 | 3.108±0.005 | $2.3_9$ $(2.0_0)$[1] | $0.41_9$ $(0.50_0)$ | 0.378 (0.301) |
| 332.2 | 3.010 | $5.6_5$ $(4.6_5)$ | $0.17_7$ $(0.21_5)$ | 0.752 (0.668) |
| 341.9 | 2.925 | $8.8_5$ $(7.3_0)$ | $0.11_3$ $(0.13_7)$ | 0.947 (0.863) |
| 346.7 | 2.884 | $14._3$ $(11._0)$ | $0.07_0$ $(0.09_1)$ | 1.155 (1.041) |
| 352.5 | 2.837 | $14._7$ $(10._1)$ | $0.06_8$ $(0.09_9)$ | 1.167 (1.004) |
| 359.7 | 2.780 | $21._7$ $(15._2)$ | $0.04_6$ $(0.06_6)$ | 1.336 (1.182) |
| 364.9 | 2.740 | $37._0$ $(22._7)$ | $0.02_7$ $(0.04_4)$ | 1.568 (1.356) |

(1) The values in parentheses are discussed in the text.

Results of the linear regression analysis of the data:

$$\log k = \frac{-3.01 \times 10^3}{T} + 9.76$$

Multiple correlation coefficient = 0.990

Standard error of the estimate (in log k) = 0.061

Standard error in the slope = $0.19 \times 10^3$

Table 3-XIV

Proton chemical exchange rate constants for the 2.5 mole % $C_6D_6$ solution.

| $T(^{\circ}K)$ | $\frac{1}{T} \times 10^3$ $(^{\circ}K^{-1})$ | $k = \frac{1}{(2\tau)}$ $(sec.^{-1})$ | $(2\tau)$ (sec.) | log k $(sec.^{-1})$ |
|---|---|---|---|---|
| 347.5 | 2.878 | $1.7_7$ | $0.56_5$ | 0.248 |
| 356.5 | 2.805 | $2.9_8$ | $0.33_6$ | 0.474 |
| 368.2 | 2.716 | $4.2_6$ | $0.23_5$ | 0.629 |
| 378.0 | 2.646 | $7.5_2$ | $0.13_3$ | 0.876 |
| 389.2 | 2.569 | $8.3_3$ | $0.12_0$ | 0.921 |

Results of the linear regression analysis of the data:

$$\log k = \frac{-2.25 \times 10^3}{T} + 6.74$$

Multiple correlation coefficient = 0.983

Standard error of the estimate (in log k) = 0.059

Standard error in the slope = $0.24 \times 10^3$

Table 3-XV

Proton chemical exchange rate constants for the 5.0 mole % $C_6D_6$ solution.

| T($^oK$) | $\frac{1}{T} \times 10^3$ ($^oK^{-1}$) | $k = \frac{1}{(2\pi\tau)}$ ($sec.^{-1}$) | $(2\pi\tau)$ (sec.) | log k ($sec.^{-1}$) |
|---|---|---|---|---|
| 341.8 | 2.926 | $1.5_4$ | $0.65_0$ | 0.188 |
| 350.0 | 2.857 | $2.3_9$ | $0.41_9$ | 0.378 |
| 354.7 | 2.819 | $3.1_3$ | $0.31_9$ | 0.496 |
| 361.2 | 2.769 | $4.6_7$ | $0.21_4$ | 0.669 |
| 369.7 | 2.705 | $10._1$ | $0.09_9$ | 1.004 |
| 379.5 | 2.635 | $13._7$ | $0.07_3$ | 1.137 |
| 384.9 | 2.598 | $17._0$ | $0.05_9$ | 1.230 |

Results of the linear regression analysis of the data:

$$\log k = \frac{-3.34 \times 10^3}{T} + 9.94$$

Multiple correlation coefficient = 0.993

Standard error of the estimate (in log k) = 0.052

Standard error in the slope = $0.18 \times 10^3$

Table 3-XVI

Proton chemical exchange rate constants for the 6.0 mole % $C_6D_6$ solution.

| T(°K) | $\frac{1}{T} \times 10^3$ (°K$^{-1}$) | $k = \frac{1}{(2\tau)}$ (sec.$^{-1}$) | $(2\tau)$.(sec.) | log k (sec.$^{-1}$) |
|---|---|---|---|---|
| 326.8 | 3.060 | $2.1_2$ | $0.47_2$ | 0.326 |
| 331.9 | 3.013 | $2.9_6$ | $0.33_8$ | 0.471 |
| 335.2 | 2.983 | $3.4_6$ | $0.28_9$ | 0.539 |
| 340.7 | 2.935 | $6.6_2$ | $0.15_1$ | 0.821 |
| 348.5 | 2.869 | $9.6_2$ | $0.10_4$ | 0.983 |
| 355.7 | 2.811 | $12._4$ | $0.08_1$ | 1.093 |
| 364.7 | 2.742 | $15._4$ | $0.06_5$ | 1.188 |
| 368.4 | 2.714 | $22._7$ | $0.04_4$ | 1.356 |

Results of the linear regression analysis of the data:

$$\log k = \frac{-2.86 \times 10^3}{T} + 9.12$$

Multiple correlation coefficient = 0.986

Standard error of the estimate (in log k) = 0.067

Standard error in the slope = $0.20 \times 10^3$

Table 3-XVII

Proton chemical exchange rate constants for the 10.0 mole % $C_6D_6$ solution.

| T(°K) | $\frac{1}{T} \times 10^3$(°K$^{-1}$) | $k = \frac{1}{(2\tau)}$ (sec.$^{-1}$) | $(2\tau)$ (sec.) | log k (sec.$^{-1}$) |
|---|---|---|---|---|
| 318.2 | 3.143 | $1.9_6$ | $0.51_0$ | 0.292 |
| 329.5 | 3.035 | $4.0_2$ | $0.24_9$ | 0.604 |
| 338.0 | 2.959 | $6.2_1$ | $0.16_1$ | 0.793 |
| 357.9 | 2.794 | $14._7$ | $0.06_8$ | 1.167 |
| 367.9 | 2.718 | $32._3$ | $0.03_1$ | 1.509 |

Results of the linear regression analysis of the data:

$$\log k = \frac{-2.73 \times 10^3}{T} + 8.86$$

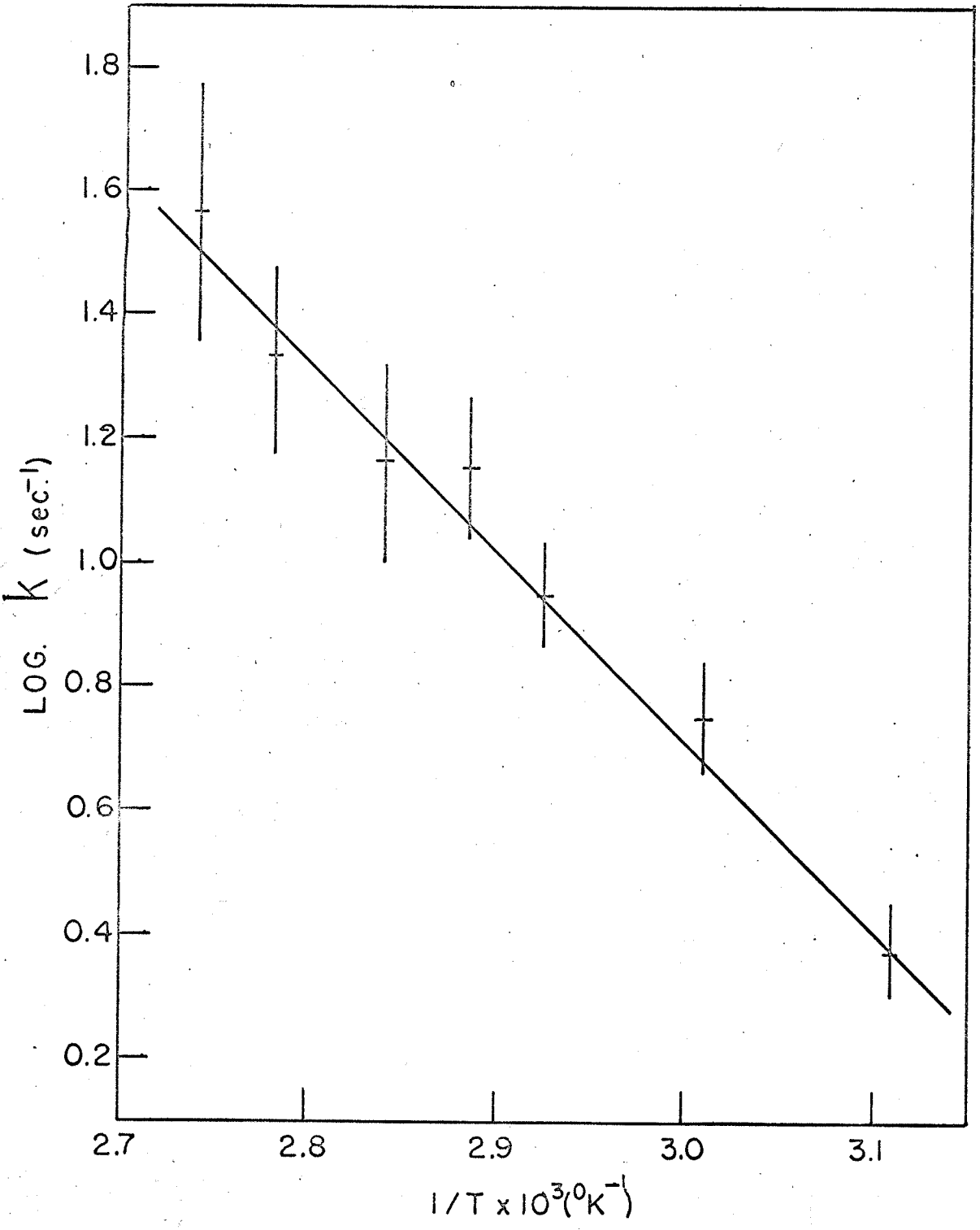
Multiple correlation coefficient = 0.995

Standard error of the estimate (in log k) = 0.057

Standard error in the slope = $0.16 \times 10^3$

Figure 3-5

A plot of log k ($sec.^{-1}$) versus (absolute temperature)$^{-1}$ for a 7.5 mole % solution of 3,5-dichlorosalicylaldehyde in $C_6D_6$.


1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
LOG. k (sec.⁻¹)
2.7
2.8
2.9
3.0
3.1
1/T x 10³(°K⁻¹)

The activation energies for the exchange processes were obtained from the Arrhenius equation (3 - 54) by multiplying the slopes of the calculated linear relationships by 2.303 R. The intercepts correspond to log A, where A is the frequency factor. The $\triangle H^{\neq}$, $\triangle G^{\neq}$ and $\triangle S^{\neq}$ values were determined at 80°C (353.2°K) by means of equations (3 - 55), (3 - 58) and (3 - 59) respectively and are tabulated in Table 3-XVIII. At 80°C a measurable exchange process occurs in all solutions, hence this temperature was chosen for evaluating the activation parameters.

The errors in the activation parameters were obtained in two ways. The first was a statistical approach and both standard errors and 90% confidence limits in the calculated activation parameters were obtained. These are included in Table 3-XVIII where the latter values are in brackets.

The estimation of the error in $\triangle E$ and $\triangle H^{\neq}$ is based on the standard error in calculating the slope of the straight line. The error in $\triangle G^{\neq}$ is a function of the standard error of the estimate in log k. The uncertainty in $\triangle E$ and $\triangle H^{\neq}$ is so much larger than in $\triangle G^{\neq}$ since the former depend on the range over which the temperature measurements are obtained. The greater the range the more accurately the slope of the straight line may be determined. The $\triangle G^{\neq}$ magnitudes are determined with a much higher precision since they are a function of log T/k (equation (3 - 58)). Because of this logarithmic relationship, an error in the temperature of $\pm$ 2°K has a negligible effect on the magnitude of $\triangle G^{\neq}$ and hence the small error in $\triangle G^{\neq}$ is due to the uncertainty in measuring k. The errors in determining $\triangle S^{\neq}$ are the largest since they depend on

Table 3-XVIII

Activation[1] parameters of proton exchange in $C_6D_6$ solutions of 3,5-dichlorosalicyl-aldehyde (A) at 80°C (353.2°K). The error limits are standard deviations from the mean and the values in brackets represent 90% confidence limits [2].

| Concentration [A] | | $E_a$ | $\Delta H^{\neq}$ | $\Delta G^{\neq}$ | $\Delta S^{\neq}$ | k |
|---|---|---|---|---|---|---|
| mole % | moles/liter[2] | kcal./mole | kcal./mole | kcal./mole | e.u./mole | $sec.^{-1}$ |
| 2.5 | 0.26±0.01 | 10.3±1.1(2.6) | 9.6±1.1(2.6) | 20.2±0.1(0.2) | -30±3.4(8) | 2.40±0.33 |
| 5.0 | 0.52±0.03 | 15.3±0.8(1.6) | 14.6±0.8(1.6) | 20.0±0.1(0.1) | -15.3±2.5(4.8) | 3.01±0.36 |
| 6.0 | 0.62±0.03 | 13.1±0.9(1.8) | 12.4±0.9(1.8) | 19.1±0.1(0.2) | -19.0±2.8(5.7) | 10.5±1.6 |
| 7.5 | 0.77±0.04 | 13.8±0.9(1.8) | 13.1±0.9(1.8) | 18.8±0.1(0.2) | -16.1±2.8(5.7) | 17.4±2.5 |
| 10.0 | 1.02±0.05 | 12.5±0.8(1.9) | 11.8±0.8(1.9) | 19.0±0.1(0.2) | -20.4±2.5(5.9) | 13.7±1.9 |

1. $J_{OH-H_B}$ in these calculations was taken as ±0.61 cps, assumed to be temperature independent.
2. The procedure for determining the error in the molarity is discussed in the text.

the sum of the errors in $\triangle H^{\neq}$ and $\triangle G^{\neq}$. In Table 3-XVIII the error limits of k are obtained on the basis of the standard error of the estimate in log k.

Allerhand et al (17) have pointed out that statistical deviations do not reflect the true errors due to the presence of systematic errors. These errors were also considered in this study.

The error in k arises from the experimental errors in the measurement of $J_{OH-H_B}$, $\triangle \nu_{\frac{1}{2}}(H_A)$ and $I/I_o$ which enter into equation (3 - 51). Consider the 7.5 mole % solution as an example. The standard deviations from the mean values of $\triangle \nu_{\frac{1}{2}}$ and $I/I_o$ for this solution are given in Table 3-X. Then, assuming that the magnitude of $J_{OH-H_B}$ is known exactly, the effects on the k values obtained using equation (3 - 51) of changing the ratio $I/I_o$ and $\triangle \nu_{\frac{1}{2}}$ by amounts corresponding to the standard deviations were considered. It was found that the greatest deviation in k occurred when the ratio $I/I_o$ was made smaller by an amount corresponding to the standard deviation from the mean and the $\triangle \nu_{\frac{1}{2}}$ values were made larger also by an amount corresponding to the standard deviation. Using these error limits of $I/I_o$ and $\triangle \nu_{\frac{1}{2}}$, a new set of k values were calculated at each temperature using equation (3 - 51). For example, at 48.5°C values of 0.43 and 0.30 cps were used for $I/I_o$ and $\triangle \nu_{\frac{1}{2}}$ respectively. These k values are given in Table 3-XIII in brackets and correspond to the maximum uncertainty in measuring k. This uncertainty is indicated in the Arrhenius plot (Figure 3-5) by the vertical line passing through each point. The uncertainty in the temperature ( $\triangle T = \pm 0.5^{\circ}K$) is indicated by the horizontal line and the uncertainty in the measurement of each point is thus represented by a rectangle. Two straight lines were drawn with maximum and

minimum slopes in such a manner as to pass through each rectangle (38) and the maximum error in the slope (hence in $\Delta$ E) was thus obtained. The Arrhenius plot indicates that the uncertainty in k and not in the temperature is the determining factor in the uncertainty in measuring the slopes.

In this manner an error of $\pm$2.1 kcal./mole in $\Delta$ E was determined. This error is overestimated since the maximum possible uncertainty in k was used based on the standard deviations in $\Delta\nu_{\frac{1}{2}}$ and $I/I_o$. Still it is not much larger than the 90% confidence limit estimate for this solution (1.8 kcal./mole) based on statistical calculations. The same conclusion was arrived at for the other solutions. Therefore only statistical errors are tabulated in Table 3-XVIII and the 90% confidence limits in $\Delta$ E may be treated as maximum errors.

Systematic errors may arise from other sources. The first is the choice of the magnitude of $J_{OH-H_B}$ in the complete absence of exchange effects. The value used in this study (0.61 cps) was obtained in both the 1 and 2.5 mole % solutions at temperatures just above the freezing point of benzene when exchange effects are expected to be small. If this value is in error, the true magnitude could only be larger. Calculations were carried out by increasing $J_{OH-H_B}$ by +0.06 cps. The k values increased slightly at each temperature and the new straight line was nearly parallel to the original. The corrected $\Delta$ E value was well within the previously determined error limits of the original $\Delta$ E. The effect on $\Delta G^{\neq}$ was negligible due to the logarithmic relationship of $\Delta G^{\neq}$ on k. Blears (24) also found that overlap between the two resonances and an incorrect

selection of J were not particularly important.

A systematic error may arise from a small long-range coupling between the CHO proton and ring protons $H_A$ and $H_B$ and between the OH and $H_A$ protons. Double resonance experiments were carried out in which the CHO and OH protons were irradiated while the ring proton spectra were studied. Only very slight, negligible effects were observed. Any long-range couplings besides $J_{OH-H_B}$ are therefore nearly zero, or zero.

Finally the applicability of equation (3 - 51) to the study under consideration must be considered. This equation was derived from Bloch's classical phenomenological equations to which a quantum correction must be applied (21). In this study the correction was negligible. The application of this equation also assumes that the magnitude of $J_{OH-H_B}$ is temperature independent and decreases only due to proton exchange effects. This is in analogy with conformational studies based on the measurement of variations of coupling constants with temperature where the assumption is made that the coupling constants in the various isomers are temperature independent. The results obtained from such studies may be subject to errors (110). Coupling constants are expected to show an intrinsic variation with temperature (111) which has been observed for F-F and H-F coupling constants (112).

The exact dependence of $J_{OH-H_B}$ on temperature (excluding exchange effects) is not known. However it is expected to be very small for two reasons. First, the $J_{AB}$ couplings for all the $C_6D_6$ solutions over all temperature ranges are constant with a maximum range of only 2.49 to 2.55 cps (Tables 3-VI to 3-XI). Secondly the long-range coupling $J_{CHO-H_C}$ in 5-chlorosalicylaldehyde (Table 3-V) is also temperature independent.

## B. MECHANISM OF THE PROTON EXCHANGE REACTION IN $C_6D_6$ SOLUTIONS OF 3,5-DICHLOROSALICYLALDEHYDE

### 1. Introduction

The pseudo first order rate constants k in Table 3-XVIII increase as the concentration [A] of 3,5-dichlorosalicylaldehyde in $C_6D_6$ increases. This suggests that a possible proton exchange reaction occurs via the collision of 2 molecules of A which may be represented as

3-60
$$A + A^* \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A^* + A \text{ where } [A] = [A^*] .$$

The mean lifetime of A between exchanges, $\tau_A$, is related to the conventional chemical rate constant $k_1$ by (10)

3-61
$$\frac{-d[A]}{dt} = k_1 [A^*] [A] = \frac{[A]}{\tau_A}$$

so that

3-62
$$k = \frac{1}{\tau_A} = \frac{1}{(2\tau)} = k_1 [A^*] = k_1 [A].$$

If equation (3-62) is valid, k is linearly dependent on [A] and a plot of k versus [A] for each solution should be a straight line passing through the origin with a slope equal to $k_1$.

The k values for each solution together with the solution concentrations in mole % and molarity units at 80°C are given in Table 3-XVIII. At this temperature the exchange process occurred in all the solutions.

The conversion of the solution concentrations from mole % to molarity units will now be described. First of all the concentrations in molarity units were evaluated at room temperature by weighing out the solute A, $C_6D_6$ and TMS. The results indicated that at room temperature the volume of TMS used as an internal reference had only a slight effect

on the total volume of the solution (1-2%) and hence on the molarity of A (moles of A per liter of solution). At 80°C the volume of TMS in solution must be even less since TMS boils at 26.5°C (113). This volume was neglected in the calculations.

Several other assumptions were made in these calculations. The total volume of each solution was obtained by adding the volumes of pure benzene and pure solid A- an ideal solution assumption. This is an approximation which may be made, as will be seen, since the errors in determining the rate constants exceed those in the concentration determinations. The volume of benzene is readily obtained since its density at 80°C is 0.815 gms./cc. (114). The density of 3,5-dichlorosalicylaldehyde was not known and was determined experimentally in the following manner. The solid A was immersed in various solvents of known densities in which it was insoluble. When the two densities were nearly equal the solid remained suspended in the solvent. The density was determined as $1.65 \pm 0.1$ gms./cc. at 25°C with a precision of about 5-10%. Assuming that the density of solid A remains unchanged at 80°C, its volume, and hence the molarity of each solution was calculated.

In the final solutions the volume contribution from solid A is less than 10%. Therefore the significance of the errors associated with the density determinations of A decreases by about a factor of 10 in the total volume and molarity calculations. This justifies the method of determining the density of the solid.

The main source of error in determining solution concentrations in molarity units lies in the assumption of additive volumes. This error is not known and is estimated at approximately 5%.

Table 3-XIX

Results of a linear regression analysis correlating the pseudo first order rate constants [1] k ($sec^{-1}$) with the concentration[1] of 3,5-dichlorosalicylaldehyde [A] in $C_6D_6$ at 80°C.

a. [A] - expressed in units of mole %.

3-63 k ($sec^{-1}$) = 1.7 (±0.5) [A] -1.0 (±3.0)(*)

Multiple correlation coefficient: 0.87

Standard error of the estimate in k: 3.9 $sec^{-1}$.

b. [A] - expressed in moles/liter of solution.

3-64 k ($sec^{-1}$) = 16.8 (±4.8) [A] -1.1 (±3.0).

Multiple correlation coefficient: 0.87

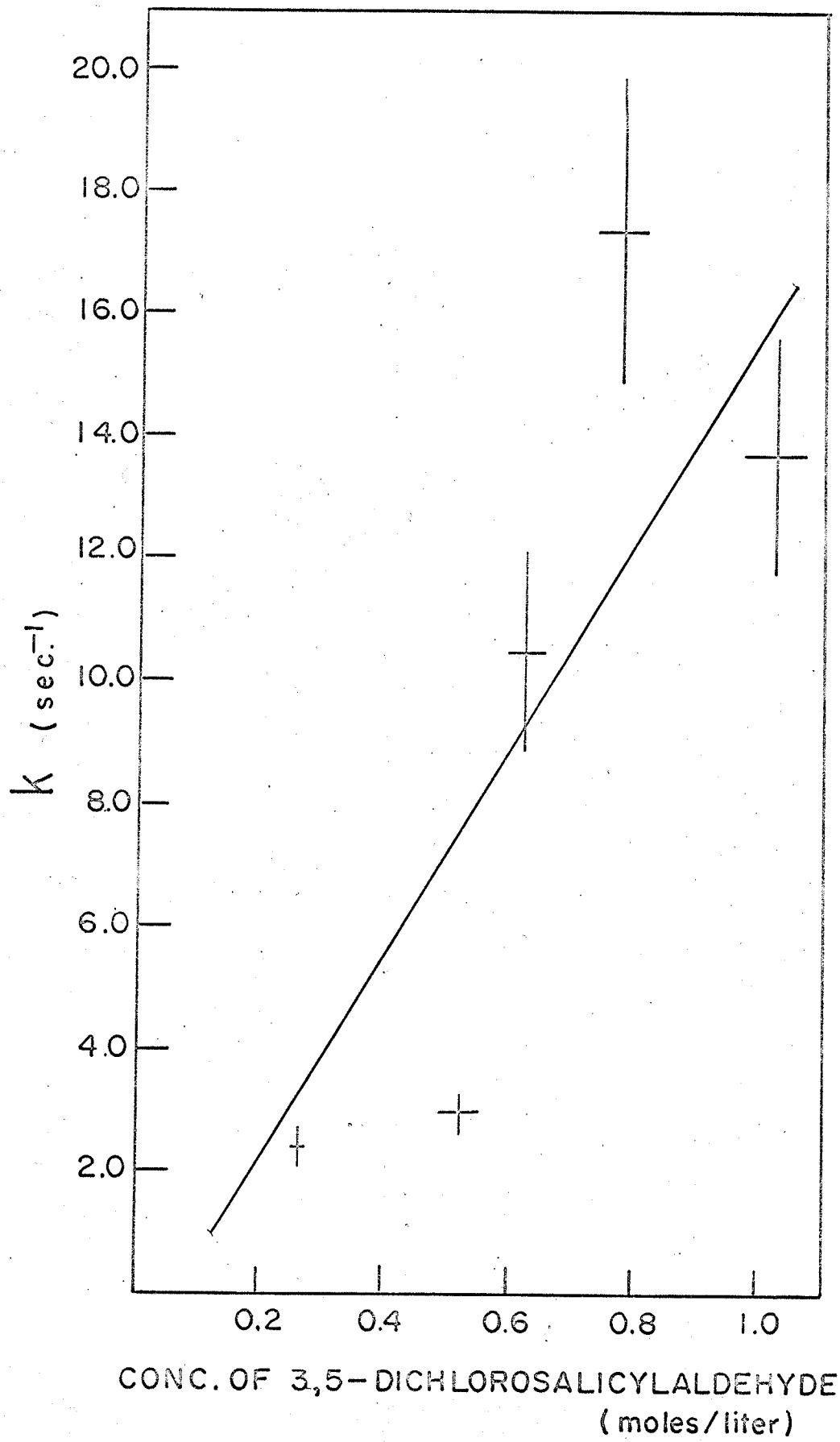
Standard error of the estimate in k: 3.9 $sec^{-1}$.

1. Given in Table 3-XVIII. A value of k = 0 when [A] = 0 is included in this analysis.

* Values in brackets are standard errors in the regression coefficients (slope and intercept).

Figure 3-6

A plot of k ($sec.^{-1}$) versus the concentration of 3,5-dichlorosalicylaldehyde [A] in moles/liter in $C_6D_6$ solutions at 353.2°K (80°C).


20.0
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
k (sec.⁻¹)
0.2
0.4
0.6
0.8
1.0
CONC. OF 3,5-DICHLOROSALICYLALDEHYDE
(moles/liter)

A regression analysis was carried out to find the best linear relationship between the concentration of A in solution and the k values at 80°C to check the validity of equation (3 - 62). Two sets of calculations were carried out with the concentrations in molarity and mole % units. In these calculations the origin was also included (k = 0 when $[A] = 0$). The results are given in Table 3-XIX. A plot of k versus $[A]$ (moles/liter) is given in Figure 3-6.

From the Figure and the multiple correlation coefficients it is seen that there is a large scatter of points about the straight line. The intercepts of both equations (3 - 63) and (3 - 64) are nearly equal and this indicates that the conversion from mole % to molarity units is accurate. Comparing equations (3 - 62) and (3 - 64) gives the magnitude of $k_1$ as $16.8 \pm 4.8$ liters mole $^{-1}$ sec.$^{-1}$ (standard deviation from the mean). The intercept of $-1.1 \pm 3.0$ sec.$^{-1}$ is compatible with a zero intercept. Hence the data support the linear dependence of k on $[A]$ and the mechanism given by equation (3 - 62).

The deviations of the points from the calculated straight line do not arise from errors in solute concentrations since the correlation coefficients are equal for calculations using mole % and molarity units. As well, the error limits of k for each solution do not account for the deviations. This scatter of the points as seen in Figure 3-6 is hard to explain and may arise from traces of impurities present in the solutions. The concentration of these impurities in solution must be small as was indicated by confirmatory temperature studies on a 5 mole % solution that was independently prepared. The solute was recrystallized from ether,

dried, and then degassed. Then the correct volumes of $C_6D_6$ and TMS were vacuum distilled to prepare the solution. Yet the same relative heights $I/I_o$ and widths at half height $\Delta\nu_{\frac{1}{2}}$ ($H_A$) were obtained as for the original solution.

The various effects on the magnitude of the rate constant $k_1$, on the possible exchange mechanism and on the activation parameters will now be discussed.

## 2. Solvent Effects and Dimer Formation

The solvent has a definite effect on the rates of proton exchange in solutions of 3,5-dichlorosalicylaldehyde since this process was observed in $C_6D_6$ but not in $CS_2$, $CCl_4$ and $C_6H_{12}$ solutions. This may be related to the low solubility of 3,5-dichlorosalicylaldehyde in the latter solvents (< 5 mole %).

Intermolecular hydrogen bonds exist between hydroxyl protons of phenols and aromatic $\pi$ -electron systems (71, 115-122). The energy of hydrogen bond formation $\Delta H^o$ between phenol and benzene is -1.6 kcal./mole at 25°C (53, 117). However, in a system where the phenolic proton is strongly intramolecularly hydrogen bonded as in salicylaldehyde or 3,5-dichlorosalicylaldehyde, the experimental evidence indicates that this bond is not broken in a benzene solution by the competing interaction with the $\pi$ -electrons. This is based on dipole moment measurements in benzene, paraxylene and dioxane solutions (59-62) and on photoreaction studies in benzene solutions (63).

The data obtained in the study under consideration support the intramolecularly hydrogen-bonded species in $C_6D_6$ solutions. The long-

range coupling constant $J_{OH-H_B}$ in 3,5-dichlorosalicylaldehyde is of the same magnitude in both $CCl_4$ and $C_6D_6$ solutions (Table 3-I). If a fraction of the solute phenolic protons were intermolecularly hydrogen bonded either with the $C_6D_6$ solvent $\pi$ -electrons or in a dimer formation with other solute molecules, the magnitude of this coupling would be smaller.

Secondly, if either of these intermolecular hydrogen bonds were present, the OH proton shift would be concentration dependent whereas for an intramolecular hydrogen bond the OH shift is concentration independent (46, 71). The concentration shift of the OH proton of phenol in benzene solutions is approximately 1.4 ppm over a concentration range of 2 to 24 mole % (121). However, for 2,6-di-t-butyl-p-methylphenol in benzene the OH shift is independent of concentration since the bulky ortho-substituents shield the OH proton from the solvent environment (121). The large concentration shifts that are possible on intermolecular hydrogen bond formation in aromatic solvents have been described (46, 123). In the study under consideration, at room temperature the OH proton shifts in $C_6D_6$ vary from +11.436 ppm (Table 3-VI) in the 1 mole % solution to +11.389 ppm (Table 3-XI) in the 10 mole % solution, a change of 0.047 ppm (2.8 cps) which is negligible in comparison with the values for phenol in benzene solutions. Also, small variations were observed for the OH proton shift in concentration studies of salicylaldehyde in seven solvents (69).

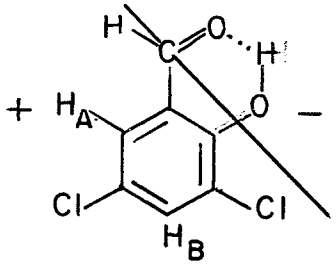
The measured C = O infrared stretching frequencies also support the monomeric, intramolecularly hydrogen-bonded species of 3,5-dichlorosalicylaldehyde in $C_6D_6$ solutions at all concentrations.

However, another weak interaction in these solutions is possible.

Recent studies (124, 125) of the solvent effects in p.m.r. spectroscopy have shown that the solvent shifts $\Delta$ ( $\Delta = \delta_{CDCl_3} - \delta_{C_6H_6}$ ) induced by benzene in saturated ketones are positive for protons lying behind a reference plane drawn through the carbonyl carbon atom and perpendicular to the C = O bond (benzene leads to an increase in the shielding of these protons). Protons that are in front of this reference plane are deshielded and hence have a negative $\Delta$ value while those lying in or near the plane have small or zero $\Delta$ values (126). This generalization also appears to hold for $\alpha$, $\beta$ -unsaturated ketones (126 and references therein). These results are consistent with an interaction between the solute carbonyl compound and the solvent benzene (124 - 126).

This generalization has been applied to the solute molecule under consideration, 3,5-dichlorosalicylaldehyde.

E.




A reference plane is drawn as indicated through the carbonyl carbon atom and perpendicular to the C = O bond (E). From (E) it is seen that protons $H_B$, $H_A$ and CHO should be shielded (positive $\Delta$) in going from $CDCl_3$ to $C_6D_6$ solutions whereas the OH proton should be deshielded (negative $\Delta$). Table 3-I indicates that these $\Delta$ values are +0.534, +1.052, +1.107 and -0.080 ppm respectively for 5 mole % solutions. This supports the intramolecularly hydrogen bonded species in benzene solution.

The above generalization is also applicable to the temperature

dependence of the shifts which have been observed on cooling solutions of ketones in toluene $-d_8$ mixtures (126). These shifts are roughly proportional to the $\Delta$ values. The chemical shifts in toluene $-d_8$ solution are temperature variable because on lowering the temperature the equilibrium

3-65 ketone + toluene $\rightleftharpoons$ complex

is displaced towards complex formation. This also applies to benzene, but toluene was chosen as the aromatic solvent since lower temperatures may be obtained.

For the molecule under consideration, on lowering the temperature, proton shifts $H_B$, $H_A$ and CHO shift to higher fields (increased shielding, + ve $\Delta$) whereas the phenolic proton in the deshielding region shifts to lower fields (-ve $\Delta$) (Tables 3-VI to 3-XI). These results also support the presence of the intramolecularly hydrogen-bonded species as well as the presence of a complex between the solute and $C_6D_6$ solvent molecules. However, a phenolic proton shift to lower fields on decreasing the temperature is also consistent with a stronger hydrogen bond (46). (A phenolic proton shift to high field on increasing the temperature has been interpreted in terms of the breaking of the hydrogen bond).

The magnitude of the interaction (3-65) must be considered. The temperature variations in the chemical shifts of proton resonances in some steroidal ketones in toluene solution have been determined (127). Assuming a 1:1 complex, its heat of formation was estimated from the temperature studies as approximately -0.65 kcal./mole. This value is regarded only as an order of magnitude in view of the many assumptions made in the cal-

culations. Solvent shifts induced by benzene and toluene together with temperature studies were extended to methoxybenzenes (128) where the $\triangle H$ values of the assumed 1:1 complexes were approximately -1.0 kcal./mole and varied slightly with the ring substituents. Finally an averaged value of $\triangle H = -0.9 \pm 0.2$ kcal./mole was obtained for the association of four para-substituted benzaldehydes in toluene - $d_8$ solutions (129). No correlation with substituent was apparent.

These interactions are very weak. The magnitudes are approximate because of the assumption of 1:1 complexes between solute and solvent. Also, temperature shifts may be associated with dispersion forces (127). The magnitude of this interaction was not calculated for the solutions under consideration due to the many approximations in the calculations and since this interaction is known to be very weak.

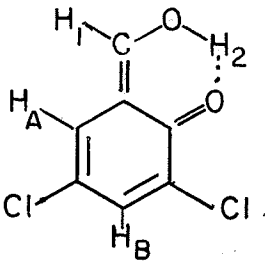
3. Contributions to the Phenolic Proton Line Widths

In all the solutions that were studied the OH proton line widths at half height $\triangle\nu_{\frac{1}{2}}$ (OH) were always slightly broader than the corresponding $H_B$ proton line widths $\triangle\nu_{\frac{1}{2}}$ ($H_B$). As the solution temperature was increased, the phenolic proton resonance doublet collapsed and further broadened whereas the $H_B$ proton resonance doublets collapsed and became sharper. For the 5 mole % solution at 111.7°C, the OH width at half height $\triangle\nu_{\frac{1}{2}}$ (OH) was $1.65 \pm 0.03$ cps whereas $\triangle\nu_{\frac{1}{2}}(H_A)$ and $\triangle\nu_{\frac{1}{2}}(H_B)$ were $0.28 \pm 0.03$ and $0.30 \pm 0.02$ cps respectively.

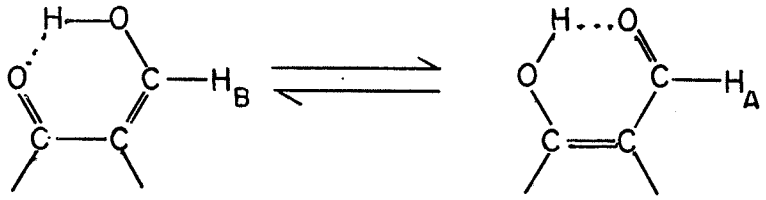
The exact reason for this additional broadening is not known but several processes besides proton exchange are probably effective. First of all the OH proton may have a shorter relaxation time than the

other protons. For example, the OH proton resonance in salicylic acid in the absence of exchange is a single, sharp line whose width is slightly greater than that of the hydroxyl proton resonance of p-bromophenol ($1/T_2$ = 10 and 7 $sec.^{-1}$, respectively) (130). Secondly, the main resonance will consist of a strong line for $O^{16}$—H absorption. There may be a small isotopic shift for the $O^{18}H$ and $O^{17}H$ resonances with the larger contribution arising from the latter resonance (5). The $O^{17}$ isotope has a spin of 5/2 which may lead to a quadrupole relaxation process (5). A contribution to the OH resonance broadening may also arise from molecules existing in solution in the form F.

F.




If the OH shift in F is slightly removed, even by 0.5 cps, from that observed in the species E, this will lead to resonance broadening. However the concentration of F in the solutions is expected to be small since the $H_1CO$ proton resonance was always sharp and never broadened. A coupling constant $J_{12}$ was never observed. This may be compared with the study of keto-enol equilibria of β-keto aldehydes (131) in which the coupling constant $J_{OH-H_B}$ in the hydroxymethylene ketone tautomer G ranged from 1 to 12 cps.



G. H.

the magnitude depending on the system and on the equilibrium between G and H tautomers in solution (H is the aldo-enol tautomer).

Finally, phenolic impurities, dimer, trimer etc. formations in very low concentrations in solution, in which the OH proton resonances vary slightly from the main phenolic resonance, may cause additional broadening (69).

4. The Magnitude of the Bimolecular Rate Constant $k_1$

The data in Table 3-XVIII and Figure 3-6 indicate that the proton exchange reaction is second order and bimolecular (132) with respect to 3,5-dichlorosalicylaldehyde. The second order rate constant $k_1$ (equations 3-60 to 3-62) is 16.8±4.8 liters $mole^{-1}$ $sec.^{-1}$ (equation 3-64). The error is the standard deviation from the mean.

Very few studies have been carried out on proton exchange reactions involving intramolecularly hydrogen-bonded protons. A concentration study of the p.m.r. spectra of salicylaldehyde in methanol solutions (69) has shown that protons exchange between the OH group of the alcohol and that of salicylaldehyde. The upper limit for the exchange rate was estimated at 330 $sec.^{-1}$ from the separation between the two phenolic resonances when they were both present. Consequently a proton contributing

to a strong intramolecular hydrogen bond is capable of exchanging. Further studies were not carried out on this system.

Forsen and Hoffman (101, 133) have applied the nuclear magnetic double resonance technique to the study of exchange processes. They measured the lifetimes of the OH protons in a mixture of t-butylalcohol and 2-hydroxyacetophenone in $CS_2$ (133) and in the system salicylaldehyde and 2-hydroxyacetophenone with a trace of acetic acid in $CS_2$ (101). However these were only exploratory studies, sensitive to the concentrations of the catalyst, which only served to illustrate the principles of the method.

The deprotonation rate of the OH proton in salicylaldehyde by the $OH^-$ ion in water is $> 10^{10}$ liters $mole^{-1}$ $sec.^{-1}$ (134). This very fast rate of proton exchange may be explained by the formation of hydrogen bonds to water solvent molecules. Further, it has been pointed out (134) that when an intramolecular hydrogen bond is present at the reaction site, the proton involved is not available for reaction unless this bond is broken.

The rates of exchange of carboxyl and hydroxyl protons of salicylic acid with the OH protons of methanol have been measured (130). In this system the methanol solvent molecules also take part in the proton exchange mechanisms.

Finally, Garbisch (131, 135) has pointed out that nuclear spin state averaging resulting from rapid proton exchange should only occur for the intermolecular process since the spin state of a rapidly exchanging proton is preserved during an intramolecular exchange (keto-enol equilibria). This is further evidence in support of the bimolecular mechanism under

consideration.

The system under consideration is novel since it appears to be the first studied with the proton exchange reaction occurring between two molecules, both with their exchangeable protons intramolecularly hydrogen-bonded. $k_1$ is about ten orders of magnitude smaller than the deprotonation rate of salicylaldehyde by the $OH^-$ ions in water.

The exact mechanism for proton transfer is not known but the intramolecular hydrogen bond must first be broken. The nature of the transition state is also not known but two solute molecules must react in the rate determining step. Consequently the exchange process probably occurs via dimer formation in the transition state. Due to the weak solute-solvent interaction the solubility of 3,5-dichlorosalicylaldehyde in $C_6D_6$ is greater than in $C_6H_{12}$, $CS_2$ or $CCl_4$. The exchange process was too slow to be observed in the latter solvents. In acetone solutions the rates of proton exchange were too fast to be measured. Hence the solvent does have an effect on the rates and the exchange process in $C_6D_6$ solutions is solvent-assisted.

A rather large standard deviation ( $\sim$ 30%) is associated with the magnitude of $k_1$. The exact reason is not known for this. However, traces of impurities probably affect the rates and hence cause the scatter of the points as seen in Figure 3-6. Consequently the rate expression probably should include a term for catalyst (impurity) concentrations. Even so, the data indicate that a proton exchange process in a system such as this may occur, that this process is bimolecular and that it may be measured by p.m.r. techniques.

The proton exchange mechanism is discussed further in the next section together with the associated activation parameters.

5. The Magnitudes of the Proton Exchange Activation Parameters

The magnitudes of the activation parameters of proton exchange in $C_6D_6$ solutions of 3,5-dichlorosalicylaldehyde at 80°C are given in Table 3-XVIII. For a reference, the heat of formation $\Delta H^\circ$ of the intramolecular hydrogen bond in salicylaldehyde was estimated by applying the linear relationship between $\Delta H^\circ$ and the OH stretching frequency shift $\Delta\nu_{OH}$ in the infrared on intermolecular phenol-base association (55). Using magnitudes of 3611 $cm^{-1}$ for $\nu_{OH}$ in phenol (66, 74, 90) and 3150 $cm^{-1}$ in salicylaldehyde (70, 80), $\Delta H^\circ$ is -8 kcal./mole. An alternate linear relationship (reference 53, equation 4) gives $\Delta H^\circ$ as -7 kcal./mole. These values are approximate since the linear relationships were derived for intermolecular hydrogen bond formation, the $\nu_{OH}$ shift in salicylaldehyde is not definite (70, 80, 90), the effect of the two chlorine atoms is neglected as is the conjugation arising from the formation of the 6-membered ring. The latter effect would tend to increase the magnitude of $\Delta H^\circ$. However these values will serve as a guide in the interpretation of the kinetic data.

The activation energy $E_a$ is considered to be the minimum energy difference between the reactants and the transition state or the height of the energy barrier opposing the reaction (136). The $E_a$ values were obtained from the integrated form of the Arrhenius equation in which it is assumed that $E_a$ is temperature independent. All of the experimental Arrhenius plots are linear and deviations from this equation are expected to be small (136).

None of the activation parameters with the exception of $\Delta G^{\neq}$

show a definite trend with concentration. The magnitude of $\Delta G^{\neq}$ decreases as the rates increase, with the exception of the 10 mole % solution, in agreement with equation (3 - 58). The magnitudes of $E_a$, $\Delta H^{\neq}$ and $\Delta S^{\neq}$ of the 2.5 mole % solution fall outside the 90% confidence limits of all the other solutions.

The activation energies are considered first of all. The intramolecular hydrogen bond must be broken and for this to occur the phenolic group must overcome the barrier hindering its internal rotation about the C-O bond. The barrier height for phenol vapor is 3.4 kcal/mole (104, 105). It is easier for the phenolic group, rather than for the CHO group to break the intramolecular hydrogen bond by twisting out of the plane of the ring. For benzaldehyde, based on far infrared studies, the barrier to rotation about the C-CHO bond is 4.7 kcal./mole in the gas phase and 6.7 kcal./mole in the liquid phase (the latter value may be in error) (137). Other values have been obtained for liquid benzaldehyde ranging from 5.90 to 6.37 kcal./mole and are summarized in reference (137). These magnitudes are in agreement with the barriers to internal rotation obtained in other aliphatic and aromatic aldehydes (138, 139).

The barriers to internal rotation are different in the liquid and gas phases because of the effect of neighbouring molecules, reflected by the lower torsional barriers in gases as compared with the liquids (140). This is supported by the free energy of activation $\Delta G^{\neq}$ for the hindered internal rotation in dimethylnitrosamine obtained from p.m.r. coalescence temperature measurements. This value is about 2 kcal./mole greater in the liquid than in the vapor phase (141).

A comparison of this data with the experimental activation energies in Table 3-XVIII indicates that the activation energies may be reasonably accounted for by the energy required to break the intramolecular hydrogen bond ( > 8 kcal./mole) and to twist the phenolic proton out of the plane of the ring ( > 3.4 kcal./mole). The latter value is also probably larger than that measured for the vapor by analogy with the above discussion and results. A similar approach in accounting for the magnitude of the activation energy was used by Meakins (142) in his dielectric absorption studies of ortho disubstituted phenols.

Another possible explanation of the magnitudes of the activation energies is to assume that the hydrogen bond is broken by a partial twisting of both groups out of the plane of the ring. Since a proton exchange process is measured, the correct hydrogen bond-breaking mechanism must give the phenolic group enough freedom of rotation so that the proton may associate itself with another solute molecule in the transition state and thus exchange.

Due to the large stabilization energy associated with the CHO group in the plane of the ring, the experimental data suggest that this group retains its hydrogen-bonded orientation while proton exchange takes place. The planar configuration of the CHO group is supported by the p.m.r. temperature studies of 5-chlorosalicylaldehyde in $C_6D_6$ (Table 3-V). At 95°C. when the proton exchange process is measureable and the splitting $J_{OH-H_B}$ has nearly disappeared, the splitting $J_{CHO-H_C}$ remains unchanged from that observed at 30°C. Hence the aldehydic long-range coupling still follows the zig-zag path. This splitting was also observed at 115°C.

The effect of the solvent on the activation energies and hence on the transition state is not known.

Considering the free energies of activation $\Delta G^{\neq}$ for the proton exchange process, the measured values cannot be compared with literature values since so few studies have been carried out on a system such as this. $\Delta G^{\neq}$ values for many other exchange processes, hindered internal rotation and ring inversion studies are summarized in the review articles (5, 10). Anet and Ahmad (102) have determined $\Delta G^{\neq} = 7.9$ kcal./mole for the internal rotation of benzaldehyde in vinyl chloride solution at -123°C from the temperature dependence of the p.m.r. spectrum. This contributes in part to the measured $\Delta G^{\neq}$.

The most interesting results in Table 3-XVIII are the entropies of activation $\Delta S^{\neq}$ for the proton exchange process since these values are large and negative. At first sight this is unexpected since a hydrogen bond-breaking process is involved which leads to greater disorder, associated with an increase in entropy.

However the entropy of activation reflects "the difference in the number and character of the translational, rotational and vibrational degrees of freedom between transition state and reactants" (143). Hence the negative entropy of activation is an indicator of the nature of the transition state and may be viewed in terms of the shape of the potential energy surface of the reaction (144).

Consider a three-dimensional potential energy diagram with the Z -direction representing the energy, the Y -direction representing motion along the reaction coordinate and the X -direction representing all other

degrees of freedom. This three-dimensional surface has a valley representing the reactants and is separated from a valley representing the products by a ridge of high energy. This ridge may be viewed as an energy barrier. It is not of uniform height but contains a saddle point in it, the transition state. For any given reacting molecule this is the highest energy that it must surmount in order to form a product. In terms of the potential energy surface, the saddle point is broad when a large number of typical reaction paths are possible and the entropy of activation is positive. However, if unusual constraints arise in the transition state, the saddle point is constrained by steep side walls and lies in a narrow defile. Then there are relatively fewer paths over the energy barrier. This represents a transition state for a reaction associated with a negative activation entropy. Such a transition state "is one for which very few motions other than that along the reaction coordinate are possible without a large increase in energy" (144).

The observed $\Delta S^{\neq}$ values imply that the transition state, which is thought to involve the formation of a dimer between two solute molecules for proton exchange to take place, forms with difficulty. For example, one solute molecule may have to be in the correct steric configuration with respect to another solute molecule for dimer formation to take place. Solute - solvent interactions may contribute to or hinder the formation of the transition state. As well, both intramolecular hydrogen bonds interfere with proton exchange and are constraints which must be overcome. The exact nature of the transition state and hence the mechanism of proton exchange is not known except that it involves the formation of a stereospecific dimer between two solute molecules.

Large and negative $\Delta S^{\neq}$ values have also been obtained in the study of the racemization of sterically hindered biphenyls (145). These activation entropies ranged from -1.6 e.u. to -26.9 e.u., with the average about -10 e.u. They were interpreted in terms of an "unlikely arrangement" that must be formed in the molecule so that the formation of the transition state could be possible (145).

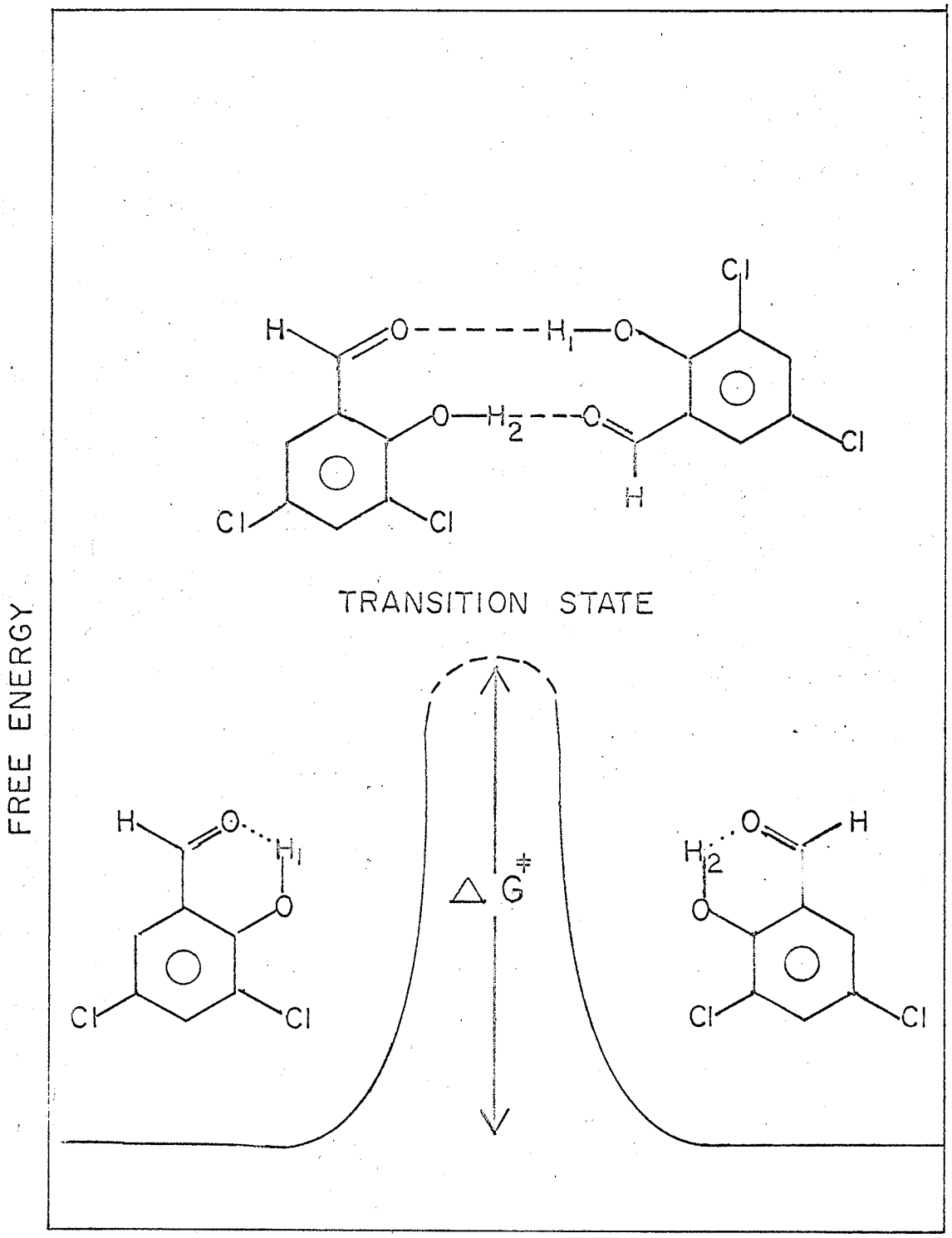
In Table 3-XVIII emphasis is not placed on the actual magnitudes of $\Delta S^{\neq}$, since large uncertainties are associated with them, but only on the signs which definitely are negative. The uncertainty in $\Delta S^{\neq}$ is mainly proportional to the error in $\Delta H^{\neq}$ (143, 146) since the error in $\Delta G^{\neq}$ is small. A transmission coefficient $\kappa$ of unity was assumed in calculating $\Delta G^{\neq}$ using equation (3 - 58) and this may be done without introducing appreciable error (143). As well, $\kappa$ enters equation (3 - 58) as a log $\kappa$ function which minimizes the uncertainty of $\kappa$ on $\Delta G^{\neq}$.

The above discussion may be summarized by a graphical representation of the free energy change associated with the proton exchange reaction in $C_6D_6$ solutions of 3,5-dichlorosalicylaldehyde (Figure 3-7). Due to the uncertainty in the exact nature of the transition state, it is represented by a dotted line. The configuration in the region of the transition state is unknown but may include a "stable intermediate" (147), a possible stereospecific dimer formation such as is shown in Figure 3-7.

In conclusion an estimate can be made of the $\Delta G^{\neq}$ for 3,5-dichlorosalicylaldehyde solutions in $CCl_4$ in which proton exchange could

Figure 3-7

A graphical representation of the free energy change for the proton exchange reaction in $C_6D_6$ solutions of 3,5-dichlorosalicylaldehyde. A possible stereospecific dimer involved in the formation of the transition state is shown.


FREE ENERGY
TRANSITION STATE
$\Delta G^{\neq}$
REACTION COORDINATE

not be measured. However, assuming that a coalescence of the splitting $J_{OH-H_B}$ occurred at the highest temperature studied (114°C), the pseudo first order rate constant k was evaluated by applying equation (3 - 47) at this temperature. Bringing in a factor of 2 for intermolecular proton exchange and assuming $J_{OH-H_B}$ = 0.57 cps (Table 3-XII), k = 2.5 sec.$^{-1}$ and $\Delta G^{\neq}$ = 22.2 kcal./mole (equation (3-58)). This $\Delta G^{\neq}$ is higher than all the values in Table 3-XVIII and is the lower limit for $CCl_4$ solutions. If the coalescence temperature is higher, $\Delta G^{\neq}$ will be still larger. Unfortunately, the activation energy for this solution cannot be estimated.

# SUMMARY AND CONCLUSIONS

A study has been carried out on the proton exchange reactions and the intramolecular hydrogen bond in benzene solutions of 3,5-dichlorosalicylaldehyde using proton magnetic resonance techniques.

By increasing the temperature of the above solutions the magnitude of the long-range splitting $J_{OH-H_B}$ decreased until at temperatures near the boiling point of benzene this splitting could be nearly eliminated. Therefore the pseudo first order rate constants for proton exchange for each solution were obtained by measuring the relative heights of the ring proton peaks ($H_B$) associated with the exchanging OH proton with respect to the heights of the ring proton peaks unaffected by proton exchange ($H_A$). The relative peak heights and the rate constants are related by equation (3 - 51). The activation parameters were obtained by applying the Arrhenius equation (3 - 54) and the theory of absolute reaction rates.

The pseudo first order proton exchange rate constants were found to depend on the concentration of 3,5-dichlorosalicylaldehyde in solution and the results indicate that the process is bimolecular (equation (3-60)) with respect to the solute molecules. The magnitude of the second order proton exchange constant is $16.8 \pm 4.8$ liters $mole^{-1}$ $sec.^{-1}$. The error is the standard deviation from the mean. It is rather large, possibly due to traces of impurities in the solutions. However the data do indicate the order of magnitude of the proton exchange reaction in which the exchangeable protons are intramolecularly hydrogen-bonded. A proton exchange reaction in a similar system has never before been studied.

The concentration and temperature effects on the ring proton, aldehydic and phenolic proton shifts indicate the presence of a weak

interaction between the solute and solvent molecules. Hence the proton exchange reaction is solvent-assisted. This is further supported by temperature studies carried out on $CCl_4$, $C_6H_{12}$ and $CS_2$ solutions of 3,5-dichlorosalicylaldehyde in which the proton exchange rates were too slow to be measured. In acetone solutions they were too fast.

The magnitudes of the activation parameters for the various solutions are listed in Table 3-XVIII. The activation energies are explained by the energies required to break the intramolecular hydrogen bond and to twist the phenolic (and perhaps the aldehydic) group out of the plane of the ring. The entropies of activation are large and negative which suggests that unusual constraints must be overcome in forming the transition state. The exact nature of the transition state (and hence the proton transfer mechanism) is not known except that it must involve the formation of a stereospecific dimer between two solute molecules.

The rate constants could not be obtained by measuring the phenolic proton line widths at half height as a function of temperature since these were always slightly broader than the corresponding $H_B$ ring proton line widths. The exact reason for this is not known but may be due to a shorter relaxation time of the phenolic proton with respect to the ring proton, a small isotopic shift for the $O^{18}H$ and $O^{17}H$ resonances or traces of phenolic impurities, or dimer, trimer etc. formations in the solutions in addition to the proton exchange reaction.

The value of this study is that it shows that proton exchange reactions may occur in a system such as this, that intramolecularly

hydrogen-bonded protons may exchange and that this rate of exchange may be measured.

8.

# RECOMMENDATIONS FOR FUTURE RESEARCH

Very much work remains to be done on this system. Temperature studies should be carried out on $CDCl_3$ and $CH_2Cl_2$ solutions of 3,5-dichlorosalicylaldehyde at various concentrations. These studies will indicate the solvent effects on the rate constants and mechanisms. Both solute and solvents must be purified before use. In conjunction with p.m.r. measurements, infrared studies should be carried out on the OH stretching frequencies of solid 3,5-dichlorosalicylaldehyde and in the various solutions. This molecule should also be studied in methanol where the solvent will definitely play an important role.

At least several of the above studies should be repeated with 3,5-dibromosalicylaldehyde as the solute molecule. The effect of ring substituents on proton exchange rates can thus be studied. These may then be extended to ring-substituted 2-hydroxyacetophenones in which the intramolecular hydrogen bond is stronger than in the corresponding salicylaldehydes.

Finally, an X-ray structural determination of phenol should be carried out so that approximate bond angles and bond lengths need not be used in calculations of the barrier to internal rotation in phenol.

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