

The University of Manitoba

PROTON MAGNETIC RESONANCE STUDY OF
CONFORMATIONAL EQUILIBRIA OF THE
PYRIDINEALDEHYDES IN SOLUTION

by

Werner Danchura

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ABSTRACT

This thesis is concerned with the use of nuclear magnetic resonance in the prediction of the conformations of pyridinealdehydes.

Long range spin-spin coupling constants of the pyridinealdehydes are determined by accurate analysis of the proton magnetic resonance spectra. These coupling constants are a precise measure of the conformational equilibria in solution. Thus, the ON-trans form of 2-pyridinealdehyde is found to be more stable than the ON-cis form by at least 2.3 kcal/mole in a CS₂ solution, and 1.6 kcal/mole in an acetone solution. The ON-trans form of 3-pyridinealdehyde is more stable than the ON-cis form in both polar and non-polar solutions. Classical solvation theory predicts that the ON-trans form of 2-pyridinealdehyde is more stable by about 7.0 kcal/mole in the vapour phase, which is at variance with the value predicted by the INDO-FPT approximate molecular orbital theory. The results obtained from the N.M.R. data are compared with those from other experiments.

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INTRODUCTION

1. Indirect Nuclear Spin-Spin Coupling Constants

Hahn and Maxwell (1a) and others (1b) discovered a multiplet splitting in the nuclear magnetic resonance spectra of liquids and liquid solutions which were not attributable to any chemical shift effect. They reported that the experimental splittings were caused by a coupling of the nuclear spins and could be calculated from an empirical expression of the form

$$E_{NN'} = \hbar J_{NN'} \tilde{I}_N \cdot \tilde{I}_{N'} \quad [1]$$

where $E_{NN'}$ is the energy of the spin-spin coupling of nuclei N and N', \hbar is Planck's constant divided by 2π , I_N and $I_{N'}$ are the respective nuclear spin angular momentum vector operators of N and N', and $J_{NN'}$ is the isotropic nuclear spin-spin coupling constant.

Ramsey and Purcell (2) proposed a mechanism for the transmission of spin information between nuclei. They suggested a nucleus N spin polarizes an electron in one of its orbitals, this electron then spin polarizing another electron in the bonding orbital, and so on along the bonds of the molecule, until the spin polarized electron in the orbital of nucleus N' spin polarizes this nucleus.

This mechanism was given mathematical form by Ramsey (3). The spin Hamiltonian for the interaction was a sum of three terms corresponding to three types of

possible interactions between the nuclear and electron spins.

$$H = H_1 + H_2 + H_3. \quad [2]$$

H_1 is the interaction of the nucleus with the magnetic field produced by the orbital motions of the electrons and is given by the expression

$$H_1 = 2\beta\hbar \sum_k \sum_N \frac{\gamma_N \tilde{L}_{kN} \cdot \tilde{I}_N}{r_{kN}^3} \quad [3]$$

where β is the Bohr magneton, γ_N is the magnetogyric ratio of nucleus N , L_{kN} is the operator for the orbital angular momentum of electron k about nucleus N , and r_{kN} is the distance of electron k from nucleus N .

H_2 is the magnetic dipole-dipole interaction of the nuclear and electron spins given by the expression

$$H_2 = 2\beta\hbar \sum_k \sum_N \gamma_N \left[\frac{3(\tilde{S}_k \cdot \tilde{r}_{kN})(\tilde{I}_N \cdot \tilde{r}_{kN})}{r_{kN}^5} - \frac{\tilde{S}_k \cdot \tilde{I}_N}{r_{kN}^3} \right] \quad [4]$$

where S_k is the spin angular momentum operator of electron k .

H_3 , called the Fermi contact interaction, is similar to H_2 but applies to the case where r_{kN} is zero and is only effective for electrons in s orbitals since only these have a finite density at the nucleus. It is given by the expression

$$H_3 = \frac{16\pi\beta\hbar}{3} \sum_k \sum_N \gamma_N \delta(r_{kN}) \tilde{S}_k \cdot \tilde{I}_N \quad [5]$$

where $\delta(r_{kN})$ is the Dirac delta function which causes the expression to be evaluated only when r_{kN} is zero.

Calculations showed that for protons the Fermi contact term, equation [5], made the greatest contribution to the coupling constant, the other terms being negligible. Most treatments of the proton coupling constants are restricted to the evaluation of the contact term. Contributions to the coupling from terms other than the Fermi contact term may not be negligible where other nuclei are concerned.

Variational and perturbational methods can be used to evaluate the coupling energy. The former are successful for small molecules (4) but the mathematical complexities arising in the considerations of large molecules preclude their use in these cases. The perturbational methods have been employed in the majority of theoretical calculations of coupling constants.

Equation [1] suggests that the expression for the coupling energy should be bilinear in \tilde{I} . The spin Hamiltonian is linear in \tilde{I} . In a perturbational approach, the bilinearity is achieved by the use of the second order energy correction

$$E^{II} = - \sum_n \frac{\langle 0 | H | n \rangle \langle n | H | 0 \rangle}{E_n - E_0} \quad [6]$$

The superscript on E designates second order. The summation is over the n excited states. E_n is the energy of the nth excited state and E_0 is the energy of the ground state denoted by 0. H is the spin Hamiltonian, equation [2].

For protons the contact term predominates, and so H can be replaced by H_3 in equation [6]. Then substitution of equation [5] into equation [6] leads to the expression

$$E_3^{II} = -\frac{1}{3} \left(\frac{16\pi\beta h}{3} \right)^2 \sum_N \sum_{N'} \gamma_N \gamma_{N'} \tilde{I}_N \cdot \tilde{I}_{N'} \quad [7]$$

$$\times \sum_n \langle 0 | \sum_k \delta(r_{kN}) \tilde{S}_k | n \rangle \langle n | \sum_{k'} \delta(r_{k'N'}) \tilde{S}_{k'} | 0 \rangle$$

$$\times (E_n - E_0)^{-1} .$$

The subscript 3 denotes that only the contact term is considered. Comparison of equation [7] with equation [1] yields an expression for the coupling constant J_{NN}^3 ,

$$J_{NN}^3 = -\frac{2}{3h} \left(\frac{16\pi\beta h}{3} \right)^2 \gamma_N \gamma_N \quad [8]$$

$$\times \sum_n \langle 0 | \sum_k \delta(r_{kN}) \tilde{S}_k | n \rangle \langle n | \sum_{k'} \delta(r_{k'N}) \tilde{S}_{k'} | 0 \rangle$$

$$\times (E_n - E_0)^{-1} .$$

To avoid the sum over excited states in equation [8], the energy difference, $E_n - E_0$, can be approximated by an average excitation energy ΔE , and using the matrix sum rule, the expression can be written as

$$J_{NN}^3 = -\frac{2}{3h} \left(\frac{16\pi\beta h}{3} \right)^2 \frac{\gamma_N \gamma_N}{\Delta E}$$

$$\times \langle 0 | \sum_{k,j} \delta(r_{kN}) \delta(r_{jN}) \tilde{S}_k \cdot \tilde{S}_j | 0 \rangle .$$

Equations [8] and [9] require the excited and/or ground state wave functions of the molecule. Work to date

has primarily used both valence bond and molecular orbital (MO) theory to calculate the wavefunction, the latter becoming prevalent due to its relative mathematical simplicity in calculations on large molecules. The employment of both formulations in the calculation of spin coupling constants has been reviewed and the strengths and shortcomings of each compared (5).

2. Finite Perturbation Calculations

A finite perturbation theory was formulated by Pople et al. (6) and was used with self-consistent field (SCF) molecular orbitals to give an alternative expression to equation [8] for the coupling constant. If the interaction energy, equation [1], is rewritten as

$$E = K_{NN'} \tilde{\mu}_N \cdot \tilde{\mu}_N \quad [10]$$

where μ_N is the magnetic moment of nucleus N defined by the expression

$$\tilde{\mu}_N = \gamma_N \hbar \tilde{I}_N \quad [11]$$

and $K_{NN'}$ is a reduced coupling constant related to $J_{NN'}$ by the expression

$$J_{NN'} = \frac{h\gamma_N\gamma_{N'}}{2\pi} K_{NN'} \quad [12]$$

then considering equations [8], [10], and [12], and the Hellman-Feynman theorem, the reduced coupling constant can be written as

$$K_{NN'} = \frac{\partial}{\partial \mu_{N'}} \left(\langle \psi(\mu_{N'}) | H'_N | \psi(\mu_{N'}) \rangle \right). \quad [13]$$

H'_N is defined as

$$H'_N = \frac{16\pi\beta}{3} \sum_k \delta(\tilde{R}_{kN}) \tilde{S}_{kZ} \quad [14]$$

where R_{kN} is the position vector of electron k relative to the nucleus N' .

$\psi(\mu_{N'})$ is an unrestricted single determinant wavefunction of the system when only the perturbation due to nucleus N' is considered, and is calculated from the Roothaan equations, i.e. the Hartree-Fock equations in the LCAO (linear combination of atomic orbitals) approximation. The wavefunction is unrestricted in that electrons of α spin and electrons of β spin are assigned to completely independent sets of molecular orbitals in order to accommodate the uneven distribution of α and β spins caused by the perturbation. This condition results in two Fock Hamiltonian matrices, one each for the α and β electrons, and the perturbation h_{pert} is added or subtracted as the term

$$h_{\text{pert}} = \frac{8\pi\beta\mu_{N'}}{3} \int \phi_\mu \delta(r_{N'}) \phi_\nu dr \quad [15]$$

to the one electron core part of the α or β Fock matrices respectively. ϕ_μ and ϕ_ν are atomic orbitals of the chosen basis set.

Using the LCAO SCF wave function $\psi(\mu_{N'})$, equation [13] becomes

$$K_{NN'} = \frac{8\pi\beta}{3} \sum_{\mu,\nu} \int \phi_\mu(R_N) \phi_\nu(R_N) dR \quad [16]$$

$$\times \left[\frac{\partial}{\partial \mu_{N'}} \rho_{\mu\nu}^{\text{spin}}(\mu_{N'}) \right]_{\mu_{N'}} = 0$$

where $\rho_{\mu\nu}^{\text{spin}}(\mu_{N'})$ is the spin density due to the perturbing moment $\mu_{N'}$ and is defined as the difference in the SCF bond orders $P_{\mu\nu}$ of the α and β matrices,

$$\rho_{\mu\nu}^{\text{spin}} = P_{\mu\nu}^{\alpha} - P_{\mu\nu}^{\beta} . \quad [17]$$

Any level of approximation can be used to calculate $K_{NN'}$ from equation [16]. In the semi-empirical INDO (intermediate neglect of differential overlap) approximation the term [15], now designated $h_{N'}$, becomes

$$h_{N'} = \frac{8\pi\beta\mu_{N'}}{3} S_{N'}^2(0) \quad [18]$$

where $S_{N'}(0)$ is the function for the valence s orbital of atom N' . The reduced coupling constant is now

$$K_{NN'} = \left(\frac{8\pi\beta}{3} \right)^2 S_N^2(0) S_{N'}^2(0) \times \left[\frac{\partial}{\partial h_{N'}} \rho_{S_N S_{N'}}^{\text{spin}}(h_{N'}) \right] h_{N'} = 0 \quad [19]$$

where $\rho_{S_N S_{N'}}^{\text{spin}}(h_{N'})$ is the diagonal spin density matrix element of the valence s orbital of atom N.

The method of finite differences can be used to evaluate $K_{NN'}$ and in this case equation [19] can be approximated by

$$K_{NN'} = \left(\frac{8\pi\beta}{3} \right)^2 S_N^2(0) \frac{\rho_{S_N S_{N'}}^{\text{spin}}(h_{N'})}{h_{N'}} . \quad [20]$$

From this expression and equation [12] the spin-spin coupling constant $J_{NN'}$ can be calculated.

The coupling constant values calculated from

equation [20] are semi-empirical. The results reproduce both general and experimental trends, and to a good extent, the signs and magnitudes of the experimental values (7). However, this is not the case for results obtained when single determinant wavefunctions are used in ab initio calculations. Some general experimental trends have been reproduced, but actual experimental values of the coupling constants have been poorly predicted. There is doubt that single determinant wavefunctions in ab initio calculations can yield values in agreement with experiment.

Theoretically, the finite perturbation method is not equivalent to the sum over states perturbation method (9) and thus there will be differences in the numerical values of the properties calculated by the two methods. This is due to the fact that in the FPT (finite perturbation theory) singly excited states cannot be introduced into the perturbed wavefunction without also introducing doubly excited states in a restricted manner. These differences are most noticeable in spin-spin coupling constant calculations when configuration interaction is included in the unperturbed wavefunctions.

3. σ - π Interactions

If a molecule contains only σ bonds the spin-spin coupling can be calculated by substituting a wavefunction Ψ

for the system into the above perturbation expressions. If the molecule also contains π bonds, substitution of the wavefunction describing the system will yield the value of the spin-spin coupling which is calculated if the π system were not included in the wave function, that is, the π contribution to the coupling is zero. This is the case when the contact Hamiltonian is solely considered; to have a non-zero matrix element the orbital function must have a non-zero value at the nucleus which is not true for π orbitals.

In order to produce a spin polarization in the system a σ - π exchange interaction must be considered. This can be done by including a Hamiltonian for the σ - π interaction, equation [21],

$$H_{\sigma\pi} = \sum_{\sigma,\pi} \frac{e^2}{r_{\sigma\pi}} P_{\sigma\pi} \quad [21]$$

in the total Hamiltonian for the system. $P_{\sigma\pi}$ is a permutation operator which interchanges σ and π electrons. In self consistent field calculations the σ - π interaction is accounted for by the exchange operators present in the SCF Hamiltonian.

The assumption that the mechanism responsible for the hyperfine splittings in π electron radicals is the same as that responsible for transmission of spin polarization from the σ system to the π system, allowing the latter to contribute to the nuclear spin-spin coupling,

can simplify the theory and calculation of the π contribution. Two early theories which employed this simplification were those of McConnell (10) and of Karplus (11).

McConnell considered the contributions of the electrons to the coupling of aromatic protons. Using the empirical equation

$$a_N = Q\rho_N \quad [22]$$

where a_N is the hyperfine splitting due to the proton N, ρ_N is the unpaired electron density at the carbon atom to which proton N is bonded, and Q is a proportionality constant. An effective Hamiltonian analogous to the contact Hamiltonian, equation [5], can be formed from this expression.

$$H = g\beta Q \sum_{k,N} \Delta_N(k) \tilde{S}_k \cdot \tilde{I}_N \quad [23]$$

$\Delta_N(k)$ is defined by

$$\langle \phi_N(k) | \Delta_{N'}(k) | \phi_{N''}(k) \rangle = \delta_{NN'} \delta_{N'N''} \quad [24]$$

and $\phi_N(k)$ is a p- π atomic orbital centred on atom N. Substitution of equation [23] into equation [6], and using the average energy approximation and matrix sum rule, yields an expression for the π contribution to the coupling, $J_{NN'}^\pi$, analogous to equation [9].

$$J_{NN'}^\pi = - \frac{2(g\beta Q)^2}{3h\Delta E} \langle 0 | \sum_{k,j} \Delta_N(k) \Delta_{N'}(j) \tilde{S}_k \cdot \tilde{S}_j | 0 \rangle \quad [25]$$

The ground state molecular wavefunction describes only the molecular π system and is justified by the σ - π

separability approximation (12). It is given as a single antisymmetrized product of π molecular spin orbitals which are linear combinations of atomic orbitals.

Karplus, unlike McConnell, modified the wavefunction rather than the Hamiltonian in equation [8] which can be rewritten as

$$J_{NN'} = \frac{2}{3h} \sum_{\tau} \langle \psi_S | \xi \sum_k \delta(r_{kN}) \tilde{S}_k | \psi_T \rangle \quad [26]$$

$$\times \langle \psi_T | \xi \sum_j \delta(r_{jN'}) S_j | \psi_S \rangle (E_S - E_T)^{-1}$$

where ψ_S is the ground state singlet wavefunction, ψ_T is an excited triplet state wavefunction, and ξ designates the remaining constants in equation [8].

The σ - π Hamiltonian [21] was assumed to be a perturbation and was used with the Rayleigh-Schrödinger first order perturbation expression to find the ground and excited state wavefunctions used in equation [26].

E.S.R. was again used to simplify the calculations. The hyperfine coupling constant a_N is given by the expression

$$a_N = \frac{2}{h} \langle \psi_D | \xi \sum_k \delta(r_{kN}) \tilde{S}_k | \psi_D \rangle \quad [27]$$

where ψ_D is the ground state doublet wavefunction of the π electron radical corresponding to the molecule under consideration. The matrix elements of equation [26] can be written in terms of the hyperfine constant a_N , an example being,

$$\begin{aligned} \langle \Psi_S | \xi \sum_k \delta(r_{kN}) \tilde{S}_k | \Psi_T \rangle & \quad [28] \\ & = \frac{1}{2} (1 + \lambda)^{-\frac{1}{2}} (h) \frac{(\Delta\sigma)^2}{(\Delta\sigma)^2 - (\Delta\pi)^2} a_N \end{aligned}$$

where λ is a parameter determining the ratio of ionic and covalent contributions, $\Delta\sigma$ is a σ doublet excitation energy, and $\Delta\pi$ is a π singlet to triplet excitation energy. If an LCAO MO description of the π orbitals is used, the expression for the π contribution to the nuclear spin-spin coupling is

$$\begin{aligned} J_{NN'} & = -h a_N a_{N'} & [29] \\ & \times \sum_{r,s} \frac{C_{Nr} C_{Ns} C_{N'r} C_{N's} \Delta\sigma_N^2 \Delta\sigma_{N'}^2}{\Delta\pi_{rs} (\Delta\sigma_N^2 - \Delta\pi_{rs}^2) (\Delta\sigma_{N'}^2 - \Delta\pi_{rs}^2)}. \end{aligned}$$

The sum is over all triplet excited states in the system and the C's are atomic orbital expansion coefficients.

An unsatisfactory feature of equation [29] is the fact that it becomes non-applicable in the fortuitous circumstance that $\Delta\sigma$ is equal to $\Delta\pi$. Two approaches were presented to obviate this difficulty.

Ditchfield and Murrell (13) modified the Ramsey perturbation expression for the nuclear spin-spin coupling such that it included both the σ - π exchange interaction and the Fermi contact interaction as perturbations. This was done by using double perturbation theory. The Hamiltonian for the perturbed system is written as

$$H = F + \lambda V + \mu W. \quad [30]$$

F is the Hamiltonian of the unperturbed system, V is the

σ - π exchange Hamiltonian [21], W is the spin Hamiltonian [2], and λ and μ are perturbation parameters. Following the procedure of Ramsey as described above, the expression for the nuclear spin-spin coupling can be extracted from the expression for the energy of the perturbed system, which is solved by the Rayleigh-Schrödinger method. If the LCAO MO approximation is used in the description of the π orbitals, the π contribution to the coupling is given by

$$\begin{aligned}
 J_{NN'} = & - \frac{a_N a_{N'} h}{4} \sum_{r,s} C_{Nr} C_{Ns} C_{N'r} C_{N's} \Delta\sigma_N \Delta\sigma_{N'} \\
 & \frac{1}{\Delta\pi_{rs}} \left[\frac{1}{\Delta\sigma_N \Delta\sigma_{N'}} + \frac{1}{\Delta\sigma_N (\Delta\sigma_{N'} + \Delta\pi_{rs})} \right. \\
 & + \frac{1}{(\Delta\sigma_N + \Delta\pi_{rs}) \Delta\sigma_{N'}} \\
 & \left. + \frac{1}{(\Delta\sigma_N + \Delta\pi_{rs}) (\Delta\sigma_{N'} + \Delta\pi_{rs})} \right]. \quad [31]
 \end{aligned}$$

All terms are as defined for equation [29].

Cunliffe, Grinter and Harris (14) also modified the Karplus method in order to overcome the difficulty of the possible zero denominator. Rather than solve for new wavefunctions which included the σ - π interaction as a perturbation, they used a variational method with $H_{\sigma\pi}$ included in the Hamiltonian of the system. Diagonalization of the variational Hamiltonian matrix yields a set of wavefunctions which are linear combinations of the original functions. Substitution of these wavefunctions

in the Ramsey perturbation expression gives

$$J_{NN'} = - \frac{2}{3h} \sum_r \langle \psi_S | \xi \sum_k \delta(r_{kN}) \tilde{S}_k | \psi_T^r \rangle \quad [32]$$

$$\times \langle \psi_T^r | \xi \sum_j \delta(r_{jN'}) \tilde{S}_j | \psi_S \rangle (E_r)^{-1}$$

where E_r is the energy of the r th triplet state. If the LCAO MO approximation is used to set up the π molecular orbitals and the E.S.R. hyperfine constants are used to approximate certain integrals, equation [32] becomes

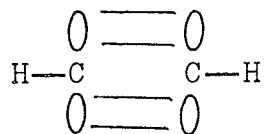
$$J_{NN'} = - \frac{h}{4} \frac{a_N a_{N'} \Delta \sigma_N \Delta \sigma_{N'}}{\gamma_N \gamma_{N'}} \sum_T \frac{W_N^r W_{N'}^r}{E_r} \quad [33]$$

where γ_N is the matrix element

$$\langle \phi_N(1) \sigma_N(2) | H_{\sigma\pi} | \phi_N(2) \sigma_N^*(1) \rangle$$

and W_N^r is a sum of coefficients of the molecular orbital wavefunctions resulting from the diagonalization of the variational matrix. ϕ_N is the $2p\pi$ atomic orbital of carbon atom N , and σ_N and σ_N^* are the bonding and anti-bonding σ molecular orbitals localized in the $C-H_N$ bond.

In the above cases, the π contribution to the coupling could be directly calculated because of the choice of wavefunctions. As illustrated below



only the electrons in the $C-H$ fragments and in the π

bonds are considered, the electrons in the remaining σ bonds being neglected.

However, in the finite perturbation theory applied to the self consistent field molecular orbitals as described above, all the valence electrons are considered. Since exchange operators are present in the Fock Hamiltonian the σ - π exchange interaction is included in the evaluation of the coupling constant, and thus would give the total coupling between two nuclei. This is true when the semi-empirical INDO approximation is used in the calculation. However, if the CNDO (complete neglect of differential overlap) approximation is used, the one-centre exchange integrals are neglected and so only the coupling through the σ system is calculated. The difference between the CNDO and INDO values roughly indicates the π contribution to the spin-spin coupling if slight differences in parameterization are ignored.

In order to differentiate between σ and π contributions to the experimental coupling, which is, in the assumption of σ - π separability the sum of the respective contributions, certain generalizations have been inferred from coupling constant data, both theoretical and experimental.

The coupling through the σ system is greatly attenuated as the number of bonds between the coupling nuclei increases. In most cases the σ coupling between nuclei separated by six or more bonds is negligible.

On the other hand, though the π coupling is slightly attenuated with increasing number of bonds, it is measureable over six or more bonds. Thus any coupling which does occur in those circumstances should be suspected of being a π coupling.

In planar molecules the π coupling should be quite insensitive to the orientation of the bonds joining the two nuclei. Thus, the π coupling should be nearly the same for the cis and trans orientation of atoms while the σ coupling should differ for the two orientations. This, however, does not allow the conclusion that, because two orientations have the same coupling, it is necessarily a π coupling.

In conjugated molecules replacement of a proton bonded to an sp^2 hybridized carbon atom by a methyl group causes the π coupling from some other proton to the methyl group to be of the same magnitude but of opposite sign as to the replaced hydrogen (15). The methyl group must be freely rotating. This phenomenon can be explained by noting the proportionality of J^π to the hyperfine coupling constant which is approximately equal but of opposite sign in the two radical fragments $\dot{C}-H$ and $\dot{C}-C-H$. The effect of methylation on the π system has been assumed to be negligible. Using this technique the five-bond para coupling in benzene and the six-bond benzylic coupling in toluene have been thought to be solely due

to the π system.

In the special case of aromatic molecules it has been proposed from experimental and theoretical investigations that substituent effects on nuclear spin-spin couplings in these molecules depend on the polarization of the σ system of the molecule by the substituent (16). If there is a negligible effect on the coupling upon introduction of a substituent a possible consideration is that the greater part of the coupling is through the π system.

As mentioned previously the above criteria are only general. They are an indication that a π coupling mechanism could be present, but each case must be considered individually, there being many parameters influencing the values of the coupling constants.

4. Nuclear Magnetic Resonance Parameters and Conformation

To this point the discussion has concerned the theoretical calculation of nuclear spin-spin couplings. In this area of research experimental data is used as a gauge of the accuracy of the calculations. Experimental data can also be used to predict or assign the conformation or structure of molecules under consideration.

In order to infer the structure of a molecule using experimental coupling values some correlation between the structure and these values must be found. This can be done in a number of ways, usually observing the change in coupling with the change in structure of

a series of test molecules of known geometry, or using data from test molecules to verify theoretically derived correlations. The latter method was used to develop the most general correlation of structure with coupling, the Karplus rule (17), while the former was used to show the stereospecificity of the five-bond "zig-zag" coupling, mainly in aromatic systems (18).

a) Vicinal Couplings

The Karplus rule concerns the correlation of vicinal coupling constants with the dihedral angle and is usually given by the expressions

$$J = J^0 \cos^2 \phi - C \quad (0^\circ \leq \phi \leq 90^\circ) \quad [34]$$

$$J = J^{180} \cos^2 \phi - C \quad (90^\circ \leq \phi \leq 180^\circ)$$

where J is the experimental coupling constant, J^0 , J^{180} , and C are constants particular to the system under investigation, and ϕ is the dihedral angle. These expressions followed from valence bond calculations performed by Karplus, and were subsequently verified by experiment.

However, other factors than the dihedral angle affect the vicinal coupling constant but which are not considered in the equations. These factors can be substituent electronegativities and orientation, hybridization of the carbon atom, and bond angles and lengths. Neglect of these factors in the application of the Karplus rule can lead to erroneous conclusions (19).