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SUBSŢĮTUENT EFFECTS

PROTON-PROTON AND CARBON-PROTON.

by . . b

CJohn A. Hiltz

. A Thesis

Submitted to the faculty of Graduate Studies

for the Degree.

DOCTOR OF PHILOSOPHY

July 1984

Department of Chemistry Dalhousie University Halifax; Nova Scotia Canada

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Carbon-proton coupling constants have been measured for series of ethyl and ethanoic acid derivatives and 2,2-diphenylmethylcyclopropane and 1-(1-deutero butylcyclohexyl)methane derivatives. The coupling constants have been correlated with electronegativity and Swain-Lupton Field factors in an attempt to obtain useful. correlations between observed coupling constants and substituent parameters.

Abstract

Good correlations are obtained with electronegativity when compounds are compared within sets in which other parameters such as Periodic Table Row and dihedral angles are constant.

Ratios of carbon-proton to proton-proton coupling constants have been obtained which have better predictive ability than the single ratio that is currently in use in, the chemical literature.

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NB a	Xi.
PXN'YN'	- charge density-bond order matrix element for p _x and p _y orbitals on nucleus N ¹ with <u>alpha</u> and <u>beta</u> spins.respectively
¢Ω _{YN'YN} ,	- imaginary part of the charge density- bond order matrix for py orbitals on nucleus N ¹ with <u>alpha</u> and <u>beta</u> spins
o _{JN,N} ,	- orbital-dipole contribution to the coupling constant
PXN'YM	- chargen density-bond order matrix element for the $p_{\rm X}$ and $p_{\rm Y}$ orbitals on nucleus $\rm N^{-}$.
CJNON	- Fermi contact contribution to the coupling constant
s ² (0)	- s'electron density on nucleus N
P SNSN'	- diagonal element of the charge density- bond order matrix for s electron spin orbitals on nucleus N ¹ with an <u>alpha</u> spin
ὰ,β	- with reference to spin +1/2 and -1/2 respectively
Φ,	- dihedral angle between vicinally coupled nuclei
۲. 0 ^۲	- value of vicinal coupling constants when is 180 degrees
E	substituent electronegativity
·S', S"	- bond angles along a vicinal coupling path
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JĘ .	- trans vicinal coupling constants where the substituents are trans to each other
Jg	 trans vicinal coupling constant where the substituents are gauche to each other
gj ^{HX} H	<u>gauche</u> vicinal proton-proton coupling constant with substituents H and X <u>trans</u> to the coupled protons

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, ¹		۹.۲	•	ethane-like fragment
	in	· _{@ee}	د د	dihedral angle between euatorial protons in
, ,		- ,	•	an ethane-like fragment
. •	Ð	, ŵ	-	dihedral angle between axial and equatorial
•				protons in an ethane-like fragment - '
R	•	R,		Ratio
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_	*			trans coupling constant , "
, ,	-	J ^C .	8	<u>cis</u> coupling constant
6	2.	MO		molecular orbital
4 .		VB	°	valence bond
	5 P	V 1.	ı	
	÷ -	Ac	~ 100 A	acetyl (-COCH ₃)
• •		^r cc [*]		carbon-carbon bond length
		r ² ° '.		correlation coefficient
· ·	<u>^</u>	φ ••• 1	•	
8	~	Jops	6 em	observed coupling constant
-	اد د	AE :		rotational energy barrier
		R	^ =	gas constant
	•	۰ ۳	5	temperature (Kelvin)
	v	• 4 · · · ·	· ,	
		` G		statistical weighting factor
2		`e [`] _	° =	natural logarithm
10 • •	ł	A.B.M_X.	<u>دسم</u>	spin system where A, B, M, and X refer to
* *	~	%− <u>λ-,</u> Ω	Àr .	groups of magnetically equivalent nuclei,
•	<i>r</i> ,	• _ 0	۰.	subscripts x, y, z, and t refer to the number of magnetically equivalent nuclei
,	~ * ~	v , t s	£	in each group and the proximity of the
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4 D 17		AB doublet of doublets
s \$	т ₂	- spin-spin relaxation time
9 <u>6</u> 1	$\delta_{\alpha \alpha}$	- chemical shift in parts per million from
		Tetramethylsilane for proton spectra
		- porte por million
, B ,	ррш	- barra ber wittioù
·	EE.	- ethyl
۰ ۲ ۲	Ph	- phenyl .
	Me	- methyl
۶ ^۴	DNPH .	- dinitrophenylhydrazone
	F ´	- Swain-Lupton field factor
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CHAPTER

INTRODUCTION

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ONE

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1.1. CARBON-PROTON AND PROTON-PROTON COUPLING CONSTANTS

1.1.

The measurement of carbon-13 natural abundance nuclear magnetic resonance (13 C-NMR) spectra has become widely available with the development of pulsed Fourier transform (PFT) NMR spectrometers (1). This instrumental development has helped overcome the inherent insensitivity of the 13 C nucleus (62 times less than that of the hydrogen nucleus at constant field) and its ' low natural abundance (1.1%). Both proton decoupled and undecoupled 13 C NMR spectra are now routinely acquired (vide infra).

Prior to the development of PFT NMR spectrometers, costly and inconvenient ¹³C sample enrichment techniques were often required to observe ¹³C nuclear magnetic gesonance phenomena (2-6). Some one-bond carbon proton coupling constants $(J_{C,H})$ were measured from the ¹³C satellite peaks in the proton (¹H) NMR spectra but long range carbon-proton coupling constants, i.e., two-bond (²J_{C,H}) and three-bond (³J_{C,H}) carbon-proton coupling constants, were less readily accessible by this technique unless the coupling were large (4, 7, 8). Other special techniques (9-13) have been developed but have not found widespread application.

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Pulsed Fourier transform techniques have made the measurement of carbon-proton coupling constants easier but generally not as easy as the measurement of proton-proton coupling-constants $(J_{H,H})$. The proton (^{1}H) has a high natural abundance (99.985%) and is approximately 62 times more sensitive than the ^{13}C nucleus which has allowed the measurement of high resolution ^{1}H spectra by conventional continuous wave (CW) techniques.

A large volume of proton, NMR data, including both chemical shifts and coupling constants, has been, recorded. The availability of this data has allowed the development of numerous relationships in which proton chemical shifts and coupling constants are related to molecular structure, substituents effects and stereochemistry. It has been assumed for a long time (5) that ¹³C chemical shifts and carbon-proton coupling constants could be utilized in an analogous manner to predict structural parameters.

Experimentally, the acquisition of a natural abundance ¹³C NMR spectra using a PFT spectrometer can be time consuming. Furthermore, relatively concentrated samples are required to increase the sensitivity when proton undecoupled spectra are desired. As the concentration of the solute in a solution increases, so do solute-solvent and solute-solute interactions which adversely effect spectral resolution.

At present, 100 megaHertz (MHz) ¹³C NMR spectrometers

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are available which reduce both the acquisition time and sample concentration requirements for the acquisition of proton undecoupled ¹³C NMR spectra. These higher magnetic field instruments also reduce the complexity of the spin systems under observation allowing easier analysis of the proton undecoupled spectra and extraction. of the desired doupling constants.

In complex systems it is just about impossible to extract all the carbon to proton coupling constants. A proton undecoupled oarbon 13 NMR spectrum of 2-methylpiperidine is shown in Figure 1.1. Complete analysis of spectra of such complexity can be difficult and time consuming. It would then be expedient if a simple relationship existed which allowed one to calculate with some degree of certainty, the expected carbon-proton coupling constant from a measured proton-proton coupling 'constant for a structurally similar compound.

Much work has been directed toward the determination of a simple ratio (selationship) between proton-proton and carbon-proton coupling constants. Correlations established by several authors (14-19) have been used to propose the use of a ratio in predicting carbon-proton coupling constants $(J_{C,H})$ Grom measured proton-proton coupling constants $(J_{H,H})$. However, close examination of these correlations indicates that a single ratio applied to all coupling constants is quite inappropriate. The ratio of the value of $J_{C,H}$ to $J_{H,H}$ for structurally



Figure 1.1. Proton undecoupled ¹³C natural abundance NMR spectrum of 2-methylpiperidine. The complexity of the proton undecoupled carbon spectra makes measurement of all long range carbon-proton coupling constants difficult and time consuming.

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Similar compounds is found to vary from one series of compounds to another, suggesting that further study of the effect of structural and substituent effects on carbon-proton coupling constants is required. These studies may allow a better understanding of the coupling mechanisms for carbon-proton coupling pathways and allow comparison of 13C and 1H coupling data.

The theoretical basis of coupling, both proton-proton and carbon-proton is reviewed in the following section. This is pertinent as the mathematical treatment of the coupling phenomena suggests that carbon-proton and proton-proton coupling constants have similar physical basis.

1.2. THEORETICAL BASIS OF NUCLEAR MAGNETIC RESONANCE

Field independent splittings in nuclear magnetic spectra were first observed by Gutowsky et.al. (20,21) and Hahn and Maxwell (22,23). The energy $(E_{N,N})$ of interaction responsible for these splittings is given by equation (1.01)

 $b E_{N,N} = h J_{N,N} I_N I_N I_N$ (1.01) where h is Planck's constant, and $J_{N,N}$ is the indirect nuclear spin-spin coupling constant between nuclei N and N' with spins I_N and I_N , respectively.

Ramsey and Purcell (24) pointed out that the

6
coupling, J_{N,N¹}, might arise due to the magnetic interaction of the nuclei with the electron spin magnetic" moments which are in turn coupled together. In a subsequent paper Ramsey (25) delineated three types of interactions that could give rise to spin spin coupling constants. These were dipole-dipole interactions, orbital-dipole interactions, and Fermi contact

The dipole-dipole interactions take place between the magnetic dipoles of the electrons and the nuclear spins. Within a self-consistent perturbation framework (26) the contributions from the dipole-dipole interactions to the coupling ${}^{(D}J_{N,N^{0}})$ is given by equation (1.02) $J_{c}^{D}(nn') \Rightarrow \frac{\mu_{O}\mu_{D}^{2}}{10\pi^{2}} = \frac{\gamma_{n}\gamma_{n}}{\gamma_{n}\gamma_{n}} \langle r_{a}^{-3} \rangle_{p} \langle r_{b}^{-3} \rangle_{p} [2P_{2n}^{\alpha\alpha} - P_{xn'xn}^{\alpha\alpha} - P_{vn'yn'}^{\alpha\alpha} + 3P_{xn'yn'}^{\alpha\beta} - 3Q_{yn'yn'}^{\alpha\beta}]$ (1.02)

where μ_0 is the permeability of a vacuum, μ_b is the Bohr magneton, γ is the magnetogyric ratio, $\langle r^{-3} \rangle_p$ is the expectation value of the inverse cube of the separation between the mucleus and its p electrons, $P_{ZN'ZN}^{\alpha\alpha}$ is the diagonal element of the charge density-bond order matrix for the p_z orbitals on nucleus N' with an α spin, $P_{XN'YN'}^{\alpha\beta}$ is the charge density-bond order matrix element for the p_x and p_y orbitals on nucleus N' with α and β spins respectively, and $Q_{YN'YN'}^{\alpha\beta}$ is the imaginary part of the charge density-bond order matrix for the p_y orbitals on nucleus N' with α and β spins.

The orbital-dipole term arises from the interaction

between the magnetic dipoles of the electrons and the nuclear spin. Using a self consistent perturbation treatment (26) Ramsey calculated the contribution of the orbital-dipole interactions to the coupling $({}^{O}J_{N,N'})$. This orbital term is given in equation (1.03)

 $J_{n}^{o}(nn^{2}) = \frac{\mu_{0}\mu_{b}^{2}}{3\pi^{2}} \bar{n} \gamma_{n} \gamma_{n'} \langle ra^{3} \rangle_{p} \langle rb^{3} \rangle_{p} \left[P_{xn'yn'} + P_{zn'yn'} + P_{xn'zn'} \right]$ (1.03)

where $P_{XN'YN'}$ is the charge density-bond order matrix element for the p_X and p_y orbitals on atom N'.

Fermi contact interactions arise between electron and nuclear spins. Ramsey (26) calculated the Fermi contact contribution to the coupling constant ($^{C}J_{N,N}$) to be given by equation (1.04)

 $\int_{J^{c}(nn)}^{J^{c}} = \frac{16}{9} \pi \mu_{0} \mu_{b}^{2} \gamma_{n} \gamma_{n'} s_{n}^{2} = 0 s_{n'0}^{2} p_{sn'sn'}^{\alpha}$

where $s^2(0)$ is the s electron density on nucleus N, and $P_{SNSN'}^{\alpha}$ is the diagonal element of charge density-bond order matrix for s electron spin orbitals on nucleus N' with an α spin.

(1.04)

Inspection of the dipole-dipole, $({}^{D}J_{N,N'})$, and orbital-dipole, $({}^{O}J_{N,N'})$, contributions to the coupling constant, given in equations (1.02) and (1.03) respectively, reveals that these terms can be non zero only when both the coupled nuclei have p electrons. That is, both equations include an expectation value for the inverse cube of the separation between a coupled nuclei and its p electron. For a hydrogen nucleus this value tends to zero. Therefore, coupling involving the proton; either proton-proton or carbon-proton, should be independent of the orbital-dipole and dipole-dipole terms and should be adequately described by the Fermi contact term (25) where p electron density is not involved in the equation.

Researchers have used molecular orbital (27,28) and valence bond approaches to calculate the Fermi contact contributions to coupling constants. The calculations have been plagued by the difficulty in constructing suitable excited state wave functions. Such perturbation treatments in general can be no better than the ground state wave functions used and are limited by the construction of such wave functions. This has resulted in some calculated coupling constants that do not compare favourably with experiment results.

Subsequent research has been directed towards the use of larger basis sets of functions to construct the molecular orbitals of the ground state wave functions in an attempt to produce better approximations of the relevant excited state wave-functions (see reference 29). An excellent review of theoretical calculations of coupling constants has recently been published (26). Although theory is hard pressed to quantitatively

Although theory is hard pressed to quantitatively predict the magnitude of a coupling constant, the theoretical approach has been successful in predicting qualitative trends for both geminal (^{2}J) and vicinal (^{3}J)

coupling constants. Equations (1.02-1.04) indicate that terms contributing to the coupling constant are sensitive to factors that alter the s electron density at the nuclei of interest, or change the energy levels of the excited states of the molecular orbital wave functions. Such changes can then be expected to cause measurable changes in observed coupling constants.

Applied NMR spectroscopy deals with these changes and attempts to relate the variation in magnitude of a coupling constant to changes in molecular structure, stereochemistry, or substituent effects. The dihedral angle subtended by vicinally coupled nuclei. (see Figure 1.2), substituent orientation with respect to the coupling path, the electronegativity of a substituent, bond angles and bonds lengths, carbon hybridization, and medium effects have all been found to influence the magnitude of coupling constants. In the following sections these parameters and their effect on the magnitude of both proton-proton and carbon-proton Vicinal (^{3}J) and coupling constants are reviewed. geminal (²J) proton-proton and carbon-proton coupling constants are discussed separately.' Emphasis is placed on illuminating the similarities of the effect of various parameters on vicinal proton-proton and carbon-proton coupling constants and geminal proton-proton and carbonproton coupling constants. Finally, the relationships between proton-proton (and carbon-proton coupling

11 Figure 1.2. Newman projection of an ethane-like fragment showing the dihedral angle o between the coupled protons H and H1. H J. D.

constants in structurally similar compounds are reviewed.

1.3. FACTORS AFFECTING THE MAGNITUDE OF VICINAL PROTON-PROTON COUPLING CONSTANTS

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1.3.1. The Dihedral Angle Between the coupled Nuclei

The first suggestion that the magnitude of the vicinal proton-proton coupling constant was dependent upon the dihedral angle subtended by the coupled nuclei (Figure 1.2) was made by Lemieux (30). Using a valence bond, approach Karplus (31) derived, for the ethane molecule, the well known equations (1.05) and (1.06)

 ${}^{3}J_{H_{\rho}H'} = 8.5 \cos^{2}\Phi - 0.28$ $0^{\circ} < \Phi < 90^{\circ}$ (1.05) ${}^{3}J_{H_{\rho}H'} = 9.5 \cos^{2}\Phi - 0.28$ $90^{\circ} < \Phi < 180^{\circ}$ (1.06) where ${}^{3}J_{H_{\rho}H'}$ is the vicinal coupling constant between protons H and H' and Φ is the dihedral angle shown in Figure 1.2.

In an attempt to accommodate an ever increasing amount of experimental data relating the vicinal proton-, proton coupling constants to the dihedral angle, Karplus modified the equations for ethane or substituted ethanes. The new expression was given by equation (1.07)

 ${}^{3}J_{H_{\gamma}H} = A + E \cos \Phi + C \cos 2\Phi$ (1.07) where A, B and C were arbitrary constants which varied from one series of compounds to another. It soon became

evident that the form of equations (1.05) and (1.06) were correct but the constants J^0 and J^{180} in the more general equations (1.08) and (1.09),

 ${}^{3}J_{H_{g}H^{3}} = J^{0} \cos^{2}\bar{\varpi} - C$ $0^{0} < \bar{\varpi} < 90^{0}$ (1.08) ${}^{3}J_{H_{g}H^{3}} = J^{180} \cos^{2}\bar{\varpi} - C$ $90^{0} < \bar{\varpi} < 180^{0}$ (1.09) had to be varied from one series of compounds to another to accommodate the ever increasing volume of experimental coupling data. The original Karplus curve for the ethane molecule is shown in Figure 1.3 and a series of Karplus type curves for $J^{0} = J^{180}$ from 5.7 Hz to 14.7 Hz are shown in Figure 1.4.

The Karplus curve was criticized by numerous authors (32, 33, 34) on the grounds that factors other than the dihedral angle, which were known to affect vicinal coupling constants, were ignored. Nowever, Karplus (31), aware of the limitations of his valence bond approach, cautioned against the blind application of his equation nôting that factors such as substituent electronegativity, carbon hybridization, bond angles and bond bengths could affect the magnitude of the vicinal : coupling constant. These factors had to be kept as constant as possible to derive useful information regarding molecular geometry using a Karplus curve.

1.3.2. Electronégativity of the substituent

In a study of a series of ethyl halides, Glick and

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Bothner-By (35) found that the observed vicinal coupling constant could be related to the electronegativity of the substituent. The linear relationship was given by equation (1.10), p^2

 ${}^{3}J_{H_{r}H} = A - B E$ (1.10) where A and B are constants (8.4 and 0.4 respectively, for the ethyl halides) and E is the Huggins electronegativity (36). In a subsequent study of the isopropyl halides, the constants A and B were found to be 8.0 and 0.5 respectively. Thus, although the relationship was not general in the sense that A and B were not universal constants, the equation did show that ${}^{3}J_{H_{r}H}$ was dependent on substituent electronegativity and generally decreased with increasing substituent electronegativity. This trend was verified by experimental and theoretical results (37, 38, 39).

In a study of disubstituted ethanes Abraham and Pachler (40), found an additive substituent effect; the measured coupling constants varied with the sum of the substituent electronegativities. This dependence is shown in equations (1.11) and (1.12)

> $J = A - B \sum E$ (1.11) $J = J^{O} (1 - C \sum E)$ (1.12)

where A_r , B_r , and C were constants, E is the Huggins electronegativity and J^O represents the coupling constant is the absence of substituent effects. Although this additive dependence was not found to be general, it did

adequately describe the dependence of ${}^{3}J_{H_{r}H}$ on E for the mono and disubstituted ethanes. For example, equation (1.12) can predict the vicinal proton-proton coupling constants for the monosubstituted, and 1,1 and 1,2-disubstituted ethanes to within 0.3 Hz of the measured values.

1.3.3. The Orientation of the Substituent with respect to the Coupled Nuclei

In a study of isomeric steroids, Williams and Bhacca (41) observed that the gauche ($\Phi=60^{\circ}$) vicinal protonproton coupling constants, (${}^{3}J_{\mathrm{H},\mathrm{H}}$), shown in Figure 1.5 were not identical. Neither a Karplus type dihedral angle dependence nor substituent effect relationships of the type discussed above could explain the observed difference. They postulated that the orientation of the substituent with respect to the coupled nuclei was critical. This has been verified experimentally.

A general substituent effect that accounts for this `phenomenon was proposed by Booth (42). The proposal was . that a substituent exerts its maximum effect when it is trans antiperiplanar (Φ =180°) or eclipsed (Φ =0°) with part of the coupling path. This is illustrated in Figure 1.5. The substituent (OR) is equatorial in isomer I and is <u>gauche</u> (Φ =60°) to proton H_B. In isomer II proton H_A is axial and <u>trans</u> (Φ =180°) to the substituent. In both

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Figure 1.5 Two isometric steroids showing the relative orientations of the coupled nuclei and the substituent (OR). The effect of the substituent is dependent upon its orientation with respect to the coupled nuclei, ise, the value of ${}^{3}J_{Ha,Hc}$ and ${}^{3}J_{Hb,Hc}$ are different, and exerts Wes maximum effect when it is antiperiplanar to the coupling path.



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 $J_{H_{b}H_{c}} = 4.5 - 5.5 hz$ $J_{H_{a}H_{c}} = 2.5 - 3.2 hz$

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compounds the coupled nuclei, H_C and H_B in compound I_r and H_C and H_A in compound II_r subtend dihedral angles of 60° . Furthermore, the substituent is the same in both isomers. Only the orientation of the substituent with respect to the coupling path has changed, and it exerts its maximum effect, $({}^{3}J_{H_rH}$ decreases), when it is <u>trans</u> to one of the coupled protons.

Pachler (43); using molecular orbital (MO) calculations has shown that phase shifts occur in plots of vicinal proton-proton coupling constant's against the dihedral angle subtended by the coup $ot\!\!/ ext{ed}$ nuclei in The phase shift was found to substituted ethanes. increase as the electronegativity for the substituent increased. The plots of the values of $J_{H_{e}H}$ for ethane and ethyl fluoride molecules against the dihedral angle between the coupled protons are shown in Figure 1.6. Although Pachler's treatment is found to be qualitatively correct for some molecules, it fails to predict the magnitude of the measured coupling constant. For instance, ³J_{H,R} for ethane and ethyl fluoride are predicted to be 4.3 and 3.8 Hz respectively while experimentally the couplings are found to be 8.0 and 7.1

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Figure 1.6. A Karplus type plot of the value of ${}^{3}J_{\rm H,H}$ for the ethane and ethyl fluoride molecules against the dihedral angle between the coupled protons.

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1.3.4. Bond Angles, Bond Lengths, and Carbon Hybridization

The effect of changing bond angles and bond lengths on the magnitude of vicinal coupling constants is experimentally difficult to study in sp^3 hybridized carbon frameworks. A theoretical treatment predicts that ${}^3J_{H,H}$ is inversely proportional to the bond length and should decrease as the angles, s' and s", shown in Figure 1.7, are increased.

Changes in bond angles and bond lengths are usually the result of a change in substituent or a change in carbon hybridization. Substituents are known to influence the magnitude of coupling constants, but the separation of electronic effects from the effect of changes in bond angles and bond lengths is extremely difficult.

The change in the hybridization of the carbon framework has been related to changes in the magnitude of the vicinal proton-proton coupling constant. It is found that ${}^{3}J_{H,H}$ increases as the degree of s character of the hybrid orbital increases. Nonetheless, the interdependence of carbon hybridization, bond angles and bond lengths has precluded the development of relationships of the type found for the dihedral angles and substituent electronegativity effects.

As Karplus (30) has noted, the utilization of.



measured coupling constants to gain insight into the structure of an organic molecule requires that all factors that influence the magnitude of the coupling constant be considered. If all other parameters are kept as nearly constant as possible, then the effect of the variation of one parameter can be related to changes in magnitude of the observed coupling constant. Empirical relationships developed in this way provide powerful tools for structural analysis. Some of these empirical relationships are discussed below.

1.4. EMPIRICAL CORRELATIONS UTILIZING VICINAL PROTON-PROTON COUPLING CONSTANTS

1.4.1. Parameterization of Substituent Effects on Vicinal Proton-Proton Coupling Constants in Ethane-Like Fragments

In an attempt to relate the effects of substituent electronegativity on the measured coupling constants in disubstituted ethane like fragments, Abraham and Gatti (44) plotted the observed coupling constants for these, fragments against the sum of Huggins electronegativity (E) of the substituents. The coupling constants were taken from both cyclic and acyclic fragments of the type shown in Figure 1.8. In the notation, J^Q, the superscript refers to the orientation

Figure 1.8. Newman projections of a disubstituted ethane-like fragment showing the various vicinal coupling constants. In the notation J⁹ , the superscript refers *to the orientation of the coupled nuclei, and the subscript to the orientation of the substituents with respect to each other.



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of the coupled protons and the subscript refers to the orientation of the substituents with respect to each other

The	results	s are giv	ven in equations	(1.13) to	(1.16) .
	, រម្ព	= 1.35	$\div 0.63 (E_x + E_y)$	¢	· (1.13)
ŧ	, `Jţ	= 18.07	-0.88 ($E_x + E_y$)	•	`(1.]4)
•	Jg	= 8.94	-0.94 (E _x +E _y)		(1,15)
٩ţ	+ Jg'=	2Ġ.92 -	2.03 (E _x +E _y)		(1.16)

It was observed that substituent effects were not additive but that they were dependent upon each other, i.e.,

 $J_{f}^{t} \neq J_{g}^{t}$ and $J_{g}^{g} \neq (J_{f}^{g} + J_{g}^{g})^{\prime}/2$

Furthermore, equation (1.13) predicted that gauche proton-proton coupling constants increase with increasing substituent electronegativity when the substituent is not trans antiperiplanar to part of the coupling path. In all other cases the coupling constants decrease with increasing substituent electronegativity as predicted by equations (1.14) to (1.16).

1.4.2. Equation for the Quantitative Prediction of <u>Gauche</u> Vicinal Proton-Proton Coupling Constants

Forrest (45) has developed an equation which allows quantitative prediction of <u>gauche</u> coupling constants in ^Omolecules with well defined conformations and which takes into consideration substituent orientation. He assumed

that a linear relationship between the coupling constant and substituent electronegativity existed and that the difference in magnitude of the coupling constants ${}^{g}J_{H_{\rho}H}^{H_{\chi}}$ and ${}^{g}J_{H_{\rho}H}$ were mainly due to substituent orientation. In the notation ${}^{g}J_{H_{\rho}H}^{H_{\chi}}$, the left superscript refers to the orightation of the coupled nuclei, the right superscript to the substituents <u>trans</u> to the coupled nuclei, and the subscript to the coupled nuclei. See Figure 1.9.

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The ratio of these two couplings can then be written ${}^{g}J_{H_{\gamma}H}^{H\chi} / {}^{g}J_{H_{\gamma}H} = (a/a - \gamma \Delta E_{\chi}) - (\beta/a - \gamma \Delta E_{\chi}) \Delta E_{\chi}$ (1.17) where $a_{\tau} \beta$ and γ age constants and ΔE_{χ} is the difference in Huggins electronegativity of the substituent, χ , and hydrogen. Since a substituent exerts its maximum effect, when it is antiperiplanar to a coupled nuclei, γ was assumed to be smaller than β and $\gamma \Delta E_{\chi}$ small compared to a_{τ} The ratio becomes that shown in equation (1.18). ${}^{g}J_{H_{\tau}H}^{H\chi} / {}^{g}J_{H_{\tau}H} = (a/a) - (\beta/a) \Delta E_{\chi}$ (1.18)

A plot of ${}^{g}J_{H,H}^{HX}/{}^{g}J_{H,H}$ versus ΔE_{x} gave a straight line defined by equation (1.19).

 ${}^{g}J_{H,H}^{HK}/{}^{g}J_{H,H} = 1.009 - 0.462 \Delta E_{x}$ (1.19) Abraham and Gatti have shown that for ethane-like fragments the <u>gauche</u> vicinal proton-proton coupling constants can be given by equation (1.20):

 $g_{J_{H,H}} = 4.1 + 0.63 \Sigma \Delta E_i$ (1.20) Combining equations (1.19) and (1.20) gives equation (1.21).

 $g_{J_{H,H}^{HX}} = (4.1 + 0.63Z\Delta E_i) (1.009 - 0.462 \Delta E_x) (1.21)$



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Figure 1.9. Newman projections of an ethane-like. fragment showing the orientation of the coupled nuclei and substituents described by the notation $g_{H_{X}}^{H_{X}}$. The left superscript refers to the orientation of the coupled nuclei, the right superscript to the nuclei trans to the coupled nuclei, and the subscript to the coupled nuclei. Using this equation Forrest has calculated the <u>gauche</u> vicinal coupling constants for 25 cyclic compounds in the chair conformation (assuming $\Phi = 60^{\circ}$) and has found a RMS error of 0.3 Hz from the measured <u>gauche</u> coupling constants.

It is apparent that empirical correlations of the type discussed above can give the experimentalist quick information concerning molecular conformation and stereochemistry. However, care must be taken to ensure that these relationships are used only on structural fragments similar to those used to derive them.

1.4.3. Method for the Calculation of the Degree to which Six-Membered Rings Deviate from the Standard . Chair Conformation

Six-membered rings form one class of compounds which can yield useful NMR coupling data, vicinal coupling constants, in particular. In the standard chair conformation of a six-membered ring, the vicinal axialaxial protons subtend a dihedral angle of approximately 180° , whereas the vicinal equatorial-equatorial or equatorial-axial protons subtend an angle of approximately 50° .

Buys (46), following the essentially qualitative work of Lambert (47), has derived an equation which allows quantitative prediction of the degree to which 6membered rings (including heterocycles) deviate from the standard chain conformation. He assumed that the ethanelike fragments shown in Figure 1.10 possessed 'pseudo trigonal projection symmetry'. Using the Farplus equation

		• • • •	
	$J = A \cos^2 \hat{w}$	• •	(1.22)
and the relationsh	ips shown in Fig	jure 1.10	۵ *
tta an	$\hat{\Phi}_{aa} = 120 \overset{\vee}{,} \Psi$	~	(1,23)
• •	⊕ _{ee} = 120 - ¥		(1.24)
v	$\hat{\Phi}_{ae} = \hat{\Phi}_{ea} = \Psi$		(1.25)
he ratio (R of the	<u>trans</u> and <u>cis</u> c	oupling const	ants (J ^t
nd J ^C respectively) could be writh	ien ;	
$R = J^{t}/J^{C} = [\hat{A}, co$	$s^2(120+\Psi) + A co$)s ^{2`} (120-₩)]/2 &	cos ² ¥
	x		(1:26)

the

and

This equation assumed an identical "multiplicative" dependence of the cis and trans coupling constants on substituent electronegativity. Solving equation (1.26) for R and cos gives equation (1.27) and (1.28).

> $R = (3 - 2 \cos^2 \Psi) / (4 \cos^2 \Psi)$ (1.27) $\cos \Psi = [3 / (2 \div 4R)]^{1/2}$ (1.28)

Thus, if the cis and trans coupling constants can be determined, the degree to which the six-membered ring deviates from the chain conformation can be estimated. The use of this relations/hip has met with some success. A thorough review of the limitations of this treatment. Appilication of this method is has been made (47). limited to a narrow range of compounds, i.e., those where



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Figure 1.10. 'Pseudo trigonal projection symmetry' in ethane-like fragments from six membered rings (after Buys). The angle between coupled nuclei in the <u>gauche</u> conformation has deviated from the standard chair conformation where the dihedral angle is 60°.

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the four proton-proton coupling constants can be measured or those where two pairs of coupling constants for rapidly equilibrating structures can be obtained.

Forrest (48) has developed a method to determine the degree to which cyclic compounds deviate from the standard chair conformation: This method requires only the measurement of one gauche coupling constant and the know, ledge of the electronegativity of the substituents attached to the ethane-like fragment. Using equation (1.21), and the Karplus equation, $J = A \cos^2 \Phi - 0.3$, a value of the gauche coupling constant can be calculated and a value of the constant A determined. As the actual value of the gauche coupling constant is known, the Karplus equation can be solved for $\cos \Phi$, the dihedral angle between the axial and equatorial protons. The results obtained using this method agree well with those obtainable with the R method, but this approach has a wider applicability.

1.5. FACTORS EFFECTING THE CARBON-PROTON VICINAL COUPLING CONSTANT $({}^{3}J_{C_{C}}H)$

1.5.1. Dihedral Angle between the Coupled Nuclei

Lemieux et al. (49) examined the dependence of vicinal carbon-proton coupling constants on the dihedral angle, subtended by the coupled nuclei for several uracil derivatives and found, as Karabatsos had predicted (5), that a Karplus type dependence existed. A similar dependence of the magnitude of the carbon-proton coupling constant on the dihedral angle subtended by the coupled nuclei had been observed for several α -glycopyranoses by Perlin and Casu (50).

Calculations, by Wasylishen and Schaefer (51) on the propane molecule suggest that, as with proton-proton coupling constants, a minimum for ${}^{3}J_{C_{\ell}H}$ occurs when the dihedral angle between the coupled nuclei is 90° , and maxima occur when the dihedral angle is 0° or 180° .

In a manner similar to the approach used for vicinal proton-proton coupling constants, vicinal carbon-proton coupling constants have been used to establish relative conformer populations in 2 phenyl succinic acid (52). Perlin and Schwarcz (53) have utilized this Karplus type dependence to help establish the conformations of carbohydrates. They measured ${}^{3}J_{C,R}$ through both carbon-carbon and carbon-oxygen coupling paths in a number of

carbohydrate derivatives and found that smaller coupling constants (0-3 Hz) were observed for dihedral angles between 60° and 100° than for dihedral angles between 140° and 180° (4.5 - 5.5 Hz).

Numerous other examples exist in the literature where the magnitude of ${}^{3}J_{C_{f}H}$ has been used as a conformational or geometric probe (vide infra). However, as was found for ${}^{3}J_{H_{f}H'}$ factors other than the dihedral angle have a profound effect on the magnitude of the observed vicinal carbon-proton coupling constant. The electronegativity. and placement of substituents, bond angles, bond lengths, and hybridization of the carbon atoms in the coupling path have all been found to exert a measurable influence.

1.5.2. Substituent Electronegativity and Placement

In a series of neopentyl derivatives, where the substituent was attached to the coupled carbon, Karabatsos (54) observed that the vicinal carbon-proton coupling constant decreased with an increase in substituent electronegativity for the substituents I, Br, Cl, OH. He found that the value of the vicinal carbonproton coupling constant decreased from 5.99 to 5.84 to 5.63 to 4.48 Hz for the iodo, bromo, chloro, and hydroxy compounds respectively. The relationship between substituent electronegativity and the measured coupling constants was not linear (correlation coefficient = 0.85

for the compounds above), but it did show a monotonic decrease in the coupling constant with increasing substituent electronegativity.

Vicinal carbon-proton coupling constants for a series of n-propyl derivatives, where the substituent is attached to the coupled carbon, have been measured by Spoormaker and de Bie (55). For the derivatives with first Row substituents, the values of ${}^{3}J_{C,H}$ increase with increasing substituent electronegativity; from 5.4 to 5.7 to 6.0 to 6.2 Hz for the methyl, amino, hydroxy, and fluoro propanes. The best fit straight line, given by linear regression analysis is shown in equation (1.29).

 ${}^{3}J_{C_{r}H} = 0.83 \text{ E} + 3.10 \text{ r}^{2} = 0.991$ (1.29) However, for the halide derivatives, ${}^{3}_{C_{r}H}$ was found to decrease with increasing substituent electronegativity; from 7.3 to 7.0 to 6.7 to 6.2Hz for the iodo, bromo, chloro, and fluoro propanes.

Forrest and Sukumar (17) have measured ${}^{3}J_{C,H}$ in a series of <u>tertiary</u>-butyl compounds and have found that the value of ${}^{3}J_{C,H}$ decreased as the electronegativity of the substituents (D, CH₃, I, Br, Cl, F) increased. Unlike the compounds studied by Karabatsos, the substituent was attached to the carbon bearing the coupled carbon instead of being directly bonded to the coupled carbon. Again, no good linear correlation between the value of ${}^{3}J_{C,H}$ for these compounds and substituent electronegativity was found. The vicinal

coupling constant and substituent electronegativity were found to be related by a quadratic equation (56) of the type shown in equation (1.30).

 ${}^{3}J_{C_{\ell}H} = A_{0} - A_{1} E - A_{2} E^{2}$ (1.30)

In the t-butyl compounds conformational effects are not significant as the methyl group has axial symmetry and is freely rotating. The measured coupling constant is the average of the one anti and two gauche orientations possible for the coupled nuclei shown in Figure 1.11.

Spoormaker and de Bie (55) have measured ${}^{3}J_{C,H}$ for a series of isopropyl derivatives with first Row substituents. The substituents (CH₃, NH₂, OH, F) were attached to the carbon bearing the coupled carbon. They found that an increase in substituent electronegativity caused a decrease in the observed coupling. The best fit straight line, given by linear regression analysis, is shown in equation (1.31).

 ${}^{3}J_{C,H} = 6.40 - 0.46E r^{2}=0.997$ (1.31) A similar decrease of the magnitude of ${}^{3}J_{C,H}$ with increasing substituent electronegativity for the first Row substituents (C, N, O, F) was found for a series of t-butyl derivatives. Again the substituent was attached to the carbon bearing the coupled carbon. The best fit straight line was given by equation (1.32).

 ${}^{3}J_{C,H} = -0.64 \text{ E} + 6.28 \text{ r}^{2} = 0.979$ (1.32) Furthermore, when the Group VII substituents (F, Cl_v Br, I) were considered, the vicinal carbon-proton

Figure 1.11. The one anti and two gauche orientations possible for the t-butyl derivatives. The measured coupling is the average of the three coupling constants shown.



coupling constant was found to decrease with increasing substituent electronegativity. The coupling varied from 5.0 to 4.8 to 4.7 to 4.6 Hz for the iodo, bromo, chloro, and fluoro derivatives respectively.

INDQ-molecular orbital calculations (48) have predicted, on the basis of an alternating substituent's effect, that when the substituent is attached to the coupled carbon that the magnitude of ${}^{3}J_{C_{LH}}$ should with an increase substituent , increase in electronegativity. Conversely, when the substituent is attached to the carbon atom adjacent to the coupled an increase in electronegativity of the carbon substituent is predicted to cause a decrease in the observed coupling constant.

It is obvious from the discussion above that the variation of the magnitude of ${}^{3}J_{C,H}$ is dependent upon both the electronegativity of the substituent and its placement along the coupling path. When the substituent is directly attached to the coupled carbon, its effect changes in going from the first Row to the halide substituents. In this instance the influence of substituents vary even when their placement along the coupling path is kept constant.

1.5.3. Carbon Hybridization, Bond Angles, and Bond Lengths

An increase in the s-character of the coupled carbon when the carbon hybridization changes from sp^3 to sp^2 to sp is found to cause a monotonic increase in ${}^3J_{C,H}$. An example of the phenomenon is shown in Figure 1.12 where the <u>cis</u> and <u>trans</u> vicinal coupling constants across alkene type fragments increase from 6.7 to 7.8 to 8.1 Hz and 11.1 to 11.9 to 14.7 H@ respectively for sp^3 , sp^2 and sp hybridized carbons (15).

Changes in bond angles and bond lengths are difficult to relate to changes in vicinal carbon-proton coupling constants experimentally. As was noted with protonproton coupling constants, changes in bond angles and bond lengths are often the result of changes in substituents and/or carbon hybridization and the isolation of effects due to these parameters is difficult if not impossible.

1.6. FACTORS AFFECTING GEMINAL PROTON-PROTON COUPLING CONSTANTS

1.6.1. Theoretical Predictions

Theoretical work on the factors affecting geminal proton-proton coupling constants, $(^{2}J_{H_{\prime},H})$, has been

Figure 1.12. The effect of the degree of the s-character of the hybridization of the coupled carbon on the magnitude of the <u>cis</u> and <u>trans</u> vicinal coupling constants across a double bond. (15)

sp³

sp²

sp



 ${}^{3}J^{t}_{C^{*},H} = 11.1 Hz$ ${}^{3}J^{c}_{C^{*},H} = 6.7 Hz$

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 ${}^{3}J_{C^{*},H}^{t} = 11.9$ Hz ${}^{3}J_{C^{*},H}^{t} = 7.8$ Hz



 ${}^{3}J_{C^{*},H}^{t} = 14.7 \text{ Hz}$ ${}^{3}J_{C^{*},H}^{c} = 8.1 \text{ Hz}$

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carried out most notably by Pople and Bothner-By (57) and by Barfield and Grant (58). The theoretical predictions made by these authors regarding the factors affecting the magnitude of the measured values of the geminal protonproton coupling constants, ${}^{2}J_{H_{f}H_{f}}$ have been supported by experimental work. These theoretical predictions are discussed below.

The Molecular Orbital (40) approach of Pople and Bothner-By, predicts that withdrawal of electron density (generally an inductive effect) from orbitals symmetric between the coupled protons in a methylene type fragment '(see Figure 1.13) should result in a positive increment ' to the geminal proton-proton coupling constant. ' Withdrawal of electron density (hyperconjugative effects) from orbitals antisymmetric between the 'coupled protons (see Figure 1.13) is predicted to result in a negative increment to the geminal proton-proton coupling constant. Corresponding but opposite effects are predicted for the donation of electrons to orbitals symmetric (between the coupled nuclei, (i.e., ${}^2J_{\rm H,H}$ should decrease), and withdrawal of electrons from orbitals antisýmmetric between the 'coupled nuclei, (i.e., $J_{\rm H,H}$ should increase):

The Valence Bond (VB) approach used by Barfield and Grant predicts similar trends. For simple hydrocarbons, the geminal proton-proton coupling constant, $({}^{2}J_{H,\Pi})$, is predicted to become more positive as the s-character of the carbon hybridization increases. An increase in the

Figure 1.13. Diagrammatic representation of the orbitals symmetric and antisymmetric between the coupled protons in a methylene fragment.

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electronegativity of a substituent on the carbon atom adjacent to the methylene (-CH₂-) fragment is predicted to cause a positive increment in the value of ${}^{2}J_{H_{r}H^{r}}$ while a substituent two carbon atoms removed from the methylene fragment should cause a negative increment to ${}^{2}J_{H_{r}H}$. These substituent effects were predicted to be operative for geminal proton-proton coupling constants across both sp² and sp³ hybridized carbon atoms. Furthermore, the geminal proton-proton coupling constant was predicted to be sensitive to π bonds and their orientation with respect to the coupled nuclei.

Anteunis (59) and Cookson and Crabbe (60) have studiel the effect of the orientation of substituent lone pairs, when the substituent is attached to the carbon atom adjacent to the coupled carbon, on the magnitude of ${}^{2}J_{H,H}$ and found that an orientation effect of 2-3 Hz on the observed geminal coupling constant was possible.

Davis and Hudek (61, 62) have checked the predictions of Pople and Bothner-By as to the effect of the orientation of heteroatoms on the magnitude of ${}^{2}J_{\rm H/H}$. The heteroatoms were attached to the carbon atoms adjacent to and two atoms removed from the coupled methylene fragment. They found that the geminal coupling constant became more positive as the lone pair of the substituent (oxygen or sulfur atoms or sulfinyl or sulfonyl groups) eclipsed one of the C-H bonds of the methylene fragment. Using compounds-where the dihedral
angle between the heteroatom lone pairs and the C-H bond of the methylene fragment were 0, 60, 180, 300, and 360 degrees, they found a dependence of the type shown in Figure 1.14. For a substituent (OH, OAC, NH₂, NHAC, Cl, Br, Ph, NO₂) two carbon atoms removed from the coupled methylene fragment, the influence of a substituent on the magnitude of the geminal coupling constant was found to be dependent upon the dihedral angle between the substituent and a C-H bond of the methylene fragment. The dependence is shown in Figure 1.15. These findings agreed well with the predictions of Pople and Bothner-By discussed above.

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.6.2. Influence of Substituent Electronegativity

In a series of mono-substituted methanes (63) the magnitude of the geminal proton-proton coupling constant, was found to increase algebraically with increasing substituent electronegativity. However, the correlation, between substituent electronegativity and the magnitude of the geminal coupling constant was not linear and the halides fell off the best fit straight line. On the basis of electronegativity alone, the value of $2_{V_{\rm H}, \rm H}^2$ for the methyl halides would be expected to decrease in the order F>C1>Br>I. However, the magnitude of $2_{\rm H, \rm H}^2$ was found to decrease from -9.3 to -9.5 to -10.10 to -10.70 Hz in going from the iodo to the fluoro to the bromo and



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chloro derivatives. The effect of substituents on the \langle magnitude of ${}^{2}J_{H_{\rho}H}$ appears to be reasonably complex and linear correlations of ${}^{2}J_{H_{\rho}H}$ and E_{ρ} even in the simplest molecules; have not been found.

1.6.3. Effect of the Degree of 's' Character of the Coupled Carbon Orbitals

The simplest example of the effect of a change of the hybridization of the coupled carbon on the magnitude of geminal proton-proton coupling constants involves the measured values of $2\overline{J}_{H,H}$ for methane and ethene. The value of ${}^{2}J_{H_{e}H}$ for the methane molecule, (calculated from ${}^2 J_{H,D}$ using the magnetogyric ratios of the hydrogenand deuterium nuclei) is -12.4 Hz. The value of ${}^{2}J_{H_{g}H}$ for ethene (calculated in a similar manner) is +2.5 Hz. Thus in going from an sp^3 hybridized carbon to an sp^2 hybridized carbon, the coupling increases from -12.4 to +2.5. This was predicted theoretically by Barfield and $\hat{\sigma}$ ant, (58), i.e., $2j_{\rm H,H}$ increases as the degree of scharacter of the carbon hybridization increases. In this example, where $2_{J_{H,H}}$ values for the methane and , ethene molecules were compared, the increment in the value of 2JN for the ethene molecule was attributed to a change in the s-character of the carbon hybrid However, changes in carbon hybridization are orbitals. accompanied by changes in the C-H bond lengths and bond

angles as well as changes in the s-character of the coupled carbon. The bond length decreases (from 1.096 to 1.07. A) and the bond angle increases (from approximately 108° to 1'20°) in going from the methane to the ethene molecule. The separation of these contributions to the change in the observed coupling constant is experimentally very difficult.

Becausé of the interdependence of bond angles, bond lengths and carbon hybridization it has been difficult to separate and study the effects of any one of these parameters independently.

1.7. FACTORS EFFECTING GEMINAL CARBON-PROTON COUPLING

The measurement of geminal carbon-proton coupling constants (${}^{2}J_{C,H}$) is now becoming widespread. Unlike geminal proton-proton coupling constants, two carbon atoms are involved in geminal carbon-proton coupling path, the carbon bearing the coupled nuclei and the coupled carbon itself. As we are essentially interested in comparing ${}^{2}J_{C,H}$ and ${}^{2}J_{H,H}$ in analogous compounds, our discussion of substituent effects on the magnitude of carbon-proton coupling constants deals primarily with substitution at the carbon bearing the coupled carbon and proton although substituent effects at the coupled carbon

1.7.1. The Effect of Substituent Electronegativity on Geminal Carbon-Proton Coupling Constants

Spoormaker and deBie (64) have studied the effect of substituents on the magnitude of geminal carbon-proton coupling constants $({}^{2}J_{C,E})$ in a series of ethyl, isopropyl and <u>t</u>-butyl compounds. Substitution on the coupled carbon caused a small change in the observed coupling; however, substitution on the carbon bearing the coupled nuclei produced a more pronounced effect. In both instances no good linear correlation of ${}^{2}J_{C,H}$ with substituent electronegativity was observed. A quadratic dependence of ${}^{2}J_{C,H}$ on E was proposed. The form of this dependence is shown in equation (1.33)

$${}^{2}J_{C_{\rho}H} = A + B E_{\chi} + C E_{\chi}^{2}$$
 (1.33)

where A_r B_r and C are empirical constants and E_x is the substituent electronegativity.

Wasylishen, Bukata, and Chum (65) have found that the geminal carbon-proton coupling constant for a series of isopropyl compounds, where the substituent is attached to the coupled carbon, is very insensitive to changes in substituent electronegativity

As little work has been done on the effect of substituent electronegativity on geminal carbon-proton or proton-proton coupling constants, discussion of the nonlinearity of the plots has been limited. The lack of measured values of ${}^{2}J_{C,H}$ (or ${}^{2}J_{H,H}$ for that matter) has

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further hindered the development of relationships between substituent effects and the magnitude of the observed geminal coupling constants.

1.7.2. Dependence of Geminal Carbon-Proton Coupling Constants on Bond Lengths

The geminal carbon-proton coupling constants have been found to vary with the carbon-carbon bond length in five-membered rings (66). A correlation relating ${}^{2}J_{C,H}$ to carbon-carbon bond length has been found (67) and is shown in equation (1.34)

 ${}^{2}J_{C,H} = 24.15 r_{CC} - 29.09 r^{2} = 0.91$ (1.34) where r_{CC} is the carbon-carbon bond length. ${}^{2}J_{C,H}$ has also been found to become less negative as the length of the coupling path in aromatic compounds (68) increases.

Again it must be stressed that the study of the effect of the variation of bond length (or bond angles) on the magnitude of coupling constants is a difficult problem. To find compounds where all other molecular parameters are kept as constant as possible and bond lengths are varied is indeed a challenging task.

1.8. CORRELATIONS BETWEEN CARBON-PRO

1.8.1. Theoretical Considerations

Consideration of the magnetogyric ratios of the carbon and hydrogen nuclei, leads one to predict on the basis of the Fermi contact term that carbon-proton coupling constants for an sp^3 hybridized carbon should be approximately one quarter the magnitude of the analogous proton-proton coupling constants. Karabatsos (3), using calculations that included mean excitation energies and electron densities, calculated a value approximately 20 per cent higher than this figure for the Fermi contact contribution to the carbon-proton coupling constant. The relationships for sp^3 , sp^2 and sp hybridized carbon are shown in equations (1.35), (1.36), and (1.37).

 $J_{C,H} = 0.30 J_{H,H} - (sp^3 hybridized C)$ (1.35). $J_{C,H} = 0.40$ $J_{H,H}^{*}$ (sp² hybridized C) (1.36) $J_{C,H} = 0.61 J_{H,H}$ (sp hybridized C) (1.37)Experimentally, Karabatsos found for a series of aliphatic carboxylic acids that the carbon-proton coupling constants were approximately 0.7 times the value of the proton-proton coupling constants for a series of structurally similar aliphatic hydrocarbons. As the predicted ratio was 0.4, Karabatsos postulated that coupling mechanisms other than the Fermi contact term might be making significant contributions to carbonproton coupling constants. More recent theoretical work (3, 12) suggests that the contributions of non contact terms (terms other than the Fermi contact term) are small.

As more darbon-proton coupling constants became available, a number of correlations of carbon-proton and proton-proton coupling constants were made. The experimental evidence suggests that although the ratios of carbon-proton to proton-proton coupling constants are generally higher than predicted in equations (1.35), (1.36), and (1.37), the correlations are such that it would appear that the coupling mechanisms For carbonproton and proton proton coupling constants are very similar. A number of these correlations will be discussed below.

1.8.2. Empirical Correlations Between Carbon-Proton and Proton-Proton Coupling Constants

Marshall and Seiwell have (14) measured Jd, H for a series of crotonic acids, methyl benzoate and acrylic acid and have found that the measured carbon proton coupling constants $(^{2}J, ^{3}J, ^{4}J, ^{5}J)$ correlate well with proton-proton coupling constants measured for geometrically equivalent, compounds. The compounds used to derive the coupling constants are shown in Figure 1.16. A plot of $J_{C,H}$ values against the $J_{H,H}$ values gave. reasonably good straight line (equation 1.36). $J_{C,H} = 0.62 J_{H,H} - 0.41$ $r_{2} = 0.975$

In spite of the variation of the ratio of the values the carbon-proton to proton-proton coupling constants

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(1.36)

Figure 1.16. Carbon-proton coupling constants (²J, ³J, ⁴J, and ⁵J) for a series of crotonic acids, acrylic acid and methyl benzoate and proton-proton coupling constants from geometrically equivalent compounds.

Type

2j 3j 4j

2_J 3J 4J J_{H,H}

2.17 16.98 -1.77

2.17 10.09 -1.41

2.50 11.60 19.10







0.48

J_{C,H}

3.12 14.50 -1.28

3.39 6.78 -0.85



J.L. Marshall and R. Seiwell, OMR, 8 ; 419 (1976)

for structurally similar compounds, (the ratio varies from 0.45 to 1.64), and the fact that the plot does not have a zero intercept, the authors still proposed that useful predictions of carbon-proton coupling constants from proton-proton coupling constants could be made using a ratio of 0.62. For individual pairs of compounds the average ratio 1s 0.76.

Vogeli and von Philipsborn (15) have compared the magnitude of ${}^{3}J_{C,H}$ for a series of alkenes to the magnitude of ${}^{3}J_{H,H}$ for geometrically equivalent compounds where H replaces CH₃, (see Figure 1.17), and found that ${}^{3}J_{C,H}$ was approximately equal to 0.6 the value of ${}^{3}J_{H,H}$ for both <u>cis</u> and <u>trans</u> vicinal coupling constants. The ratio of ${}^{3}J_{C,H}$ to ${}^{3}J_{H,H}$ (0.6), compares well with the slope found by Marshall and Seiwell (16) for equation (1.38), i.e., 0.62, but again the plot did not pass through the origin.

In a study of geminal carbon-proton and geminal proton-proton coupling constants in a number of 1,3dioxanes, 1,4-dioxanes, 1,3-benzoxazines, and 1,3dioxolanes, (see Figure 1.18), Ayras (18), found that the values of the measured carbon-proton coupling constants correlated well with the corresponding geminal protonproton coupling constants measured for structurally similar compounds where a methyl group was replaced by a proton. The best fit straight line was given by equation

(1.39).

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Figure 1.17. The vicinal carbon-proton and proton-proton coupling constants for geometrically similar alkenes.

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٥	hz	, 	hz	•
сн (се _з) ₂	17.04	10.03 .	10.7	6.6
Ph · .	17.90	11,08	77°5″	6.7
C6H4CH3	17.6	10.5 ·s.	11,2	6.0
C CH3	17.35	11.50	10.7	-6.3
CB20H	17.37	10.48	11.2	6.4 .
CH ₂ Cl	16.92	10.11	10.3 ·	5.9 .
Br	14.94	7.12	8° ð	4.6
CIIÓ	17.40 .	10.00	10.0	5.7
COOII ,	17.20	10.50	70 ° 7 '	5.7
0	,		ъ в	1945 .

U. Vogeli and W. von Philipsborn, OMR, 7, 617 (1975)



 ${}^{2}J_{C_{0}H} = 0.55 \; {}^{2}J_{C_{0}H} + 4.93$, $r^{2} = 0.99$ For the series of unsaturated acylic compounds shown in Figure 1.19, where 'the coupled methyl carbon is attached to an sp² hybridized carbon, ${}^{2}J_{C_{0}H}$ was again found to correlate well with ${}^{2}J_{H_{0}H}$ for structurally similar compounds where the methyl group was replaced by a proton. The best fit straight line was given by equation (1.40)

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 $^{2}J_{C,H} = 0.58$ $^{2}J_{H,H} + 2.68$ $r^{2} = 0.999$ (1.40) Even though the correlation coefficients were excellent, Ayras cautioned agains use of these correlations in systems other than those for which they were developed. Furthermore, he concluded that these results were reasonable if the Fermi contact term predominates in both carbon-proton and proton-proton coupling constants.

The effect of substituents on vicinal <u>cis</u> and <u>trans</u> carbon-proton coupling constants in a series of propenes has been studied (19). The measured coupling constants were compared to the proton-proton coupling constants for a series of geometrically equivalent ethenes. The compounds and their respective coupling constants are shown in Table 1.1. ${}^{3}J_{C,H}$ was found to vary linearly with ${}^{3}J_{H,H}$. The best fit straight line for the plot of ${}^{3}J_{C,H}$ against ${}^{3}J_{H,H}$ is given by equation (1.41) ${}^{3}J_{C,H} = 0.46$ ${}^{3}J_{H,H} + 158$ $r^{2} = 0.956$ (1.41)

The ratio of a particular pair of analogous carbon-

Figure1.19. Geminal proton-proton and carbon-proton coupling constants for structurally similar unsaturated compounds.'

COMPOUND ²JC,н Ju,e (Ez) formaldehyde. 11 acetaldehyde 26.7 acrylic acid 1 crotonie acid 3.9 propenal . trans-2-butenal 3.5 acrylonitrile crotononitrile 3,5 3,5-DNPH. of formaldehydea 11,0.

3;5-DNPH of acetaldahyde^a a) 9,5-DNPH-3,5-dinitrophenylhydrazone P. Agras, Acta Chemica Scandinavica, B31, 325 (1977). Tableäl.1. The vicinal carbon-proton and vicinal proton-proton coupling constants for series of analogous monosubstituted propenes and ethenes respectively.

R3	:== (CII3	ļ
R2	,	² 1	
	-	-	•
			1

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Ϋ́Σ.	R ₂	R.J. 3.	^j ch ₃ ,H	з _{је, е} .	ratio
1	Cl	H	5.6	7.30	0.77
ŢĹ.	H	Cl	8.1	14.60	0.55.
3	Ph	E.	10.0	18.59	- 0.5,4
9	E	Ph	^v 7.9 ^v .	11.48	0,69
1.	CDP .	· 11	6.4	11.75	°0.54
ĩ	H,	CN	9.3 -	17.92	, 0 . 52
Ι,	CHO '	E	5:9	10.00	0.59
•	соон	Ē	6.3.	10.20 [°] ,	0.62
•	/		" " "	، د	

 ${}^{3}J_{C,H} = 0.46 {}^{3}J_{H,H} + 1.58 {}^{2}r^{2} = 0.956$

P. Ayras, OMR, 9, 663 (1977).

proton and proton-proton coupling constant's was found to vary with the substituent electronegative and with the orientation of the substituent with respect to the coupling path, i.e., for the <u>Gis</u> coupling constants the ratio varied from 0.77 for the chloro compound to 0.62 for the carboxylic acids to 0.59 for the aldehydes to 0.54 for the cyano and phenyl compounds while the ratios for the <u>cis</u> and <u>trans</u> chloro compounds were 0.77 and 0.55 respectively.

Douglas (69) has studied ${}^{3}J_{C_{\rho}H}$ in a series of isopropenyl compounds, (see Table 1.2), and compared the observed coupling constants with ${}^{3}J_{H_{\rho}E}$ for geometrically equivalent ethene derivatives. His results indicate that the ratio of the sum of the <u>cis</u> and <u>trans</u> carbon-proton and proton-proton coupling constants is sensitive to substituent effects. The ratio varied from 0.55 for the fluoro derivatives to 0.65 for the methyl derivatives.

Forrest and Sukumar (17), in the study of substituent effects on ${}^{3}J_{C,H}$ and ${}^{3}J_{H,H}$ for t-butyl compounds and isopropyl compounds discussed earlier; (see section 1.5.2), found an excellent correlation between the vicinal carbon proton and vicinal proton-proton coupling constants. The plot of ${}^{3}J_{C,H}$ against ${}^{3}J_{H,H}$ gave the straight line given in equation (1.42). ${}^{3}J_{C,H} = 1.2 {}^{3}J_{H,H} = 3.5 {}^{2}=0.991$ (1.42) "This correlation appeared to indicate that ${}^{3}J_{C,H}$ and ${}^{3}J_{H,H}$ have a similar dependence on substituent

Table 1.2. Vicinal carbon-proton and vicinal protonproton coupling constants for series of analogous monosubstituted propenes and ethenes respectively.

N.C.C.

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X	° cis	tranş	sum	Cis	trans	sum	॰ CE/BH
F	2.5	· 7.0	, '9.5	· 4.7	12.7	17.4	.0.55
OCH3			12.5	7.0	14.1	21.1	0.59
C1	4°2	8.6	12.8	7.2	14.8.	22.0	0,58
Br	4.5	9.0`·	13.5.	7:2	15.1	22.3	0.61`
CN	• 6.4	10.1	16.5	,11.8	17.9	29.7	0.56
ся ³	b	-	17.3	· 10.0 '	16.8 •	26.8	0.65
A.W.	Donal	as. OMR.	9, 69	(1977)		•••	

electronegativity. However, the authors caution that this behavior should not be projected into situations where the substituent can assume different orientations relative to the coupled nuclei. The t-butyl and isopropyl compounds give coupling constants that are an average for the one trans and two gauche orientations possible with these freely rotating molecules. (See Figure 1.20). The orientation effect of the substituent on the individual coupling constants for both the isopropyl and t-butyl compounds are the same. It is obvious from the preceding discussion that some excellent correlations between carbon-proton and proton-proton coupling constants exist. However, none of these correlations pass through the origin and substituent effects are found to cause variations in the ratios of coupling constants for structurally similar compounds.

1.8.3. The 'Simple' Ratio

Because of the obvious desirability of having a single ratio between C-H and H-H coupling constants, some authors have proposed using the single value that they have determined in spite of the evidence that the ratio is not constant. Although a number of good correlations have been found, they are applicable only to the compounds almost identical to those used to derive the relationship. Factors such as substituent effects (for





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Figure 1.20. Newman projections showing the possible orientations of the coupled nuclei for t-butyl derivatives and isopropyl derivatives. instance, electronegativity and substituent orientation) have been found to cause large variations in the ratios of carbon-proton and proton-proton coupling constants. Furthermore, the slope of the correlations varies from one series of compounds to another, regardless of the degree of s-character of the coupled carbon atoms.

The number of good correlations found does seem to indicate that the coupling mechanism for carbon-proton and proton-proton coupling constants are similar. If this is in fact the case, the accumulation of more data on carbon-proton coupling constants and the factors effecting their magnitude should allow not only a better, understanding of the coupling mechanism for carbon and hydrogen but also aid in the efforts to find more general correlations between carbon-proton and proton-proton

1.9 Carbon-Carbon Coupling Constants

The measurement of long-range, carbon-carbon couping constants is just becoming widespread. The 2D INADEQUATE technique (70) has been used, for example, to measure the long range carbon-carbon coupling constants in the 1 and 2-naphthalenes (71). Prior to pulse sequences such as that of INADEQUATE, carbon-13 labelled compounds were required to measure carbon-carbon coupling constants over more than one bond (72, 73). Carbon-carbon coupling constants have been used for structural elucidation (74, 75, 76). Berger (71) has found a Karplus-type relationship (equation 1.43) between the vicinal carbon-carbon coupling constant and the dihedral angle subtended by the coupled nuclei for alicyclic compounds.

 ${}^{3}J_{C,C} = 1.67 + 0.176 \cos \Phi + 2.24 \cos^{2} \Phi$ (1.43)

Earlier, Barfield <u>et ál.</u> (77), using an INDO-MO approach, predicted a similar dependence (equation 1.44) between the magnitude of the vicinal carbon-carbon coupling constant and the dihedral angle.

 ${}^{3}J_{C,C} = 2.73 + 0.579 \cos \Phi + 2.17 \cos 2\Phi$ (1.44) It has been suggested that the geminal carboncarbon coupling constant may be a better probe of molecular stereochemistry than vicinal carbon-carbon coupling constant, as ${}^{2}J_{C,C}$ is sensitive to substituent orientation (78). Barfield (79) has investigated nonbonded interactions in cyclic compounds using an INDO-FPT approach and found that non-bonded interactions can dominate ${}^{3}J_{C,C}$. When such interactions are dominant, the dihedral angle is not related to ${}^{3}J_{C,C}$ by a Karplustype relationship.

Several reviews of the factors affecting the magnitude of one, two, and three bond carbon-carbon coupling constants have been published (80, 81, 82). On the basis of the observed vicinal carbon-carbon coupling constants for a series of [5 - 13C] benzanthracenes, Cox

and Levy (83) have suggested that carbon-carbon coupling constants should depend on substituent electronegativity, the dihedral angle between the coupled nuclei, and the hybridization of the coupled carbons.

The structural dependence of two bond carbon-carbon coupling constants has been assessed (84). The magnitude of. $^{2}J_{G_{\nu}C}$ was found to vary with the bond angle in a manner similar to $^{2}J_{H,H^{\circ}}$

Recently, Kamienska-Trela <u>et al.</u> (85) have studied the effect of substituent electronegativity on the magnitude of the one-bond, caffon-carbon coupling constant across the triple bond of a series of acetylene dérivatives. For the series of compounds studied (substituent = H, CMe₃, Cl, Br, I, Li, Sn, Si), ${}^{1}J_{C,C}$ was found to correlate well with the substituent electronegativity ($r^{2} = 0.994$).

Marshall (86) has recently completed a thorough review of carbon-proton and carbon-carbon coupling constants, focussing on the ratio of carbon-carbon to carbon-proton coupling constants for structurally similar environments. He observed that the ratio varies from one series of compounds to another. As more carbon-carbon coupling constants become available, correlations between carbon-carbon and carbon-proton coupling constants may allow the experimentalist to predict the value of one coupling from the observed value of the other coupling constant.

1.10. MEDIUM EFFECTS

Although chemical shifts show a larger dependence on the solvent that coupling constants, evidence clearly supports a solvent dependence for the coupling constant (87). In the absence of any specific association effects, this dependence is related to the polarity of the solvent (88). The dependence of the observed coupling constant on the solvent has been studied theoretically by the means of three models; the reaction field model (89), the cubic closest pack cluster model (90) and the solution model (91). Such studies have met with varying degrees of success.

The results obtained often depend upon the complexity of the system being studied. For instance, conformationally labile system are known to be effected by the dielectric constant of the solvent if conformers with different dipole moments are possible. The solvent favored conformer will vary as the dielectric constant of the solvent changes. As the measured coupling constant is an average of several coupling constants, it will, reflect the change in dielectric constant (see Figure 1.21).

Temperature effects on the coupling constant are primarily reflected through the solvent medium. When conformers of yarying energy, exist, changes in temperature of the solvent may cause a change in

Figure 1.21. The two conformations of a conformationally labile cyclohexane ring. The conformer populations are dependent upon the temperature and the preference of the substituent groups for the equatorial position.

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conformer populations and thus the magnitude of the observed coupling. The temperature dependence of the coupling constant, in a system with two conformers, is given by equation (1.45)

 $J_{dbs} = [J_A + (J_A - J_B)]/[1 + e^{(\Delta E/RT)/G}]$ (1.45) where J_A and J_B are the coupling constants of conformers A and B, T is the temperature (\mathbb{R}°), ΔE is the rotational energy barrier, R is the gas constant, and G is a statistical weighting factor.

In a study of a series of compounds care must be taken to ensure that the temperature and solvent effects are kept as nearly constant as possible, especially when comparing substituent effects. If variations of temperature and solvent conditions occur, it is essential to consider these when comparing the measured coupling constants.



.2.1,1. Reasurement of the Desired Geminal Carbon-Proton Coupling Gonstants 7 The compounds investigated and the experimental conditions for the acquisition of the proton undecoupled carbon spectra are listed in Table 2.1. Both the proton decoupled carbon spectra and the proton undecoupled carbon spectra were acquired on a 'Varian CFT-20 NMR Spectrometer at ambient instrument temperature. The spin system of interest for the ethyl derivatives, designated an $A_3B_2X_2$, is shown in Figure 2.1. In the formalism A3B2X, the letters represent groups of magnetically equivalent nuclei; the subscripts represent P the number of magnetically equivalent nuclei in each " group, and the proximity of the letters alphabetically reflects the difference in chemical shift of the various sets of magnetically equivalent nuclei. Using Figure 2.1 the methyl protons are designated A3, the methylene protons Bog and the coupled carbon' X. Due to the complexity of the carbon (X) portion of . the proton undecoupled carbon spectra (see Figure 2.2)

the $A_3 \dot{B}_2 X$ spin system requires that the proton $(A_3 B_2)$.

Complete solution of

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ETHYL DERIVATIVES

the iterative least squares program LAOCN4A (92) was used

to aid in the extraction of the desired geminal carbonproton coupling constants $\lambda^2 J_{CH}$).

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	pro	ton un	decoup	led ca	rbon	spec	tra of	the o	ethyl	ian i v r
•	der:	ivatives	, CH ₃ C	Ĩ2Zo:	*		Ş	. 0	. *	· · ·
		e e	٠		۱	*	с 1		7	* · ·
`		Ζ-	sw Q	AT [•]	BM	PD	DE	DP .	Solvent	, ° N
,			r, 0° 4	,	° °	• •	~		¢	
\$		Sietz	420	9.752	19	0.Q	~7901 ·	8192	CDC13	· · · · · ·
۰ ۲		·SnEtz	400	10.239	19	00	. 2131	8192;	, @Cl ₃	۰ ۴ ٦ .
Ere 17	υ,	Cesta .	500 _	8.191	16 ,	0.0	1482	8192	COCl3	1 сн
5.4.5	p	Poet3	500	8.191	. 16	0.0	8216	8192	ĆOCl3	550 in toluene
,	т. Ч	EgEt3	1000	- 4:095	21	6.0	5602	8192	r @Çl3 -	م بر (به :
-	,*** -	oer :"	500 _.	8 .191 .	21	6.0	1847	8192	COCI.3	•
•		0 NEE2	1502 ·	2.727	21 2	6.0	1498	8192	CDC1 ₃	1 1 - 6
,		set	1000	. 4.095	21.	6.0	.4026	8192	$CDCl_3$.	с 1
2	•	seel	° 800	5.119	21	6.0	3425	8192	COCl ₃	
4.		TeBt		4.095	21	Ğ.Ö	8251	.8192	CDCl3	` · ·
•		Į.	1000	4 .095	21	6.0	4561		CDCl ₂	•
	٦.	SN - 50	ectral n	ත්තන්තන		•		' '.	ني ب	•
		AT - 20	guisitic leo mid	n time		1	2 ~~	ti d		-
•	•	PD - pu	jze dója Tze miou	3Y .	- e ¹	/	•	-d *	· ·	,
Q.		Mr. – tur DP. – dat	nder of ta point	transle :s	nts	<i>.</i>	•	,	٤,	• '
•		١	3					,	a' .	49
		~	•	· ·	-		•)	•	•
				F	* a					• g, '

Figure 2.1. Spin designations of the coupled nuclei of the $\Lambda_3 B_2 M$ spin system for the monosubstituted ethyl derivatives, CH3CH2Z, listed in Table 2.1. Å ₿B \mathbf{Z} R HA ER 1, 2. R 8 З, Q Z is as shown in Table 2.1 ۵



spectra be solved rigorously to yield the chemical shifts of protons A and B, $\gamma_0 \delta_A$ and $\gamma_0 \delta_B$ respectively, and the . vicinal proton-proton coupling constant (${}^3J_{\rm HE}$). Again LAOCN4A was used to extract the values of the proton chemical shifts and vicinal coupling constants which are shown in Table 2.2.

To ensure that the concentration of the solute did not affect the proton proton coupling constants, the proton spectra were run as both 5 and 5.0 percent solutions in deuterated chloroform (CDCl₃). Although chemical shift differences were observed, the coupling constants calculated by LAOCN4A were constant within 0.10 Hz for the 5 and 50 percent solutions.

All proton undecoupled carbon spectra were run as 50 wpercent solutions in CDCl₃. The lead tetraethyl was used as a 65 per cent solution in toluene.

The LAOCN4A analysis is discussed below.

2.1.2. Determination of Geminal Carbon-Proton Coupling Constant's using the Iterative Least-Squares Program

The input parameters required for the solution of the X part of the A_3B_2X spin system to yield the desired geminal-carbon proton coupling constant $({}^2J_{B,X})$ are listed in Table 2.2 and Table 2.3. The values of the chemical shifts of protons A and B, $(\gamma_0\delta_A \text{ and } \gamma_0\delta_B)$,

The proton chemical shifts and vicinal Table 2.2. proton-proton coupling constants (for the ethyl derivatives, CH3CH2Z, calculated using the iterative" least squares program, LAOCN4A (92). . . .

		`			*	•		-
	\$1~ a	2 0	708a -	$\gamma_{o}\delta_{b}$	~~ o	Nobab	з _{ј к, й}	
			60	44	(Hz)		• ,	· · · ·
•	· ·	Si(Et) ₃	74.07ª `	40.53	• •	-33.54	· 7.92 ^b	, b
0	۵	Sn (Et) 3	- 93.30 ··,	. 63.36	,	-29.94	.8.04	*
٥	0 ¹	Ge(Et) ₃	80.83	56°.56	•	-24.27	7。93	
	•	Pd (et) 3	115.50	,115.50		°, 0°00	8.18	÷
		Hg(Et)3	103.31	81.01	•	-22, 30	` & _• 03	de juint
		Teet	128.82	209.31		80.49	. ø 7.61	δ τ ζι
ر		SeEt	 110.56	203.86 [.]	•	93.30	7 _° 50- [°]	ت ب (
•		OEt	95.70	277.50.	o	181.80	-7.02	· J.
•	, ,, ,,	N(Et) ₃	81.40	200.90	ø	119 ₄ 50	7°10	* a * * *
	۰ ۹	Set	99.90 .	202.80	•	 102.90.	₹.32·	• • •
	¢). I	146.50	254.10	•	107.60 ·	7.46	a, é
-		•						

a) all chemical shifts in Hertz downfield, from TMS.

at 0.00 Mertz, accurate to 0.20 Hz. b) all coupling constants accurate to 0.08 Hz.

13 Table 2.3. The carbon chemical shifts and one and two bond carbon-proton coupling constant data for the ethyl derivative's, CH3CH2Z.

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	• •	i H	H.	· · · ·	۰. ک.	-	· · · · · · · · · · · · · · · · · · ·
	2.	δc _a	δcb	l _{Jča,H} .	l _{JCb,H}	2 _{JCa,H}	· 1/AT'
		्(1	opal D	ə -	(BZ)	.	
	Si(Et) ₃	7 ° 27 °	,'3.10, [`]	`125_8 ′	117.4	-5.22	0.11 ^{0*} · · ·
ۍ. دی	Sn (Et) ₃	10.84	-0.42) 125.5 .	128.0	-4.62	0.10
G/	.Pb(Et)3	13.80	9.70 °	125.4	, 134.5	-3.86	
	Ge (Et) _{3.}	• •	ų a	125.5	126:0	-4.76,5	0.13
-	$Eg(Et)_{3}$	13.23	35:79	124.8	130.0	-4 [°] .52	0.25 .
-	SEt `	14.04	24.74	127.2 -	137.4	-3.51.	0:25
	OEt	15.3Å	65.96	125.8 <	138.0p	-2.64	0.13 .
- ¹ .e	'M(Et) ₂	10.87 .	45.55	125.5	131.5	-3.03	0.37
,	SeEt , ^{vi}	15.89	15.25	126.9	140.3	-3.22	0,20 ~··
	Teeť	17.23	-6.62	127.0	140-0-2	-3.22	0.25
•	° I	20,32 .)	-1.21	128.5 -	150.5	-2.74.	0.25
	Br	19.55	27:55	128.1	150.7	-2.'65	0.13.
,	Cl	19.15	`40.36 [']	127:9	150.0	-2.85	0.13 🔨 🕆
	F ^ .	16.42	83.60	126.3	150.3	-1.86	0.13
ı	CH3	16.82	16.98 '	124.3	. 125.3	-4.20	0.13 %.
	н, ⁸ .	5.90	5.90	125.0	125.0 ·	-4.80	0.13 .
	* ° •		Ρ		•	۹ ۱	•

a) chemical shifts referenced to middle resonance of CDC1₃ at 77.05 ppm relative to TMS at 0.00 ppm
b) digital resolution Hz (1/AT) for the geminal coupling constants, AT - acquisition time

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and the geminal proton-proton doupling constant $({}^{3}J_{AB})$ are required as well as estimates of the chemical shift differences between the doupled carbon and the A and B protons ($\gamma_{0}\delta_{AX}$ and $\gamma_{0}\delta_{BX}$ respectively) and the one bond carbon-proton coupling constant $({}^{1}J_{A,X})$. To allow the selection of a reasonable starting value of $J_{B,X}$ for the iterative process, a number of theoretical spectra with various values of $J_{B,X}$ were calculated. When the calculated spectrum resembled the actual spectrum, this value of $J_{B,X}$ was used as a starting point in the iterative calculation. The iterative calculations are made against the line frequencies of the proton undecoupled carbon spectra.

Three parameters were allowed to vary during the iterative process; the chemical shift of the coupled methyl carbon, the one bond carbon-proton coupling constant of the methyl carbon' (C_X) , and the desired geminal carbon-proton coupling constant. The chemical shift of the methyl carbon was set arbitrarily to -2000 The mathematics of the A3B2X spin system require Ez. that the coupling constants, $J_{A,X}$ and $J_{B,X}$, be small compared to the chemical shift difference between the coupled carbon and the protons A and B, $\gamma_0 \delta_{AK}$ and $\gamma_0 \delta_{BK}$; to ensure that the criterion for the X approximation are satisfied. A chemical shift of -2000 Hz for the coupled carbon sufficed as second order. terms did not make significant costributions to the calculated spectra.

-17;

In all cases the final calculated spectra gave line positions within 0.2 Hz of those measured from the sactual spectra. The LAOCN4 calculations were checked using the program LAME (93). An alternative approach was also used to measure the desired geminal coupling constants from the acquired spectra. This is discussed below.

.1.3. The Composite Particle Approach/(94)

Quantum mechanics predicts that in a case where a spin system is composed of groups of mechanically equivalent nuclei that the Hamiltonian for the spin system can be factorized. Factorization is the process of neducing a complex spin system to yield a simpler system. This can lead to spin systems that are well documented and more readily analysed to yield the desired

The factorization of complex spin systems has been termed the 'Composite 'Particle approach' and is dependent upon two féatures common to groups of magnetically equivalent nuclei.

1. Coupling between spins within a group of magnetically equivalent nuclei does not contribute to the observed spectrum, i.e., for groups of magnetically equivalent nuclei A, B and X.

 $J_{A,A} = J_{B,B} = J_{X,X} = 0$ 2. There is no mixing between wave functions having different values of $I_{T,T}^{2}$ the square of the spin angular
momentum of the group. This second feature implies that 'each group of magnetically equivalent nuclei may be thought of as a composite particle with a maximum total spin, Imax. Each spin state will then have different values of I^2 . If we have n nuclei then Imax = n/2 and I may assume the values n/2, (n/2)-1,... 0 if n is even and n/2, (n/2)-1,... 1/2 if n is odd.' It follows that there are (n/2)+1 spin states for n even and (n+1)/2 spin states for n odd. The permitted eigen values of I are of the form $h^2I_m(I_{m+1})$ where I_m is the total spin 'quantum number associated with I and the selection rule is $AI_m = 0$.

As in electronic spectroscopy the multiplicity of a particular spin state is given by $(2I_m + 1)$. Values of $I_m = 0$, 1/2, 1, 3/2, and 2 correspond to singlet (S), doublet (D), triplet (T), quartet (Qt) and quintet (Q) states respectively. The eigen value m may assume the values, T_{max} , I_{max} -1, ... - I_{max} .

В

1

1,0

3,1

Х

1/2

1/2

2

For the A3B2X spin system,

3/2

3/2, 1/2

4,02

Imax

2I_m+1

Im

States Qt_A, D_A T_BS_B D_X The composite particle of A is composed of the quartet (Qt) and doublet (D) state; B a triplet (T) and singlet (S) state and X a doublet (D) state.

§ 79.

The A3B2% spectrum is composed of the following subspectra

 $A_{3}B_{2}X = Qt_{A}T_{B}D_{X} + Qt_{A}S_{B}D_{X} + D_{A}T_{B}D_{X} + D_{A}S_{B}D_{X}$ From this it is easy to show that the $D_{A}S_{B}D_{X}$ and $D_{A}T_{B}D_{X}$ states are the components of an $AB_{2}X$ spin system.

AB2X

А

 $\cdot 1/2$

1/2

DA

Imax

21_m+1

States

Im

В

1

1,0

T_B,S_B

3,1

The A_3B_2X spin system can then be written $A_3B_2X = AB_2X + Qt_AT_BD_X + Qt_AS_BD_X$

The X transitions of the AB₂X system are well known, and proper choice of m_B values yields a pair of lines separated by $[2I_BJ_{B,X} + J_{A,X}]$ hertz. When the number of B nuclei is even, and here it is, states with $I_B = 0$ contribute a pair of lines separated by $J_{A,X^{*}}$. Isolation of these lines gives $J_{A,X}$. Knowledge of the magnitude $J_{AX^{*}}$ and isolation of the lines separated by $[2I_BJ_{B,X}+J_{A,X}]$ yields $J_{B,X}$. The geminal coupling constants measured from the splittings in the acquired spectra and those calculated from LAOCN4A analysis of the AD₂X and the LAME analysis of the A₃B₂X spin systems compared well within the limits of experimental error and

80

1/2

<u>]</u>/2

DX

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finite line width. They are shown in Table 2.4.

2.2. The ETHANOIC ACID DERIVATIVES

2.2.1. Measurement of the Geminal Coupling Constants

... The proton decoupled and proton undecoupled C-13 NMR ______spectra of the mono substituted acetic acids were run on a Varian CFT-20 NMR spectrometer at ambient instrument temperature. The compounds of interest, acquisition parameters, and solvents are listed in Table 2.5.

The spin system of interest is an A_2X (see figure 2.3). The criterion for the X-approximation is met, i.e., the chemical shift of the A protons from the carbon(X) is large compared to the carbon(X)-proton(A) geminal coupling constant $(^2J_{A_{\rho}X})$, i.e., $J_{A_{\rho}X} << \gamma_0 \delta_{AX}$. A typical spectrum is shown in Figure 2.4.

Reported couplings are the mean of two measurements per spectrum and at least two spectra were run for each compound. The method of measurement of splittings is shown in Figure 2.5. The geminal carbon-proton coupling constant (${}^{2}J_{A,X}$) was taken as the average of the separation of adjacent resonances of the $A_{2}X$ triplet at the peak of each resonance. The geminal carbon-proton coupling constants are shown in Table 2.6.

Table 2.4. The geminal carbon-proton coupling constants for the ethyl derivatives, CH_3CH_2Z . The analyses of the $A_3B_2AB_2X$, and A_3B_2X spin systems of the ethyl derivatives were done using the program LAOCN4 (92). The analysis of the A_3B_2X spin system was checked using the program LAME (93). The geminal carbon-proton coupling constants listed in the last column were measured from the splittings in the experimental spectra.

	1		,			a .	
Z	3 _{JHH} a	$2_{\rm J_{CH}}$	error ^b	2 _{JCH}	ERROR	2 ³ CH	
	A3B2 (AI	B2 [™] °	A3	B ₂ X	SPLITTING	
Si	7.92	-5.21	.0.186	-5.22	d .045	-5., 25	
·Sn	8.04	-4.63	0.026	-4.62	0.035	-4.65	
Pb	8.18'	°-3.94	0068	-3.86	0.076	<i>=</i> 4.00	
* Ge	7.93	-4.77	0.047	-4.76	0.058	-4.80	
Eg	8.03	-4.52	. 0.344	-4.52	0.105	-4.70	
S	7.32	-3.56	0.232	-3.51	0.076	-3.45	
0 0	~7.02 '	-2.53	0.047	-2.64	0.112	-2.45	
N	7.10	-2.84 -	0.199	-3.03	0.120	-2.90	
Se	7.50	-3.23	0.193	-3.22	0.098	-3.15	
Te	7.6L	-3.14	0.103	-3.22	. 0.112	-3.10.	
I	7.44	-2.72	0.193	-2.74	0.106	-2.73	,
				1			

a) all coupling constants are in Hertz

b) rms error is the difference between the calculated and measured line positions.

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Parameters for the acquisition of the proton Table 2.5. undecoupled carbon spectra of the ethanoic acid derivatives, CH₂ZCOOH.

			•					
[°] Z	SW	AT	PW	PD	NT	DP .	Solvent	с -
OH [°]	ໍ 200	20.479	21	б.0	, 1615	8192	DMSO-d6	
Br	500	8.191	, 19	2.0	2404	81 92 [`]	COCl ₃	
CN ·	500	8.191 -	[′] 19	2.0	1358	8192	CDC13	
Ph	500	8.191	Ø.	2.0	3680	8192	CDC13/20%	MeOH
COOH	. 500	8.191	12	₁°0	5046	8192	COCl3	.e 1
` <u>C1</u>	500 _.	8.191	19	1.0	, 902	8192	CDCl3	
I	500	8.191	19	2.0	7001	[•] 8192	CDCl3	•
SH	500 -	8.191	21	[°] 7.0	_ 448	8192 [°]	ODCl3	
OCH3	500	8% 191	21	5.0	131	8192	CDCl ₃ .	
H	250	10.000	20	2.0	626	8192	CDCl ₃	
F	500	8.191	19 -	10.0	^e 2415 °	8192	CDCl ₃	•
NAĊ	500	· 8.191	15	5.0	4019	8192	CDCl3	4
							•	•

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SW - spectral window AT - acquisition time FW - pulse width FD - pulse delay MT - number of transients DT - data points

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· 83.

Figure 2.3. Spin designations of the coupled nuclei of the A_2X spin system of the ethanoic acidderivatives, CH₂ZCOOH, listed in Table 2.5.

 $\mathbb{E}_{\mathbb{A}} \xrightarrow{\mathbb{C}} \mathbb{C}_{\mathbb{K}} \mathbb{O} \mathbb{O} \mathbb{E}$

Z is as listed in Table 2.5.





Figure 2.5. Schematic of the X part of the A₂X spectra of an ethanoic acid derivative showing the method used to measure the geminal carbon-proton coupling constant.

The reported couplings are the average of the separation of the peaks of the adjacent splittings. That is, the separation of resonances 1 and 2 and resonances 3 and 2.

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Table 2.6. The geminal carbon proton coupling constants for the monosubstituted ethanoic acid derivatives.

۰ <u>،</u> .	,	~ · ·
SUBSTITUENT "	^{`` 2} JCOOH ∂H	liati
	(HZ)	2°0 . A
CH3	, -6.97.	`````````````````````````````````````
OH ,	-4.4]	° 0°02
·. OCH3 ·	-4.40	0.13
NHAC .	·· -5.73	0.13
ŇD ³ , "	-5,82	0.13
. F (-3., 45	· 0.13
·- Sei	-5.52.	0.13.
Cl	-5.23	0.13 ·
Br ·	-4.64	° 0°13
I, '	-4.4]	0.13
°CN '。 ·	-8.00	0.13
, Ph	7.75	0.13
CO2Et .	7: -7.36	0.06

i) digital resolution (1/AT) in Hz, AT - acquisition time

de la

2.3. CONFORMATIONAL EFFECTS

2.3.1. Ethyl Derivatives

For the ethyl derivatives conformational effects can only be significant if the substituent (Z) does not have axial symmetry. When the substituent has axial symmetry, the influence of the orientation of the substituent on the measured coupling constant is the same for all possible orientations the substituent can assume with respect to the coupling pathway. When the substituent does not have axial symmetry, its orientation with respect to the coupling path may vary from one compound to another and influence the magnitude of the observed coupling constant.

2.3.2. Ethanoic Acid Derivatives

As was noted for the ethyl derivatives, when the substituent (2) has axial symmetry conformational effects are not important. However, if the substituent does not have axial symmetry then its orientation with respect to the coupling path may vary from one compound to another and influence the magnitude of the measured coupling

. . 2.4. METHYL DERIVATIVES

2.4.1. Source of the Geminal Proton-Proton Coupling Constants

As we are interested in comparing substituent effects on geminal carbon-proton $({}^{2}JC_{r}H)$ and geminal protonproton $({}^{2}J_{H_{r}H})$ coupling constants in analogous compounds, a series of methyl derivatives was used to obtain values for the geminal proton-proton coupling constants. All values of the geminal proton-proton coupling constants for these compounds were taken from the literature (63) and are listed in Table 2.7.

It should be noted that the values of the geminal . proton-proton coupling constants were calculated from geminal deuterium-proton coupling constants using the ratio of the proton and deuterium magnetogyric ratios, i.e., ${}^{2}J_{H,H} = {}^{2}J_{H,D}$ %, 6.514. The accuracy of geminal proton-proton coupling constants calculated from geminal proton-deuterium coupling constants has been questioned. Fraser <u>etal.</u> (95) note that a primary isotope effect and/or efficient quadrupole relaxation may lead to incorrect geminal deuterium-proton coupling constants and thus incorrect geminal proton-proton coupling constants. Mislow (96) has shown that rapid quadrapelar relaxation of the deuteron is theoretically capable of decoupling the deuteron from the proton. More recently, researchers Table 2.7. The geminal proton-proton coupling constants for the series of monosubstituted methyl derivatives used to compare with the geminal carbon-proton coupling for constants of the ethyl and ethanoic acid derivatives.

		0
ទប	BSTITUENT	2 _{JH,H} a
, ~	r .	`(Hz) '
٠	Снз	-12.56
	NHAC	, -11'.73 ·
ч. •	oe , och ³	-10.60 (, ·
- ,	F`'	- 9°.50
¥	Si	-14.05
	S . *'	-11.87
,	ີCl ເ	-10.70 🖒
Ч.с. Ч.с.	Ge	-12.96
٥	Br .	-10.10
	Sn · "	-12.37
	¢ I 2	··- 9.36 .
	, H	-12.40 ~
	CN ·	-16.90 /
,	Ph	-13.80
	° CO ₂ Et	-14.50 . 5

a)all geminal proton-proton coupling constants taken from reference 63.

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(97) have suggested that geminal tritium-proton coupling constants (${}^{2}J_{H,T}$) should be used to calculate ${}^{2}J_{H,H}$. They cite the similarity of the magnetogyric ratios of tritrium and hydrogen, (1/1.06664), the sharpness of the spectral lines and the small primary isotope effect (0.11 Hz using anisochronous methyl protons) as important. considerations. In a study of ${}^{2}J_{H,T}$ it was found (98) that ${}^{2}J_{H,H}$ calculated from ${}^{2}J_{H,T}$ did not agree exactly with ${}^{2}J_{H,H}$ calculated from ${}^{2}J_{H,D}$. (However, agreement was within 0.5 Hz for all compounds studied. In this work all ${}^{2}J_{H,H}$ values have been derived from ${}^{2}J_{H,D}$ values.

2.5. THE 2,2-DIPHENYLMETHYLCYCLOPROPANE DERIVATIVES

2.5.1. Measurement of the Desired Vicinal Carbon-Proton Coupling Constants

All proton decoupled carbon and proton undecoupled carbon NMR spectra were acquired on a Varian CFT-20 NMR spectrometer at ambient instrument temperature. The compounds were run as 10 percent solutions in CDC1₃.

The proton decoupled carbon spectra were acquired using a sweep width of 4,000 Hz, 8K data points, and a pulse angle of 90°. The chemical shifts of the ring and methyl carbons of the 2,2-dipheavlmethylcyclopropane derivatives, are shown in Table 2.8. The proton

Table 2.8. The carbon chemical shifts of the ring and methyl carbons of the 2,2-diphenylmethylcyclopropane derivatives. The one bond carbon-proton coupling constants for the methyl group are also listed.

,Ph

Ph.

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1:

				۰°		
Z	c ₁	¢ ₂	C ₃	Cłąr	l _j c,H	•
	۰ بر	, (bł	om), .		(hz)	
, , , , , , , , , , , , , , , , , , ,	ی میں میں میں میں ا	35.0 ¹ .	, 22.1	15.9	125.0 ⁱ i	
I	19.1	42.1	30:7	33.6	1-28.0 °-	,
Br · ·	40.6	42.1	28.9	29.2	128.0 '	
CI .	48.3	42.2	28 <u>;</u> ; 0	26.8	12,9.0'	
₽ ₽	80.9	39.7	ື 23 . 7	19.8	128.0	
OMe	 65.8	42.3	° 25.1	18.9	126.5	
NH2	39.7	42.0	27.0	24.3	126.1.	
CN	25.8	42.3	19.3 .	16.2		
ĊO_Me'.	30.8	43.9	24.1	18.5 °	128.5	» ,,

i)all chemical shifts are referenced to the middle resonance of CDCl₃ at 77.05 ppm relative to TMS at 0.00ppm ii)all chemical shifts are accurate to 0.05 ppm and all coupling constants are accurate to 1.0 Hz.

92`

undecoupled spectra were run in the gated decoupling mode using a sweep width of approximately 800 Hz to improve the digital resolution. The decoupler was off during the acquisition of data but turned on during the pulse delay to take advantage of the Nuclear Overhauser enhancement.

The proton undecoupled carbon spectrum is an ABM X spin system. The spin designations of the proton and carbon nuclei. of the 2,2-diphenylmethylcyclopropane derivatives are shown in Figure 2.6 and a typical proton undecoupled carbon spectrum is shown in Figure 2.7.

Complete analysis of the carbon spectra to yield the desired vicinal carbon-proton coupling constants, ${}^{3}J_{A,X}$ and ${}^{3}J_{B,X}$ (see Figure 2.8) requires solution of the AB part of the proton spin system to yield the geminal proton-proton coupling constant $(J_{A,B})$ and the chemical shifts of protons A and B, $\gamma_{0}\delta_{A}$ and $\gamma_{0}\delta_{B}$ respectively.

The proton spectrum, an ABM₃ spin system, was solved using the X-approximation and checked using the program LAME. The effect of the M spin was ignored as the chemical shift difference between the protons A and M and B and M ($\gamma_0 \delta_{AM}$ and $\gamma_0 \delta_{BM}$) were large compared to the coupling constants between protons A and M ($J_{A,M}$) and protons B and M ($J_{B,M}$).

Since the solution of the AB spin system is well known, values of $J_{A,B}$ and $\gamma_0 \delta_A$ and $\gamma_0 \delta_B$ could be calculated. The solution of the ABX part of the ABM₃X Figure 2.6. Spin designations of the coupled nuclei of the ABM3X spin system of the 2#2diphenylmethylcyclopropane derivatives listed in Table

2.8.

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Z is as shown in Table 2.8. If $Z = F_r$ then another , spin is added to both the carbon and proton spin systems. The carbon spectrum becomes an ABM₃SX spin system and the proton spectrum an ABM₃X spin system.



Figure 2.8. The vicinal <u>cis</u> and <u>trans</u> carbon-proton coupling constants, ${}^{3}J_{C,H}^{c}$ and ${}^{3}J_{C,H}^{t}$ for the ${}^{2}\eta^{2}$ -



Dihedral angle between the coupled nucleï is 0 degrees.



Dihedral angle between the coupled nuclei is approximately 144 degrees. spin for the carbon nucleus to yield the vicinal carbonproton coupling constants $({}^{3}J_{A_{\rho}X}$ and ${}^{3}J_{B_{\rho}X})$ could then be . made using the splittings in the measured proton undecoupled carbon spectrum.

The X part of an ABX spectrum is shown diagramatically in Figure 2.9. From the splittings, the quantities $(J_{A_rX} + J_{B_rX})$ and $\tilde{Z}(D_+ - D_-)$ can be measured. The quantities D_+ and D_- are defined in equations (2.01) and (2.02).

 $D_{+} = \frac{1}{2} \left(\left[\gamma_{0} \delta_{AB} + \frac{1}{2} \left(J_{A_{\rho}X} - J_{B_{\rho}X} \right) \right]^{2} + J_{A_{\rho}B}^{2} \right)^{1/2}$ (2.01) $D_{-} = \frac{1}{2} \left(\left[\gamma_{0} \delta_{AB} - \frac{1}{2} \left(J_{A_{\rho}X} - J_{B_{\rho}X} \right) \right]^{2} + J_{A_{\rho}B}^{2} \right)^{1/2}$ (2.02)

Solving these equations for $(J_{A,X}-J_{B,X})$ gives equation (2.03).

 $J_{A_{\rho}X} - J_{B_{\rho}X} = 2 (D_{+} - D_{-}) [1 + (J_{A_{\rho}B}^{2} / (\gamma_{0} \delta_{AB}^{2} - (D_{+} - D_{-})^{2})]^{1/2}$ (2.03)

As $2(D_+-D_-)$, $J_{\hat{A},B}$ and $\gamma_0 \delta_{AB}$ (the difference in chemical shift between protons A and B) are known, $J_{\hat{A},K}$ - $J_{\hat{B},K}$ can be calculated. Solving the simultaneous equations in $J_{\hat{A},K}$ and $J_{\hat{B},K}$ yields values for the desired vicinal carbon proton coupling constants, i.e.,

letting $J_{A,K} + J_{B,K} = X$, and $J_{A,K} - J_{B,K} = Y$ then $J_{A,K} = (K+Y)/2$

where X and Y are known.



2.5.2. Solution of the Proton and the Proton Undecoupled Carbon Spectra of 1-fluoro-2,2-diphenylmethyl cyclopropane

Solution of the proton and proton undecoupled carbon spectra for fluoro-1-methyl-2,2-diphenylcyclopropane is somewhat more complicated. The fluorine nucleus introduces an extra spin into both the proton and carbon spectra. The AB part of the proton spectra becomes an ABX spin system. However since the X part of the spin system was not available the values of $J_{A,X}$ and $J_{B,X}$ could not be calculated in the manner analogous to that used for the ABX spin system when the X is a carbon atom.

The mathematics for the exact solution of the ABX spin system (where X = F) is available and allows the calculation of $J_{Ha_{\ell}F}$ and $J_{Hb_{\ell}F}$ from the splittings in the proton spectrum. The AB part of the ABX spin system is shown diagramatically in Figure 2.10 .

The geminal proton-proton coupling constants $({}^{2}J_{A,B})$ can be determined by measuring the splittings between pairs of resonances, i.e., from Figure 2.10 it can be seen that $J_{A,B} = 1-3_{0} \cdot 2-4_{0} \cdot 5-7_{0} \cdot 6_{5} \cdot 8$.

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The absolute value of the sum of the fluorine-proton coupling constants, $|J_{A_{\rho}X} + J_{B_{\rho}X}|$, is given by equation (2.04)

 $(3 \div 5) - (4 \div 6) = |J_{A_rX} \div J_{B_rX}|$ (2.04) where 3, 5, 4 and 6 are the positions of the resonances

Figure 2.10. , Representation of the AB part of an ABX spectrum. The numbers refer to the line positions discussed in the text, i.e., $J_{A_{\sigma}B}$ is given by the separation of lines 1 and 3, 2 and 4, 5 and 7, and 6 and 8.





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in Hertz.

Furthermore, the values of D, and D are defined by equations (2.05) and (2.06)

 $2D_{=} = 5-1$

 $2D_{+} = 6-2$ (2.06) If $J_{A_{v}B_{v}}$ D_{+} and D_{-} are known then the value of sin $2Q_{-}$ and sin $2Q_{v}$ can be calculated using equations (2.07) and (2.08) respectively

> $\sin 2Q_{-} = 1/2 J_{A_{\rho}B}/D_{-}, \qquad (2.07)$ $\sin 2Q_{\mu} = 1/2 J_{A_{\rho}B}/D_{+} \qquad (2.08)$

From the calculated values of sin 20 and sin 20, values of 20 and 20, can be calculated and used in equations (2.09) and (2.10) to calculate values for cos $\frac{1}{2}$ 20 and cos 20,

 $1/2(\gamma_0\delta_{AB}) - 1/4(J_{A_rX}-J_{B_rX})' = \cos 2Q_ * D_ (2.09)$ $1/Q(\gamma_0\delta_{AB}) + 1/4(J_{A_rX}-J_{B_rX}) = \cos 2Q_ * D_ (2.10),$ where $\gamma_0\delta_{AB}$ is the chemical shift difference between the coupled protons. The value of $(J_{A_rX}-J_{B_rX})$ can be calculated through solution of the simultaneous equations (2.09) and (2.10) to give (2.11),

 $1/2(J_{A_{\nu}X}-J_{B_{\nu}X})^{*} = \cos 2Q_{+} = D_{+} - \cos 2Q_{-} = D_{-}$ (2.11) As we know the value of both the difference $(J_{A_{\nu}X}-J_{B_{\nu}X})^{*}$ and the sum $(J_{A_{\nu}X} + J_{B_{\nu}X})^{*}$ of the fluorine-proton coupling constants, solution of the simultaneous equations gives values for vicinal fluorine-proton coupling constants, $J_{A_{\nu}X}$ and $J_{B_{\nu}X}$.

Correct assignment of the resonances, lines 1 through

(2.05)

8 in Figure 2.10, results in calculated values of $J_{A,X}$ and $J_{B,X}$ of the same sign. Incorrect assignment yields coupling constants of different signs. Furthermore, once $J_{A,X}$ and $J_{B,X}$ are known, either equation (2.09) or (2.10) can be used to determine the chemical shift difference between the coupled protons A and B, $\gamma_0 \delta_{AB}$. The values of $\gamma_0 \delta_{AB}$ and $J_{A,B}$ are then used to solve the ABX carbon spectra.

The vicinal coupling constants of interest are shown in Figure 2.9 and listed in Table 2.9 along with the analogous proton-proton coupling constants taken from a series of monosubstituted cyclopropanes (99, 100, 101). Two observations can be made regarding Figure 2.9. For the cis vicinal carbon-proton coupling constants the dihedral angle between the coupled nuclei is 0° , whereas for trans vicinal carbon-proton coupling constants the dihedral angle between the coupled nuclei is -approximately 1440. Furthermore, the orientation of the substituent varies with respect to the coupled protons for the <u>cis</u> and <u>trans</u> coupling constants. The effect of these changes on the magnitude of the observed coupling will be discussed in a later section.

2.6. THE CYCLOHEXANE DERIVATIVES

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Cyclohexane derivatives and other six membered cyclic compounds containing heteroatoms in which the ring is

Table 2.9. The vicinal carbon-proton coupling constants $\binom{3}{J_{C_{\rho}H}}$ for the 2,2-diphenylmethylcyclopropane derivatives and the analogous vicinal proton-proton coupling constants $\binom{3}{J_{H_{\rho}H}}$ for the cyclopropane derivatives (99, 100, 101).

K	³ јС, п	З _{ЛЕ, Н}	з ^л б°н	3 ₃ 2,
· ·	'.	(н	Z) .	a the
D	5,91	8.97 4	³ .27	5_\$58
	4-94 4	7.55,	2.57	4:37
Br	4.49	- 7.16	1.98	. 3.82
Ĉl .	4.29	7.02	۷ ا ،72 ر.	ia , 5 9 i
	3.20	, 5 . 8 9	0.80	2.39
ÖCH3	3.70	`ຸ <u></u> (6.19	1:40	. 2.94
VÍ NÉ2	4.41	^γ 6.63	i.84	3.55
COZEC	4.60	8 • Q.4	2.60	·
CN	5.17	8.40	2.34	5.09

- the digital resolution (1/AT), where AT is the acquisitin time, is 0.13 Hz for the carbon-proton coupling constants.

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'locked' in a particular conformation have been used extensively by NMR spectroscopists to study the effect of the orientation of coupled nuclei or the effect of the orientation of substituents with respect to the coupled nuclei on the magnitude of vicinal proton-proton coupling constants(${}^{3}J_{H,H}$). Careful selection of these compounds ensures that the prientation of the coupled nuclei and/or the orientation of the substituent with respect to the coupled nuclei are well known. The measured vicinal coupling constants can then be related to these parameters.

Empirical correlations, which relate vicinal protonproton coupling constants to substituent orientation and electronegativity have been developed (44, 45, 47). More recently, a Karplus type relationship (dihedral anglecoupling constant relationship) of the form

 $^{3}J = A \cos^{2} \Phi + B \cos \Phi + C$

in which substituent electronegativity and orientation are taken into consideration by the empirical parameters A and B has been developed (102)

2.6.1. The 1-(1-deutero-4-t-butyleyclohexyl)methanol Derivatives

In order to study the effect of a substituent attached to the coupled carbon and the effect of the orientation of the coupled carbon and hydrogen nuclei a series of 1-(1-deutero-4-t-butylcyclohexyl) methanol derivatives have been synthesized. The compounds and the vicinal carbon proton coupling constants of interest are shown in Figure 2.11. It can be seen in Figure 2.11 that four distinct vicinal carbon-proton coupling constants can arise in the two isomers, i.e., ${}^{g_{J}}C_{C,H}^{C}$, ${}^{g_{J}}C_{C,H}^{D}$, ${}^{g_{J}}C_{C,H}^{C}$, ${}^{g_{J}}C_{C,H}^{C}$, ${}^{g_{J}}C_{C,H}^{C}$, ${}^{g_{J}}C_{C,H}^{C}$, where the left superscript refers to the orientation of the coupled nuclei, g (gauche or 60°) and t (trans or 180°), the right superscript refers to the nuclei trans to the coupled carbon and proton, and the subscript to the ${}^{s_{I}}$

*...

The chemical shift data for the proton decoupled carbon spectra of the <u>cis</u> and <u>trans</u> isomers of the cyclohexyl methanols is listed in Table 2.10. All proton decoupled carbon spectra were acquired on a Varian CFT-20. NMR spectrometer using a sweep width of 4,000 Hz, a pulse angle of 90°, and 8K data points. The compounds were run as 10 percent solutions w/w in deuterated chloroform (CDCI₃) at ambient temperature (35° C).

The proton undecoupled carbon spectra were acquired on a Bruker 100.62 M Hz carbon -13 NMR spectrometer at the University of Montreal, Montreal, P.Q. in the gateddecoupling mode (decoupler off during acquisition) using a sweep width of 4,000 Hz, a pulse angle of 60 degrees and 32K data points. The coupling constants for <u>cis</u> compounds are shown in Table 2.11 as only the coupling



2.11 Newman projections of the vicinal carbon-proton coupling constants for the <u>cis</u> and <u>trans</u> isomers of 1-(1deutero-4-t-butylcyclohexyl)methane derivatives. TABLE 2.10. ¹³C Chemical Shift Data for the 1-(1-deutero-4-t-buty1cyclohexy1) methane Derivatives.

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4	Ż	~	c_1	c ₂	^ک ر ک	Ċ4	C ₅	с _б	Ç7 *
4		çis	34.70	27.41	21.91	48.30	32.40	27.32	63 . 50
Ųđ	trans	39.95`	29.72	26.65	48.20	32.30	27.32	68.58	
	C1	<u>cis</u> ·	34.70	28,30	21.60	48.28	32 . 50 ·	27.40	46.74
CL	trans	39 . 76 🥳	31.00	26.70	47.90	32.35	27.50	50.81	
-	cis	35.00	29.30	21.50	48.30	32.55	27.50	36.72	
	DL .	trans	39.70	32,00	26.80	47.85	32.40	2760	40.50
IŲ	cis	35 .4 5	30.50	21.20	48.45	32.45	27.50	10.70	
	trans	39.60.	33.80	26.90	47.80	32.20	27.60	15.80	

i) all chemical shifts in ppm referenced to middle resonance of CDCl₃ at 77.05 ppm relative to TMS at 0.00 $^\circ$ ppm, resolution is 0.05 ppm

Table 2.11. The vicinal carbon-proton coupling constants, ${}^{t}J_{C,H}$ and ${}^{g}J^{H}\tilde{C}_{,H}$, for the <u>cis</u>-l-(l-deutero-4-t-butylcyclohexyl) methane derivatives. The line, widths (L.W.) of the CH₂X carbons of the <u>trans</u>-l-(ldeutero-4-t-butylcyclohexyl) methane derivatives are also

listed.

Substituent ^CJ_{C,H} ^GJ^HC,_H ^{LAW.} (Hz) OH 8.60 3.10 7.27 Cl- 10.50 3.60 7.60 Br 10.62 3.90 7.80 I 10.99 4.00 8.03

-reported coupling constants are accurate to 0.20 Hz

constants for the <u>cis</u> isomers could be resolved. The line widths of the <u>trans</u> isomers are also given in Table 2.11. The vicinal carbon-proton coupling constants for the <u>cis</u> isomers and line widths for the <u>trans</u> isomers were measured directly from the proton undecoupled spectra.

2,7.1. The 1-methyl-4-phenyl-3,3',5,5'-tetradeuterocyclohexane derivatives

The compounds and the vicinal carbon-proton coupling constants of interest are shown in Figure 2.12. There are four distinct coupling constants for these compounds, two for the <u>cis</u> (phenyl and methyl groups <u>cis</u>) isomer and two for the <u>trans</u> (phenyl and methyl groups <u>trans</u>) isomer, i.e., ${}^{t}J_{C,H}$ and ${}^{g}J_{C,H}^{HC}$ for the <u>cis</u> isomer and ${}^{g}J_{C,H}^{CX}$ and ${}^{g}J_{C,H}^{CC}$ for the trans isomer. The notation is the same as that used for the 1-(1-deutero-4-t-butylcyclohexyl)methane, derivatives.

With the exception of the hydroxy derivative, the <u>cis</u> isomers (the chloro, bromo and iodo derivatives) could not be synthesized in sufficient quantities to afford a proton decoupled carbon spectra. The <u>trans</u> chloro and bromo derivatives were synthesized but coupling constants for these compounds could not be measured.

Table 2.12 gives the carbon chemical shifts for the cis and trans hydroxy derivatives and the trans chloro



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110

^gCC

Figure 2.12. The vicinal carbon-proton coupling constants for the 1-methyl-3,3',5,5'-tetradeutero-4-: phenylcyclohexane derivatives. The Newman projections show the vicinal carbon-proton coupling constants for the cis and trans isomers of these derivatives. Table 2.12: Carbon chemical shift data for the ring and methyl carbons of the 1-methyl-4-phenyl-3,3' $_{6}$ 5,5'tetradeuterocyclohexyl derivatives. The vicinal carbonproton coupling constants for the 1-methyl-4-phenyl- $3_{r}3'_{r}5_{r}5'$ -tetradeuterocyclohexanols and the analogous proton-proton coupling constants for the octadeuterocyclohexanols are also listed.

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9	·	Ж	C-1	C-2	C~3	.C-4	C-5
1		вн	70.01 ^a	39.88	30.47	42.95	25.18 .
2		OH	68.24	38.47	29.54	43.09	31.29
1		Cl	• 71.22	41.21	30.36	42.89	34.06 .
1	0	Br	70.36	42.64	30.34	42.77	35.68
			· \	- and a start		P	

a) all chemical shifts referenced to middle resonance of CDCl₃ at 77.05 ppm relative to TMS at 0.00 ppm. Reported shifts are accurate to 0.05 ppm.

oupling Constant ^b	v	Ç, H.	`' H, H ^C	
tJ		5.60 .	11.11	
₫ ^Ĵ ĦĊ,	, " , "	.3.25	⁽ 4.05 .°	
gjCC	a	L.47	2.48	
gjCC		, 2.20	. 3.29	

b) all couping constants in hertz, accurate to 0.13 Hz c)reference (130) and bromo derivatives. The protion decoupled carbon spectra of these compounds were acquired on a Varian CFT-20 NMR spectrometer using a sweep width of 4,000 Hz, a pulse angle of 90 , and 8K data points. The compounds were run as 10% solutions w/w in deuterated chloroform at ambient instrument temperature.

The proton undecoupled spectrum of the <u>cis</u> hydroxy derivative was acquired on a Varian CFT-20 NMR spectrometer using a pulse angle of 60 degrees, a sweep width of 500 Hz and 8K data points. The proton undecoupled spectrum of the <u>trans</u> hydroxy, derivative was acquired on a Bruker 62.83 MHz carbon-13 NMR spectrometer using a 60 degree pulse in the gated decoupling mode by Dr. Charlies Rodgers of Bruker Spectrospin Ltd.

The vicinal carbon-proton coupling constants for the cis and trans hydroxy derivatives are shown in Table 2.12. They were measured directly from the line positions of the triplet of triplets pattern of the proton undecoupled spectra. For the cis isomer, the trans carbon-proton coupling constant was assumed to be the larger coupling constant. For the trans isomer, the carbon-proton coupling constant with the substituent (OH) trans to the coupled carbon was assumed to be the smaller coupling constant.

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2.8. Sign of the Carbon-Proton Coupling Constants

In this thesis the sign of the one-bond carbonproton coupling constants was assumed to be positive on the basis of the coupling constants reported in the literature (<u>vide infra</u>). The solution of the A_3B_2X spin system of the ethyl derivatives using LAOCN4A (${}^{1}J_{C,H}$ positive) gave geminal coupling constants with a negative "sign. The sign of the geminal coupling constants for the ethanoic acid derivatives were assumed to be negative." also. All vicinal carbon- proton coupling constants were assumed to be positive which is in agreement with vicinal coupling constants reported in the literature (<u>vide infra</u>).











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3.1. SUBSTITUENT EFFECTS ON CARBON-PROTON AND PROTON-

115

3.1.1. Ratio of JCos to JBOB

Various empirical relationships between carbon-proton coupling constants $(J_{C,H})$ and proton-proton coupling constants $(J_{H,H})$ in structurally similar compounds were reviewed in the Introduction.

Figure 3.4 shows fifty carbon-proton coupling constants $(^{2}J_{C_{a}H})$ and $^{3}J_{C_{a}H}$) that we have measured, plotted against proton-proton coupling constants $(^{2}J_{W,H})$ and ${}^{3}J_{H_{H_{H}}}$ for structurally similar compounds. The compounds and their respective coupling constants are listed in Table 3.1. The geminal carbon-proton coupling constants (${}^{2}J_{C,H}$) were measured for the series of ethyl derivatives and ethanoic acid derivatives while the analogous geminal proton-proton coupling constants were calculated from deuterium-proton coupling constants in a series of mono-deuteromethyl derivatives (63). The vicinal carbon-proton coupling constants listed in Table 3.1 are taken from a number of 2,2-diphenylmethylcyclopropane derivatives and t-butyl derivatives, while the analogous geminal proton-proton coupling constants are takén from a series of cyclopropane derivatives (99, 100, 101) and isopropyl derivatives (17)

The bept fit straight line for the plot (using a

Figure 3.1. Plot of fifty carbon-proton coupling constants $(J_{C,H})$ against fifty proton coupling constants $(J_{H,H})$ for structurally similar compounds.

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Table 3.1. Fifty Carbon-Proton and Proton-Proton Geminal and Vicinal Coupling Constants for Structurally Similar Compounds. Compounds #1 through #13 are the ethyl derivatives and #14 through #26 are the ethanoic acid derivatives while the proton-proton coupling constants are taken from the analogous methyl dérivatives. Compounds #27 through #35 and #36 through #44 are the <u>cis</u> and <u>trans</u> $2_r 2$ -diphenylmethylcyclopropane derivatives respectively. The proton analogues are a series of <u>t</u>-butyl derivatives while the proton analogues are a series of <u>t</u>-butyl derivatives.

2_{J_{H,E}}

14.05

12.37

10.94

12.96

`11.87

10.60

11.73

12.56

10.70

10.10

9.50

12,40

10.6Q

11.73

12.56

9.50

10.70

10.10

12.40

11.87

11.73

16.90

13.80

14.50

9.36

9.36

²_{JC,H} # 載な 1 5.22 Si 4.62 2 Sn 3 3.86 Pb 4 4.76 Ge 5 3.51 S б ۰O 2.64 7 3.03 N 8 Ĩ 2.74 9 С 4.20 10 C12.85 11 Br 2.65 12F 1.86 13 Η 4.80 4.41 14 0 15 5.73 NHAC 16 CH3 F 6.97 17 3.45 18 CL 5.23 . 19 Br 4.64 20 I 4.41 21 H 6.77 22 S 5.52 23 ND_3 5.82 24 8.00 CN 25 7.75 Ph 26 7.36 **BOCO**

з_{ЈН,Н} 3_{ĴС,Н} . 各 X 5.91 8.97. 27 D 4.94 7.55 28 I 29 4.49 Br 7.16 4.29 30 Cl 7.02 31 F 3.20 5.89 32 OCH2 3.70 6,19 NH2 33 4.50 6.63 34 CN 5.17 8.43 4.60 8.04 35 CO_2Me 5.58 3.27 36 Ď 37 2.57 I 4.37 38 Br-1.98 3.82 39 C13.59 1.72 40 F. 0.80 2.38 2.94 41 OCHa 1.40 42 MH_2 3.55 1.75 43 - CN 2.34 5.12 2.60 44 CO-Me 4.57 ° 6.54 45 Br 4.22 46 T 4.45 6.69 47 CH2 4.62 6.80 48 5.27 7.38 D 49 Cl4.08 6.43 50 F 6.10 3.81

ß

linear regression analysis) is given by equation (3.01). $J_{C,H} = 0.34 J_{H,H} + 1.09 r^2 = 0.511$ (3.01) The poor correlation coefficient for this plot (r^{2} = 0.51) illustrates the fact that no universally consistent correlation between carbon-proton and proton proton coupling constants can be used It should be noted that both geminal carbon-proton and geminal proton-proton coupling constants are plotted as absolute values in order to avoid the impression of a better correlation which would be obtained from two widely separated clusters of data. The variation of the ratio of the carbon-proton to the proton-proton coupling constants $(J_{C,H}/J_{H,H})$ for the series of compounds investigated indicates that a single ratio, such as that proposed by Marshall (14) is not

generally applicable. The spread of the data appears to be too scattered to allow a general correlation, but by selection of groups of data on the basis of a suitable parameter, such as the Row or Group of the Periodic Table to which a substituent belongs, some excellent correlations can be found. The series of compounds mentioned above, i.e., the ethyl derivatives, the derivatives, ethanoic acid and the diphénylmethylcyclopropane derivatives will be discussed separately and conclusions made regarding the factors (especially substituent effects) affecting the observed coupling constants.

PARAMETERS USED IN THE QUANTIFICATION OF

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SUBSTITUENT EFFECTS

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3.2.

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In this work the primary interest was in the empirical correlations between the development of inductive or field effect of a substituent and the imagnitude of carbon-proton or proton-proton coupling constants. A substituent affects the s-electron density at a carbon atom in at least two ways (103); by altering the hybridization of the carbon atom in various bonds and by causing a polarization of the carbon-substituent bond. . The change in the hybridization of the carbon atom results in a change in the s-character of the orbitals and thus in the magnitude of the observed coupling constant through the bonds. The polarization of the carbon-substituent bond results : in a change in the effective nuclear charge at, the carbon nucleus. This in turn alters the radial electron density and leads to a variation in the size of the electron cloud. The coupling constant is sensitive to the size of the electron cloud.

We have used two parameters to quantify substituent inductive effects. These are discussed in the next sections.

3.2.1. Electronegativitý

Électronegativity is generally defined as the ability of a nucleus to draw valence electrons toward itself relative to another nucleus. It is an empirical number whose magnitude depends upon the manner in which it is calculated. Various scales have been developed, the most common being those of Pauling (103) based on thermochemicaldata, Mulliken (104) based on ionization potentials and electron affinities and Huggins (36) based Scales based on quantum defects on thermochemical data. (106), .atomic energies and covalent radii (107), proton chemical shifts (108), & covalent radii (109) floating spherical gaussian orbitals (110), dielectric constants . (101)₄ effective nuclear charges (102), and <u>ab initio</u> calculations using a nonempirical electrostatic method (NEM) (113) are found in the literature.

The usefulness of the concept has been summarized well by Batsanov (114) who states

"Together with Huckel, these authors believe that the main reason for the successful application of electronegativity in chemistry is that this reflects the periodic variation of properties in Mendeliev's system.

In this work we are interested in substituent effects on one bond (^{1}J) , two bond (^{2}J) , and three bond (^{3}J) coupling constants. The use of electronegativity scales

allows convenient comparison of these substituent effects . on the observed coupling constants.

Two electronegativity scales are utilized, the Huggins scale (36) and the nonempirical electrostatic method NEM scale (113). The Huggins electronegativity scale has been used previously to relate substituent effects and changes in the magnitude of coupling constants (17, 40, 115) and has yielded useful *correlations. This scale has values for all the substituents attached to compounds used in our studies of vicinal carbon-proton coupling constants, but does not ~ have values for all of the substituents used in the geminal and direct coupling cases. Consequently, a second scale, which has values for the heavier substituents in the third and fourth Rows of the Periodic Table, was also required. The NEM scale was chosen for use-with the one and two bond coupling constants because the scale has these values for the heavier atoms and has values similar to the Huggins scale for those atoms they have in common.

3.2.2. Swain-Lupton Field and Resonance Factors

Electronegativity is often equated with the ability of, a nucleus to attract electrons by its inductive effect. Substituent effects are not necessarily all inductive effects. In an attempt to separate the field

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or inductive effects of substituents and resonance effects of substituents Swain and Lupton (116) have calculated a series of substituent field (F) and resonance (R) factors.

These factors were calculated in an empirical manner. Swain and Lupton assumed that any set of substituent parameters, i.e. σ_m , σ_p , etc. could be expressed as the sum of field and resonance components as in equation (3.02)

$G^{o} = fF + rR \qquad (3.02)$

where G is the substituent effect, F and R are the field and resonance constants respectively, and f and r are weighting factors.

They proposed that F and R were more accurately defined and more physically significant independent variables for predicting or correlating substituenteffects on physical properties than any other set they considered.

More recently Swain (117) has proposed a revised series of field and resonance factors. These are based on a larger series of data and the precision of the constants, F and R, have been calculated. Charton (113) has calculated a series of constants, σ_{I} , which he Suggests give a better measure of the inductive effect of a substituent than do the Swain-Lupton field factors, F. Recently, a series of papers have been published (119, 120, 121) which criticize the separation of field and

resonance effects given by the Swain-Lupton approach. Reynold's and Topsom (119) propose that the Swain-Lupton F and R constants provide an incomplete separation of the field and resonance effects due to the inappropriate criteria used to perform the calculations. In particular, they criticize the use of R = 0 for the -N(CH₂)₃ group. Furthermore, they suggest that the application of the resonance factor R is restricted to systems following σ and σ^+ , and fails for systems following σ , as no single resonance scale can predict the full range of aromatic reactivity resulting from the significant change in resonance effects with electron demand. Swain (122) replies that their evidence against the use of R = 0 for the $N(CH_3)_3$ group is in fact for the NH3 group. Swain also shows that the fit for both σ^+ and σ^- substituents is good and that his approach can accomodate substituents not considered in his original. (118) treatment. Swain points out that multiple parameter approach proposed by Reynolds and Topsom has several disadvantages including the arbitrary choice of lack of predictive capability, and for illparameter, fitting data leads one to conclude that another parameter should be considered rather than a change mechanism.

Hoefnagel et al. (120), on the basis of new data, propose that the Swain-Lupton F and R constants do not satisfactorily separate field and resonance factors.

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Swain suggests that these new data represents an example of the deviation from the average behavior predicted by F and R values and that Swain-Lupton field and resonance factors can be useful in accessing such deviations. Swain suggests that Hoefnagel et al. should have taken their approach one step further, <u>i.e.</u>, they did not go past the point where an optimum least-squares fit between observed and calculated data was found, and defined critical conditions to see if their parameters had physical significance.

Charton (121) has criticized the Swain-Lupton field and resonance factors on several grounds; firstly, that' σ_{I} gives a better fit than F for a majority of systems studied; secondly that $N(CH_3)_3$ must be well behaved, and Charton finds that ionic groups have a highly variable localized effect; and lastly that σ_{T} and σ_{D} give values for the transmission of localized substituent effects from the meta to the para position in benzene that agree more closely with those for model compounds and calculations than do F and R. Swain suggests that the significance of Charton's σ_T values are in question as the critical subsidiary conditions used to calculate them are not well defined. Also, Swain states that Charton adresses the question of whether F or σ_{T} is better for correlating substituent effects only for series of compounds where *r* bond resonance has little or no significance. Charton does not consider charged species

($N(CH_3)_3$, COO^7 , O^7 , SO_3^7) nor species with an hydroxylic proton (OH, COOH, CH₂OH). Finally, Swain suggests that σ_{I^*} values appear to have been adjusted to fit^w experimental data.

Swain concedes that correlations of experimental data with some substituent parameters may be slightly better than those with F, especially if more parameters are used or if the parameter is selected to ensure optimum fit. However, he feels that the advantage of using Swain-Lupton field and resonance factors is that they represent the average behavior of substituents from which deviations in substituent effects are more apparent. As such, the Swain-Lupton field factor F. will be used in this, thesis as a measure of the magnitude of the inductive effect of a substituent.

3.3. PLOTS OF CARBON-PROTON AND PROTON-PROTON COUPLING AGAINST SUBSTITUENT ELECTRONEGATIVITY AND SWAIN-LUPTON FIELD FACTORS

In the following sections the observed carbonproton coupling constants for each series of compounds studied are plotted against substituent electronegativity (E) and Swain Lupton field factors (F) in an effort to derive usable empirical correlations. These plots will allow comparison of substituent effects on one, two and three bond coupling constants and may give some insight. into the factors affecting these coupling constants.

Starting with the general plot of points for all the derivatives in a particular series of compounds, emphasis is placed on finding more specialized relationships within each plot. Substituents from Rows and Groups within the Periodic Table are considered and the resulting correlations are used as a basis for the discussion of the factors affecting the observed carbonproton coupling constants.

Finally the carbon-proton and proton-proton coupling constants from the analogous series of compounds are plotted against each other, the plot discussed, and correlations developed.

2.3.1. Plot of the One Bond Coupling Constants for the Ethyl Derivatives Against Substituent Electronegativity(¹J)

The acquisition of the proton undecoupled carbon spectra of the ethyl derivatives allowed the measurement of the one bond carbon-proton coupling constants for these compounds. A plot of the value of ${}^{1}J_{C,H}$ (for the carbon with the substituent attached) for the ethyl derivatives listed in Table 3.2 against the NEM electronegativity ($E_{\rm N}$) of the substituent is shown in Figure 3.2. It is obvious from the spread of the data points in Figure 3.2 that ${}^{1}J_{C,H}$ does not correlate well with $E_{\rm N}$. The correlation coefficient for the best fit straight line given by equation (3.03) is 0.39.

 $J_{C,H} = 9.87 E_N + 111.06$ $r^2 = 0.389$ (3.03) However, when compounds with substituents in a particular Row of the Periodic Table are considered separately, the best fit straight lines for the plots of the values of ${}^{1}J_{C,H}$ for those compounds with first \gg through fourth Row substituents are given by equations (3.04), to (3.07) respectively.¹

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Table 3.2 The one bond carbon-proton coupling constants $(l_{j_{C/H}})$, NEM substituent electronegativities (113), and Swain-Lupton field factors (117) for the ethyl (derivatives, CH₃CH₂Z.

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•	Substituent		EN	Ē	بي بي المراجع ا المراجع المراجع
	Z ,	, (Hz) ,	₹ *	د (۱۹	
	Si(Et) ₃	* <u>117.4</u> ⁱ .	1.81	-0.10 -0	- Lot
•	Sn (Et)'3	, 128.0	1.63	-0.35 ¹¹	۲. س
	Ge(Et)3	1.26.0	; :1.74	-0.278 ¹¹	
	SEt í	. 137.4	2.65	0,-52 , '-	r
,* '.	OEt	138.0	ʻ3`53	0.61	· · · · · · · · · · · · · · · · · · ·
	N(Et) ₂	131.5	, ³ .23' ·	,0.38	÷.,
4	SeEt	- 140:3	- 2,39	· 0.28	· · · ·
	ľ '	150.5	2.48	0.65.	
	Br	, 150.7	: 2.78	0.72	x
	C1 ["]	150.0	3.14	0.72	
	H	125.0	1.94	0.00 -	v
٠	CH3	124.3	2.52	-0.02	
	F · · ·	150:3	4.00	0.74	ø
1	TeEt	140:2	. 2.19	· · · · · · · · · · · · · · · · · · ·	
ł	Pb(Et) ₃	v 134.5	۵	0.42 ii	•
	Hg(Et) ₃ i)reported	130.0 coupling consta	ints accurat	e to 1.0 Hz.	ا مو
	Eurolan (ii	rated by C. R	Hamor. T	P. Poat. W P	٠

Reynolds, Can. J. Chem., <u>51</u> (1973).

Figure 3.2. Plot of the values of ${}^{1}J_{C,H}$ for the ethyl derivatives listed in Table 3.2 against the NEM electronegativity of the substituent (E_{N}) .



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⁻¹ JC,H	-	16.55 E _N +	81.33 ; $r^2 =$	0.922	(3.04)
¹ J _{С,Н}	38° 12	24.43 E _N '#	$73503 \text{ yr}^2 =$	0.999	(3.05)
^{`,1} J _{C,H}	19-	23.57 ¢ _{N'} +	,84.71 ¹ r ² =	0.997	(3.06)
ljc,t	Ē	25.83, E _N +	85.31 r ² =	0.983	(307)

The correlation coefficients for these plots are excellent in comparison to that obtained for the general plot (Figure 3.2). It is interesting to note that the, slope of the plot of ${}^{1}J_{C,H}$ versus E_{N} ($\delta^{1}J_{C,H}/\delta E_{N}$) for the first Row substituents (C, N, O, F) is considerably. different than the slope of the plots for the second, third, and fourth Row substituents, i.e., $\delta^{1}J_{C,H}/\delta E_{N}$ is 16.55 for the first Row substituents whereas $\delta^{1}J_{C,H}/\delta E_{N}$ varies between 23.57 and 25.83 for the second, third and fourth Row substituents.

In a plot of ${}^{1}J_{C,H}$ versus E for an equivalent series of methyl derivatives, Douglas (123) observed a similar variation of the one bond coupling constants with substituent electronegativity. The best fit straight line for the fourteen methyl derivatives shown in Table 3.3 is given by equation (3.08).

 ${}^{1}J_{C,H} = 6.61 E_{N} + 120.23$ $r^{2} = 0.253$ (3.08) The best fit straight lines for the plots of the values of ${}^{1}J_{C,H}$ against E_{N} for the first, second, third and fourth Row substituents are given by equations (3.09) through (3.12).

> ${}^{1}J_{C,H} = 17.53 E_{N} + 78.22 r^{2} = 0.949$ (3.09) ${}^{1}J_{C,H} = 24.49 E_{N} + 73.03 r^{2} = 0.999$ (3.10)

Table 3.3. The one bond carbon-proton coupling constants for a series of monosubstituted methyl derivatives and Pauling substituent electronegativities (104).

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* &	SUB	STITUEN	Ţ	electro)NEGAI	TIVIT	Y	l _{JC,E}	(Hz)	
· ,	•	F			4.0			149.1	*	•
		OMe			3.5	١		139.6	4	•
		NMe ₂	2	ø	3 _° 0 [°]	,	•	131.0	1982) 1	
		CMe3	Ņ	, ,	2.5			124.5		7
	,	CL			3.0		المتعاد	.150.0	3	
	•	SMe	., *		2.5			137.5		
		SiMe ₃	•170	ĩ	1.8	×		118.2		
,	۰.	Br		~	-2.8		-	152.0		
		SeMe	•	•	2.4	**	۵ '	140.2		
	;	GeMe3		•	1.8 -			124.0	•	
•		I ,			2.5			151.0		
		TeMe			2.1	• ಒ	×	140.5		
		SnMe3			1.8			127.2	1	•
	n	PbMe ₃	<i>а</i> ,	P	1.8	,		134.0	и 2	
		Ħ		``*. `	2.1	с °	-	125.0	ע	-
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(123)

A.W. Douglas, J. Chem. Phys., 45, 3465 (1966)

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 ${}^{1}J_{C,H} = 26.31 E_{N} + 77.86 r^{2} = 0.996$ (3.11) ${}^{1}J_{C,H} = 25.48 E_{N} + 85.37 r^{2} = 0.957$ (3.12) As was found for the ethyl derivatives, the correlations of the plots improve significantly over the

general plot when compounds with substituents in a particular Row of the Periodic Table are considered separately.

Figure 3.3 shows a plot of the values of ${}^{1}J_{C,H}$ for the ethyl derivatives against the Swain-Lupton field factors (F) of the substituents. The best fit straight line (for the derivatives for which Swain-Lupton F factors are available) is given by equation (3.13).

 ${}^{1}J_{C,H} = 35.8 F + 122.0 r^{2} = 0.914$ (3.13) Inclusion of the points for the germanium, tin, and lead derivatives using F factors calculated by Reynolds <u>et al.</u> (124) from chemical shift data for the trimethyl derivatives, (Ge(CH₃)₃, Sn(CH₃)₃, and Pb(CH₃)₃)', gives the best fit straight line shown in equation (3.14) for the plot of ${}^{1}J_{C,H}$ against/F.

 ${}^{1}J_{C,H} = 25.7 F + 129.0 r^{2} = 0.799$ (3.14) The slope, intercept and correlation coefficient of equation (3.14) are significantly different from those for equation (3.13); the slope decreases from 35.8 to 25.7, the intercept increases from 122.0 to 129.0, and the correlation coefficient decreases from 0.914 to 0.799 in going from equation (3.13) to (3.14). Ideally one would like to use F factors calculated for the actual

Figure 3.3. Plot of the values of ${}^{1}J_{C,H}$ for the ethyl derivatives listed in Table 3.2 against the Swain-Lupton field factor (F) of the substituent.



substituent, i.e., the F factor for the triethyl derivatives instead of the F factor for trimethyl derivatives. That this may introduce an inconsistency into the plot is illustrated by the series of substituents OH, OCH₃, and OC₂H₅ where the F factor varies from 0.46 to 0.54 to 0.61 for these three substituents. Similar variations for the tin, germanium, and lead F factors for the X-CH₃ substituents and for the X-CH₂CH₃ substituents would account for the poorer correlation for equation (3.14).

Werstiuk (125) has plotted the values of ${}^{1}J_{C,H}$ for a series of mono-substituted methanes against the Swain Lupton F factors of the substituents. (See Figure 3.4). Two distinct correlations were found for I⁺ and I⁻ groups as defined by Maciel, McIver, Ostlund and Pople (39, 126, 127, 128, 129). The best fit straight line for the plot of the I⁻ substituents (COCH₃, COOH, CN, and NO₂) against F is located 15-20 Hertz below that for the I⁺ substituent (OH, NH₂, CH₃, F, Cl, Br, I). The author concluded that this shift could be due to an attenuation of the inductive effect or the effect of other factors (such as hyperconjugative effects) which might contribute to a decrease in the value ${}^{1}J_{C,H}$.

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In summary, the one bond carbon-proton coupling constants $({}^{1}J_{C,H})$ for the substituted ethanes that we have measured do not correlate well with substituent electronegativity (E_{N}). However, if compounds with



Figure 3.4. Plot of the values of ${}^{1}J_{C,H}$ for the methyl derivatives against the Swain-Lupton field factor (F).

substituents in a particular Row of the Periodic Table are considered, good correlations of the one-bond carbon-, proton coupling constants with E_N are found.

The one-bond carbon-proton coupling constants $({}^{1}J_{C,E})$ for the substituted ethanes that we have measured correlate well with Swain Lupton F values especially if the values for the germanium, tin and lead compounds are omitted. It appears that the field factor provides a more general parameter for the comparison of substituent effects on one bond coupling constants. The substituent effect on ¹J_{C.H} is best described as varying from Group to Group of the Periodic Table and the field factors (F) reflect this variation; e.g., notice the constancy of the field factors (F) and also the magnitude of ${}^{1}J_{C,F}$ for the ethyl halides in Table 3.2 . The F factor varies from 0.72 to 0.65 while the one bond 0.74 to 0.72 to carbon-proton coupling constant varies from 150.3 to 150.0 to 150.7 to 150.5 for the fluoro, chloro, bromo; and iodo derivatives respectively.

As the substituents used in ethyl derivatives are all I⁺ substituents, the correlation of ¹J_{C,H} with Swain-Lupton field factors (F) parallels the behavior of the I⁺ substituents for the mono-substituted methyl derivatives found by Werstiuk.

It is interesting to note that the plot of the one bond carbon-proton coupling constant for the ethyl derivatives against Charton's σ_T values of the substituents (10 compounds) gives a better correlation than the analogous plot of ${}^{l}J_{C,H}$ against the Swain-Lupton field factor of the substituent. The best fit straight lines given by a linear regression analysis are shown below.

$J_{C,H} = 54.4$	⁶ 1 + 124.0	$r^2 = 0.966$	•	3.14a
$1_{\rm J_{C,H}} = 35.8$	F+122.0 .	$r^2 = 0.904$		3.14b

Swain (122) has conceded that in some instances that σ_{I} (or for that matter other substituent parameters) may give slightly better correlations than Swain-Lupton field factors. However, he still maintains that the Swain-Lupton approach affords the most generally applicable separation of field and resonance effects. In the light of the arguments given in the preceding section, it was decided that the Swain-Lupton field factor for a substituent will be used in this thesis as a parameter that approximates its inductive effect. This is not to say that better correlations are not possible in some instances with other parameters.

3.3,2. The Effect of Substituents on Geminal Carbon-Proton Coupling Constants $(^{2}J_{C,B})$

In this section the effect of substituents on geminal carbon-proton coupling constants $({}^{2}J_{C,H})$ are considered. The values of ${}^{2}J_{C,H}$ for the ethyl and ethanoic acid derivatives are plotted against substituent electronegativity (E_{N}) and Swain Lupton field factors (F) and the glots discussed. The geminal carbon-proton coupling constants are then compared to geminal protonproton coupling constants for the analogous methyl derivatives in an attempt to develop empirical correlations between the carbon-proton and proton-proton coupling constants. The relevant coupling constants, electronegativities and field factors for the compounds of interest are listed in Tables 3.4 and 3.5.

3.3.2.1 Variation of the Value of ${}^{2}J_{C,H}$ for the Ethyl and Ethanoic Acid Derivatives with E_{N} and F

Figure 3.5 shows a plot of the values of ${}^{2}J_{C,H}$ for the ethyl derivatives against the NEM electronegativity (E_N) of the substituent for the fourteen compounds, listed in Table 3.4. The best fit straight line for the plot, derived from a linear regression analysis; is given by equation (3.15).

 $J_{\rm C,H}^2 = 1.24 E_{\rm N} - 6.71 = z^2 = 0.739$ (3.15)

Table 3.4. The geminal carbon-proton and proton-proton coupling constants for the ethyl derivatives and the analogous methyl derivatives. The NEM electronegativities (113), Swain-Lupton field factors (117) and the Ratio of the carbon-proton to the proton-proton coupling constants are also listed.

		~	-		, ô	h P	
	X .	² J _{C,⊞}	² J _H ,H	RATIO ·	EN	E · · · · ·	•
		'• (H:	z) `•	•	\$	ັ້ ເຊັ່ງ ເຊັ່ນ ເຊັ່ງ ຊ	
•	C , 3	-4.20	-12.56	0.334	2.53	-0.02	
	N	-3.03	-11.73	0.258	3.23	0.38	
	0	-2.64	10.60	0.249	3.53	0.61	
	F	-1. 86 [*]	- 9.5Ò	0.196	4.00	0.74 ·	
	Si	-5.22	-14.05	0.372	1.81	-0.10	
0	ន	-3.51	-11.87	0.296	2.65	0.68	
	Cl	-2.85	-10.70	0.266	3.14	0.72.	
	Sn	-4.62	-12.37	0.373	· 1.63 、	-0.35 [.] 2	
	Se`	-3.22			2.39	0.28	•
	Br	-2.65	-10,.10	0.262	2.78	0.72	
	Ge	-4.76	-12.96	0.367	1.74	-0.278 ^a	
	Te	-3.22	، به ه ۲	s 4¥ o	2.19	, el	
	I	-2.74	~ ,9,36	0.293	2.48	0.65	
	H	-4.80	-12.40	0. 387	1.94.	0.00	
	, Pb	-3.86	2	./.	* 0	-0.420ª	
	Hg	-4.52	u .	4 	-	* * * *	
		, L		•		2	

a)calculated by G. K. Hamer, I. R. Peat, and W. F. Reynolds, Can. J. Chem., <u>51</u>, 897 (1973).

Table 3.5. The geminal carbon-proton and proton-proton coupling constants for the monosubstituted ethanoic acids and the analogous monosubstituted methanes. The NEM substituent electronegativities (113), Swain-Lupton field factors (117), and the Ratio of the carbon-proton to proton-proton coupling constants are also listed.

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X	² _{ĴC,H}	² ј _{н,н}	RATIO	EN	ŕ
• • a 1	· (H:	z) · ·	:		,
CH ₃	-6497	12.56	° @\$ 5.55	2.53	- 0.02
OH ,	-4.41	-10:60	0.416	3.53	0.46
NHÀC	-5.73	-11.73	0.488	3.23ª	. 0.77
ÈF (-3,45	9 . 50	0.363	4.00 ,	· 0°.74 ·
SH	-5,5 ²	[°] ب1. ⁸⁷	0.465	,2.65	[°] 0.52
ci.	-5.23	~`-] 0.70 j	0.489	3.14.	0.72
Br	-4.64	-10.10.	0.459	2.78.	. 0.72
I	-4.41	-9.36	0.471	2.48	0.65
CN	-8.00	-16.90	0.473	2:53ª	ູ່ 0ໍ.90
Ph	-7.75	-13.80	0.561	2.53ª	` 0,25
COOEt	-71.36	-14.50	0.508	2.53 ^a	; 0 , 47 ч
H	-6.77 -	-12.40	0.546	1.94	0.00

a) atom electronegativties



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Similarly, a plot of the values of ${}^{2}J_{COOH,H}$ for the ethanoic acid derivatives against the NEM electronegativity $(E_{\rm N})$ of the substituents is shown in Figure 3.6. The best fit straight line for the compounds listed in Table 3.5 is given by equation (3.16).

 ${}^{2}J_{COOH,H} = 1.83 \text{ E} - 11.00 \text{ r}^{2} = 0.467$ (3.16) The correlation coefficient for this plot is worse than that for the ethyl derivatives and the poor correlations for these plots preclude useful application of either equation (3.15) or (3.16) to predict carbonproton coupling constants from substituent celectronegativity.

The magnitude of the geminal coupling constants for both the ethyl and ethanoic acid derivatives increase (become more positive) with increasing substituent electronegativity. The slope of equation 3.16 is larger than that for equation 3.15, suggesting that the ethanoic acid derivatives are more sensitive to a change in substituent electronegativity than the ethyl derivatives. However, the poor correlation coefficients bring such a conclusion into doubt.

Figure 3.7. shows a plot of the values of ${}^{2}J_{C,H}$ for the ethyl derivatives from Table 3.4 against the Swain-Lupton field factors (E) of the substituents. The best Figure 3.6. Plot of the geminal carbon-proton coupling constants ${}^{2}J_{COOH,H}$ for the ethanoic acid derivatives listed in Table 3.5 against substituent NEM electronegativity.

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-4. CO

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3.00 (NEM)

3.50



4.00

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fit straight line for the plot is given by equation (3.17).

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 ${}^{2}J_{C,H} = 2.72 F - 4.49 r^{2} = 0.791$ (3.17) The points for the lead, germanium and tin compounds have been omitted in equation (3.17). If the points for these derivatives are included the best fit straight line for plot of ${}^{2}J_{C,H}$ against F is given by equation (3.18).

 ${}^{2}J_{C,H} = 1.94 F - 4.06 r^{2} = 0.703$ (3.18) As was mentioned earlier, the F values for the trialkyllead, trialkylgermanium, and trialkyltin derivatives were calculated by Reynolds for the methyl, not the ethyl derivatives of these compounds and as such may not be the correct values for the compounds used to measure the coupling constant.

A plot of the values of ${}^{2}J_{COOH,H}$ for the ethanoic acid derivatives listed in Table 3.5 against the Swain-Lupton Field factors (F) of the substituents is shown in Figure 3.8. It is obvious from the plot that no good correlation between the geminal carbon-proton coupling constant and F exists for this series of compounds. A linear regression analysis gave the best fit straight line described by equation (3.19).

 $^{2}J_{COOH,H} = 1.84 \text{ F} - 6.83 \text{ r}^{2} = 0.145$ (3.19) The geminal carbon-proton couplings constants for the ethyl and ethanoic acid derivatives, ($^{2}J_{C,H}$ and $^{2}J_{COOH,H}$ respectively), do not vary linearly with either



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substituent electronegativity (E_N) or Swain-Lupton field factors (F). The correlation coefficient for the plot of ${}^2J_{C,H}$ for the ethyl derivatives against E_N is 'better' than that for the corresponding plot of ${}^2J_{C,H}$ against F $(r^2 = 0.74 (E), r^2 = 0.70 (F))$, but neither plot yields a good correlation. For the ethanoic acid derivatives the correlation coefficient of the plot of ${}^2J_{COOH,H}$ against E_N is 'better' than that for the plot of ${}^2J_{COOH,H}$ against F $(r^2 = 0.47 (E), r^2 = 0.15 (F))$ but again neither plot gives a usable correlation.

3.3.2.2. Variation of the Value of 2 $\mathbf{J}_{C,H}$ with Substituent Electronegativity and Swain-Lupton Field Factors for Substituents from a Particular Row or Group

Grouping of the substituents in the first, second, third, and fourth Rows respectively leads to excellent correlations between the values of ${}^{2}J_{C,H}$ for the ethyl derivatives and substituent electronegativity (E_{N}). The best fit straight lines for the plots of ${}^{2}J_{C,H}$ against E_{H} for compounds with first through fourth Row substituents are given in equations (3.20) through (3.23).

monotonically in going from the first Rov (1.58) to the fourth Row (2.25) substituents whereas the y-intercept's show very little variation. For the ethyl derivatives the dependence of the observed coupling constants $({}^{2}J_{C,H})$ on substituent electronegativity (E_{N}) increases as the substituents are varied from the first to fourth Rows.

Although a similar trend is observed for the plot of ${}^{2}J_{COOH,H}$ for the ethanoic acid derivatives against substituent electronegativity, the lack of data for compounds with substituents in the second, third, and fourth Rows of the Periodic Table allowed a correlation of ${}^{2}J_{COOH,H}$ with $E_{\rm N}$ for the first Row substituents only. The best fit straight line for the four first Row substituents, (C, N, O, F), is given by equation (3.24).

 ${}^{2}J_{COOH,H} = 2.46 E_{N} - 13.31 r^{2} = 0.973$ (3.24). The slope of this plot, $(\delta^{2}J_{COOH,H}^{*}/\delta E_{N})$, is considerably larger than that for the ethyl derivatives with first row substituents, (2.46 versus 1.58), as is the absolute value of the intercept (13.31 versus 8.19). It is difficult to attach any significance to the difference in the slopes and intercepts of equations (3.20) and (3.24) as the absolute value of the geminal coupling constants for the ethanoic acid derivatives are larger than those for the ethyl derivatives and these numbers merely reflect this trend.

The excellent correlations of the plots of the value of $^{2}J_{C,H}$ for the ethyl or ethanoic acids derivatives with

substituents from a particular Row of the Periodid Table against the substituent electronegativity suggest that one should investigate the variation of ${}^2J_{C,F}$ for these compounds as the substituent varies down a Group of the Periodic Table. When the substituent was varied across a. Row, for instance, from carbon to nitrogen to oxygen to fluorine, the measured coupling was found to become less negative as the substituent electronegativity increased. However, when the substituent is varied down a Group, the coupling constant does not change monotonically as the electronegativity of the substituent decreases. The Group IVA substituents (carbon, silicon, germanium, and tin) serve to illustrate this point. For these derivatives the value of ${}^{2}J_{C.H}$ varies from -4.20 to -5.22 to -4.76 to -4.62 for the carbon, silicon, germanium and tin compounds, i.e., the value of ${}^{2}J_{C,H}$ for the carbon compound falls off the line defined by the trend shown by the silicon, gérmanium, and tin compounds. Similar variations of ²J_{C,H} for ethyl derivatives with Group VI and Group VII substituents are also observed.

If the coupling constants for the ethyl derivatives with substituents in G_{0} oup IVA, Group VIA and Group VIIA are plotted against substituent electronegativity and the coupling constants for compounds with the first row substituents, (C, O, and F), ignored, the best fit straight lines for these plots are given by equations (3.25) through (3.27). Group IVA ${}^{2}J_{C,H} = -3.15 \text{ En} + 0.57 \text{ r}^{2} = 0.829$ (3.25) Group VIA ${}^{2}J_{C,H} = -0.65 \text{ En} - 1.74 \text{ r}^{2} = 0.812$ (3.26) Group VIIA ${}^{2}J_{C,H} = -0.18 \text{ En} - 2.24 \text{ r}^{2} = 0.351$ (3.27)

Using equations (3.25), (3.26) and (3.27) it is possible to calculate the expected value of ${}^{2}J_{C_{r}H}$ for the ethyl compounds with carbon (Group IVA), oxygen (Group VIA) and fluorine (Group VIIA) substituents respectively and compare the observed and calculated value of ${}^{2}J_{C,H}$ for each substituent. The observed and calculated geminal carbon-proton coupling constants (${}^{2}J_{obs}$ and ${}^{2}J_{calc}$) and their ratios are shown below.

	••	X	2 _{Jobs}	2 _J calc *	Ratio
Group	IV	С	-4.20	-7.34	· [^] 0.57
Gróup	VI	0	-2.64	· -4.03	0.66
Groyp	VII	1	-1. 86	-2.96	0.63

This would seem to indicate that the anomalous behaviour of the first row substituents is not random. The similarity of these ratios may indicate what we might term a 'light atom effect' is operative where the observed geminal carbon-proton coupling constant is affected in an analogous manner by all the first row substituents. However, the poor correlations given by the relationship's 3.25 through 3.27 bring such a conclusion into doubt.

The variation of the magnitude of ²J_{C,H} with the
substituent Row or Group is illustrated in Figures 3.9 and 3.10 respectively. The anomalous behaviour of the first Row substituents is evident in Figure 3.9. All coupling constants for compounds with first Row substituents fall off the straight line defined by the points for the compounds with substituents in a particular Group. For instance, the value of ${}^{2}J_{C,H}$ for ethyl fluoride is larger, i.e., is less negative, than the value that would be predicted by the other halide derivatives. The monotonic increase of ${}^{2}J_{C,H}$ for the ethyl derivatives when the substituent is varied across a Row can be seen in Figure 3.10 where the value of ${}^{2}J_{C,H}$ for the ethyl derivatives is plotted against the Group to which the substituent belongs.

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The anomalous behaviour of the first Row substituents is not unique to the consideration of substituent effects on geminal coupling constants. A plot of single bond energies (I-X) for all the substituents in the first through fourth Rows and in Groups IVA through VIIA is shown in Figure 3.11. Here the first Row elements; carbon, nitrogen, oxygen and fluorine have sing Fe bond energies, that with the exception of the carbon-carbon bond, are much different from the energy which would be predicted by consideration of the single bond energies of the other elements in, their particular Group of the Periodic Table. Pauling (04) has attributed, the abnormal results for the

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Figure 3.9. Flot of the geminal carbon-proton coupling constants for the ethyl derivatives against the Row of the Periodic Table in which the substituent is found:

·CI

'S

Row

o Br

•Se

Ge

oTe

óF

152 [']

Figure 3.10. Plot of the geminal coupling constant for the ethyl derivatives against the Group to which the substituent belongs.

- 1

-2

-3

-4

-5

e. .

oPb

۰C,

∘ Sn • Ge

• Ši

·I'V

9,

J

1153

W

o Br

VII

.00

VI

۰_۲ ۱.

Group; .

o Se, Te



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Figure 3.11. The single bond energies for the elements in Group IV, Group V, Group VI, and Group VII (after Pauling).

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nitrogen, oxygen and fluorine single bond energies to the repulsion of the lone pairs of the bonded atoms and to electrons involved in other bonds (in the case of the nitrogen and oxygen atoms). We suggests that the heavier atoms do not exhibit similar effects because of the d and f character of the unshared electron pairs of these nuclei which leads to less over hap of the substituent bonding orbitals.

An analysis of the variation of ${}^{2}J_{C,H}$ with Swain--Lupton field factors (F) of the substituent, similar to -that carried out with substituent electronegativity, has been made. The best fit straight lines for the plots of ${}^{2}J_{C,H}$ for the ethyl compounds with derivatives in the first, second, third and fourth Rows of the Periodic Table against F are shown in equations (3.28) through

(3.31). (C, N, O, F) ${}^{2}J_{C,H} = 2.87 F - 4.16 r^{2} = 0.970.$ (3.28) (Si, S, Cl) ${}^{2}J_{C,H} = 2.58 F - 4.98 r^{2} = 0.948$ (3.29) (Ge, Se, Br) ${}^{2}J_{C,H} = 2.14 F - 4.06 r^{2} = 0.964$ (3.30) (Sn, I) ${}^{2}J_{C,H} = 1.88 F - 3.96$ (3.31)

Equation (3.31) is included so that the trends in the slopes of the plots $(\delta^2 J_{C,H}/\delta F)$ and the y-intercepts can be compared. Although the correlation coefficients for the plots of $^2 J_{G,H}$ against F for the ethyl derivatives with first, second, and third Row substituents improve considerably over the correlation for all compounds shown in Figure 3.7, there is nevertheless a small spread of

data points. As with the analogous plots of ²J_{C.H} against E_{N} , where the slope, $(\delta^2 J_{C,H} / \delta E_N)$, increased in going from the first to the second to the third to the 'fourth Row substituents, the slopes, $(\delta^2 J_{C,H}^2/\delta F)$, for the plots represented by equations (3.28) through (3.31) vary in a regular manner. However, the slope decreases in going. from the first to second to the third and to the fourth Row substituents. In contrast to the trend found for the plots of ${}^{2}J_{C,H}$ against; E_{W} where the absolute value of the intercept for the first Row substituents was smaller than the absolute value of the intercepts for the second, third and fourth row substituents which in turn were similar in magnitude, the y-intercept for the second Row substituents is smaller than that for the other three plots which are similar in magnitude.

Equation (3.32) gives the best fit straight line for the plot of the values of ${}^{2}J_{COOH,H}$ for the ethanoic acid derivatives against the Swain Lupton Field factor (F) of the substituents for the four, compounds with first Row substituents $\frac{1}{2}$

 $2j_{COOH,H} = 2.91$ F - 6.56 $r^2 = 0.479$ (3.32) The correlation coefficient for the plot of the derivatives with first Row substituents is much better than that for the general plot given by equation. (3.19).

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3.3.2.3. Variation of the Geminal Proton-Proton .Coupling Constant with Substituent Electronegativity and .Swain-Lupton Field Factors

As one might expect from the previous discussion, no simple relationship between the value of ${}^{2}J_{H_{0}H}$ for the methyl derivatives and substituent electronegativity is found in the plot shown in Figure 3.12. The best fit straight line has a correlation coefficient of 0.510 and no other simple relationship, for instance an exponential equation, appears to give a better fit for the data points. The spread of data points is similar to that found for the plots of ${}^{2}J_{C,H}$ for the ethyl and ethanoic acid derivatives against E_{N} shown in Figures 3.5 and 3.6.

However, the correlations between the values of ${}^{2}J_{\rm H,\dot{\rm H}}$ and ${}^{\rm E}_{\rm N}$ for compounds with substituents in a particular Row of the Periodic Table are good. The best fit straight lines for derivatives with substituents in the first through fourth Rows are given in equations (3.33) through (3.36).

 ${}^{2}J_{H,H} = 2.11 E_{N} - 18.11 r^{2} = 0.950$ (3.33) ${}^{2}J_{H,H} = 2.53 E_{N} - 18.61 r^{2} = 0.999$ (3.34) ${}^{2}J_{H,H} = 2.75 E_{N} - 17.75$ (3.35) ${}^{2}J_{H,H} = 3.96 E_{N} - 49.19$ (3.36)

The equations for the first and second row substituents are for four and three points respectively while the equations for the third and fourth row Figure 3.12. Plot of the geminal proton-proton coupling constants $({}^{2}J_{H,H})$ for the methyl derivatives listed in Table 3.4 against the NEM electronegativity of the substituents.



substituents are for two points only. Equations (3.35) and (3.36) are included so that the trends in the slopes, $(\delta^2 J_{H,H}/\delta E_N)$ and y-intercepts of the equations, as one goes from the first to the fourth row substituents, can be examined. As was found for the carbon-proton coupling constants, the slope increases monotonically from the first to the fourth row substituent plots (from 2.11 to 3.96) while the intercepts remain relatively constant (varying between 18.11 and 19.19) in going from the first to the fourth row substituents.

Equations (3.37) and (3.38) are the best fit straight lines for the plots of the values of ${}^{2}J_{H,H}$ for the methyl derivatives with substituents in Groups IV and VII, excluding the first Row substituents, against substituent electronegativity.

² J _H , Å		-8.98	E_{N}	11 1	2.38	$r^2 = 0.914$		(3.37)
2 _J	677 622	-2.02	ENT	 costi	4.40 -	$r^2 = 0.987$	•	(3.38)

The correlation coefficients indicate that the plots are reasonably linear. Group VI substituents were not included as values of the proton-proton coupling constant for the selenium and tellurium derivatives were not available. Using equations (3.37) and (3.38), values of ${}^{2}J_{\rm H,H}$ for the ethane and methyl fluoride molecules were calculated and compared to the measured coupling constants for these compounds. As was found for the geminal carbon-proton coupling constants for the ethyl derivatives, the absolute value of the calculated

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coupling constant for the compounds with first Row substituents was considerably higher than the measured value. The ratio of the measured to the calculated geminal proton-proton coupling constants was 0.62 for the carbon (Group IV) derivative and 0.76 for the fluoro (Group VII) derivative.

The geminal proton-proton coupling constants for twelve methyl derivatives are plotted against Swain-Lupton field factors (F) of the substituents in Figure 3.13. The correlation coefficient for the plot is poor $(r^2 = 0.69)$ and the best fit straight line, obtained by linear regression analysis is shown in equation (3.39).

 ${}^{2}J_{H,E} = 2.82 \text{ F} - 12.40 \text{ r}^{2} = 0.687$ (3.39) However, consideration of methyl compounds with substituents in a particular Row of the Periodic Table yields better correlations. Equation (3.40) and (3.41) are the best fit straight lines for the plots of the values of ${}^{2}J_{C,H}$ for the methyl derivatives with first and second Row substituents respectively against the Swain-Lupton field factors (F) of the substituents.

> ${}^{2}J_{H,H} = 3.82 F - 12.73 r^{2} = 0.912$ (3.40) ${}^{2}J_{H,H} = 3.50 F - 13.73 r^{2} = 0.908$ (3.41) ${}^{2}J_{H,H} = 2.86 F - 12.16$ (3.42)

Figuration (3.42) is for two points only (Br,Ge) and is dincluded so that the trends in the slopes $(\delta^2 J_{\rm H,H}/\delta f)$ and the y-intercepts of these equations can be compared. As was found for the plots of ${}^2 J_{\rm C,H}$ against F, the slope of



3.13. Geminal coupling constants $(^{2}J_{H,H})$ for the Figurę

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the plot of ${}^{2}J_{H,H}$ against F decreases in going from the first to the second Row substituents then decreases for the 'heavier' (Br and Ge) substituents. Furthermore, the absolute value of the y-intercept varies in a manner. similar to that found for the ${}^{2}J_{C,H}$ versus. F plots; it decreases from the first to the second row substituents.

The similarity of the general plots of the values of ${}^{2}J_{C,E}$ for the ethyl and ethanoic acid derivatives against $E_{\rm N}$ and F and the plots of the values of ${}^{2}J_{\rm H,E}$ for the methyl derivatives against $E_{\rm N}$ and F indicates that the effect of substituents on the observed coupling constants is much the same for both carbon-proton and proton-proton coupling constants. With these similarities in mind, geminal carbon-proton coupling constants for the ethyl and ethanoic acid derivatives are compared to the analogous geminal proton-proton coupling constants for the methyl derivatives in the next section.

3.4. CORRELATIONS BETWEEN GÉMINAL CARBON-PROTON AND PROTON-PROTON COUPLING CONSTANTS

3.4.1. General Plots of ${}^{2}J_{C,H}$ for the Ethyl and Ethanoic Acid Derivatives Against ${}^{2}J_{H,H}$ for the Mono-Substituted Methyl Derivatives

Figures 3.14 and 3.15 show plots of the geminal

carbon-proton coupling constants for the ethyl and ethanoic acid derivatives respectively against the analogous geminal proton-proton coupling constants taken from a series of monodeutero methyl derivatives. The best fit straight lines for Figures 3.14 and 3.15, calculated using linear regression analysis, are given in equations (3.43), and (3.44).

 ${}^{2}_{JC,H} = 0.70 \cdot {}^{2}_{JH,H} + 4 \cdot 46$ $r^{2} = 0.859$ (3.43) ${}^{2}_{JCOOH,H} = 0.62 \cdot {}^{2}_{JH,H} + 1.57$ $r^{23} = 0.851$ (3.44) The correlation coefficients for both plots indicate a considerable spread of data points.

Closer examination of Figures 3.14 and 3.15 reveals that, as was found for the plots of the geminal carbonproton and proton-proton coupling constants against substituent, electron egativity, some excellent correlations within these general plots can be found.

Consideration of the points for the pairs of compounds with first Row substituents (carbon, oxygen, nitrogen, and fluorine) in Figure 3.14 results in an improved correlation between the values of ${}^{2}J_{C,H}$ for the ethyl derivatives and the corresponding values of ${}^{2}J_{H,H}$, for the methyl derivatives. The best fit straight line. for the four points is given by equation (3.45).

 ${}^{2}J_{C,H} = 0.71 {}^{2}J_{H,H} + 4.91 r^{2} = 0.936$ (3.45) Although the correlation has improved from that found for the general plot shown in Figure 3.14, (r² = 0.936 versus $r^{2} = 0.859$), the point for the compounds with nitrogen

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substituents appears to fall above the other points on the plot. The value of ${}^{2}J_{\rm H,H}$ used for the nitrogen substituted compound was taken from methylacetamide (substituent NHCOCH₃) and not methylamine (substituent NH₂). This could have introduced an error into the plot as the geninal proton-proton coupling constant for methylacetamide may differ from that for methyl amine. Equation(3.46) gives the best fit straight line for the compounds with first Row derivatives excluding that for the nitrogen substituted derivative.

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 ${}^{2}J_{C,H} = 0.77 {}^{2}J_{H,H} + 5/46 r^{2} = 0.7999$ (3.46) The excellent correlation appears to indicate that the use of the geminal proton-proton coupling constant for the methylacetamide molecule may in fact introduce an inconsistency into the plot.

Equation (3.47) gives the best fit straight line for the plot of ${}^{2}J_{C,H}$ against ${}^{2}J_{H,H}$ for compounds with Group IV substituents (silicon, germanium, tin, and lead) excluding-carbon. A good correlation is found.

 ${}^{2}J_{C,H} = 0.37 \; {}^{2}J_{H,H} - 0.072 \; r^{2} = 0.984 \; (3.47)$ A similar treatment of compounds with Group VII substituents excluding fluorine does not give a good correlation. The best fit straight line is shown in equation (3.48).

 ${}^{2}J_{C,H} = 0.074 \; {}^{2}J_{H,H} - 2.00 \; r^{2} = 0.248^{\circ}$ (3.48) The closeness of the magnitude of the geminal carbon- $^{\circ}$ proton coupling constants for the ethyl halides and

geminal proton-proton coupling constants for the methyl halides results in an equation with is very sensitive to small differences in the coupling constants. Comparison of the values of ${}^{2}J_{C,W}$ and ${}^{2}J_{W,H}$ for the fluoro, chloro, bromo, and iodo derivatives of ethane and methane reveals that the magnitude of these couplings vary differently in . going faom the ethyl to methyl derivatives. The value of ²J_{C.H} for the ethyl halides increases in the graer Cl<I<Br<F from -2.85 to -2.74 to -2.65 to -1.86 Hz whereas the value of ${}^{2}J_{\mathrm{H},\mathrm{H}}$ for the methyl derivatives increases in the order, Cl<Br<F<I, from -10.70 to -10.10 to -9.50 to -9.36 Mz. The poor correlation reflects this change in relative order of magnitude of the geminal. carbon-proton and proton-proton coupling constants. The existence of a 'light atom effect' was suggested to explain the anomalous behaviour of the ethyl and ethanoic acid derivatives with first Row substituents when the geminal coupling constant was plotted against substituent electronegativity. Compounds with a first Row substituent fell off the line defined by the other compounds in a particular Group. In Figure 3.14, the heavier substituents, i.e., those in the third and fourth Rows of the Periodic Table, fall away from the line defined by the substituents in the first and second Rows of the Periodic Table. If the values of ${}^{2}J_{C,H}$ and ${}^{2}J_{H,H}$ for compounds with substituents in the first and second Rows of Periodic Table are plotted against each other,

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the best fit straight line is given by equation (3.49). ${}^{2}J_{C_{\rho}H} = 0.73 {}^{2}J_{H,H} + 5.14 r^{2} = 0.969$ (3.49)' Similar results are found when the values of ${}^{2}J_{COOH,H}$ for the ethanoic acid derivatives are plotted against the values of ${}^{2}J_{H,H}$ for the analogous methyl derivatives. Equation (3.50) gives the best fit straight line for the pairs of compounds with substituents in the first Row. ${}^{2}J_{COOH,H} = 1.15 {}^{2}J_{H,H} \div 7.57 r^{2} = 0.988$ (3.50) The correlation coefficient indicates a linear relationship between the geminal carbon-proton and proton-proton coupling constants exists for these compounds.

Equation (3.51) gives the best fit straight line for the plot of the values of ${}^{2}J_{COOH,H}$ against ${}^{2}J_{H,H}$ for the halogen derivatives of the monosubstituted ethanoic acids and the monosubstituted methanes respectively (no F).

 ${}^{2}J_{COOH,H} = 0.60 \; {}^{2}J_{H,H} + 1.28 \; r^{2} = 0.908$ (3551) The correlation of this plot has improved considerably over that for the analogous plot for the ethyl halides shown in equation (3.48). The magnitude of the geminal carbon-proton coupling constants for the halide derivatives of ethanoic acid increase in the same order as the geminal proton-proton coupling constants for the methyl halides, i.e., Cl<Br<Is This is in contrast to the trend observed for the ethyl derivatives. 3.5. The dependence of the Ratio of the Geminal Carbon-PROTON COUPLING CONSTANT TO THE GEMINAL PROTON-PROTON COUPLING CONSTANT $({}^{2}J_{C,E}/{}^{2}J_{E,E})$ on SUBSTITUENT EFFECTS

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Considerable effort has been made to find a 'simple ratio' between carbon-proton and proton-proton coupling constants. Although no 'single ratio' has been found, evidence suggests that the ratio of carbon-proton and proton-proton coupling constants is reasonably constant within series of structurally similar compounds. However, little work has been carried out on the effect of the variation of substituents on the observed ratio of ${}^{2}_{JC,E}$ to ${}^{2}_{JE,E}$.

In the following section the ratio (R) of the geminal carbon-proton coupling constants $({}^{2}J_{C,H})$ for the series of ethyl and ethanoic acid derivatives to the geminal proton-proton coupling constants $({}^{2}_{J}J_{H,H})$ for the structurally similar methyl derivatives are plotted against substituent electronegativity $(E_{\rm N})$ and Swain Lupton field factors (F) and the variation of the ratio with substituent effects discussed.

3.5.1. • Ethyl Derivatives Variation of the Ratio $({}^{2}J_{C,H}/{}^{2}J_{H,H})$ with Substituent Electronegativity (E_{N}) and Swain Lupton Field Factors (F)

Figure 3.16 shows a plot of the Ratio of J_{C,H} to

 ${}^{2}J_{\rm H/H}$ for the ethyl, and methyl derivatives respectively, against substituent electronegativity (E_N). The best fit straight line, from a linear regression analysis, is given by equation 3.52.

- Ratio $({}^{2}J_{C,E}/{}^{2}J_{E,E}) = -0.078 E_{N} \div 0.51 r^{2} = 0.925$ (3.52)

The correlation is good and from the plot it can be seen that the Ratio decreases monotonically with increasing substituent electronegativity (E_N) , i.e., the ratio is the largest for the pair of compounds with the hydrogen substituents (0.387) and smallest when the substituent is fluorine (6.196). This variation in the Ratio indicates that the geminal carbon-proton coupling constants for the ethyl compounds are more sensitive to a change in substituent electronegativity than the corresponding geminal proton-proton coupling constant for the methyl compounds.

Although the correlation coefficient of the plot shown in Figure 3.16 is good, the correlation between the Ratio of ${}^{2}J_{C_{r}H}$ to ${}^{2}J_{H,H}$ and substituent electronegativity (\underline{E}_{N}) improves if pairs of compounds with substituents in a particular Row of the Periodic Table are considered. Best flt straight lines for compounds with substituents in the first, second, and third and fourth Rows of the Periodic Table are given by equations (3.53), (3.54), and (3.55) respectively.



172 Ratio $({}^{2}J_{C,H}/{}^{2}J_{H,H}) = -0.092$ $E_{N} + 0.56$ $\tilde{r}^{2} = 0.987$ (3.53) Ratio $({}^{2}J_{C,H}/{}^{2}J_{H,H}) = -0.081 E_{N} + 0.52 \cdot x^{2} = 0.991$ (3.54) Ratio $({}^{2}J_{C,H}/{}^{2}J_{H,H}) = -0.098 E_{N} \approx .54 r^{2} = 0.999$ (3 55) These excellent correlations suggest that the effect' of the electronegativity of a substituent in a particular Row is similar for both carbon-proton and proton-proton coupling constants (although the carbon-proton coupling constants increases in an algebraic sense more rapidly) that the effect of varying substituent and electronegativity on the ratio is best described by considering pairs of compounds with substituents in a particular Row of the Periodic Table as the slope $(\delta Ratio/\delta E_{\rm M})$ of the plots yaries from one Row to another. We have calculated values of ${}^{2}J_{C,H}$ for the ethyl compounds from the values of $^{2}J_{H,H}$ for the methyl) compounds and the substituent electronegativity by rearranging equation (3.52) to give equation (3.56). ${}^{2}J_{C,H} = {}^{2}J_{H,H} (-0.078 \cdot E_{N} \div 0.51)$ (3.56) The calculated values of ${}^{2}j_{C,E}$ and those measured experimentally are shown in Table 3.5, The root mean square (rms) error of the calculated values of 2JC, H was 0.18 Hz/for all compounds. A plot of the ratio of the values of ${}^{2}J_{C,E}$ and ${}^{2}J_{H,E}$ for the ethyl and methyl compounds respectively against

Table 3.6. Comparison of the values of ${}^{2}J_{C,H}$ for the ethyl derivatives against those calculated from equation (3.56), i.e., ${}^{2}J_{C,H} = {}^{2}J_{H,H}$ (-0.070 E_N + 0.51).

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۲	20	EN	₅ 2 ⁸ 'ė	² JC, H ^a	² JC, H	diff.
		· ·.	٥	calc.	expt.,	- -
	^C	: 2.53	-12:56	-3:93	-4,20	-0.27
	N •	`3。23 ·	-11.73	-3.03	·-3.03 ·	·0.00 ,
	0 [°]	·3 . 453 ·	-10.60 °	-12.49	-2.64 .	-0.15
0	Ţ.	4.00	- 9.50	-1 <i>.</i> 88·	-].86	0-02
•	Si	1.81	-14.05	-5.19	-5.22	-0.03 [°]
	S,	2.765	-11.87	-3.60	₹3.51	°0.09
	сi	3.14	-10.70	-2.84	-2.85	-0.01
	Sn "	1.63	-:-12.37 [°]	-4.74	-4.62	0.12
ø	Br	2.78	-10.10	~2.96 ·	-2,65	0.31
*	Ge	1.74	-12.96	-4.85	-4.76 .	0.09
	I	2.48	- 9.36 -	-2.96	. \$ 3.74 .	0.22
•	H.	1.94	-12.40	-4.45	-4.80	-0.35
•	a \\ -17	aanalina	annahanha d	a Darba	ς	

a) all coupling constants in Hertz.

the Swain Lupton field factors (F) of the substituents is The best fit straight line is shown in Figure 3.17. given by equation (3.57). Ratio $(^{2}J_{C,H}/^{2}J_{H,H}) = -0.12$ F + 0.34 $r_{2}^{2} = 0.754$ (3.57) It is obvious that no general corrélation for all points exists. _ However, plots of the ratios of the coupling constants for pairs of compounds with substituents in a particular Row of the Periodic Table against F-leads to much improved correlations. Equations (3.58), (3.59), and (3.60) give the best fix straight lines for the plots of the ratio of coupling constants of pairs of compounds with substituents in the first, "second, and third and fourth rows respectively against F. Ratio $({}^{2}J_{C,H}/{}^{2}J_{H,H}) = -0.16 F \pm 0.34 r^{2} = 0.937$ (3.58) Ratio $(^{2}J_{C,H}/^{2}J_{H,H}) = -0.11F + 0.36$ r² = 0.931 (3.59) $Ratio({}^{2}J_{C_{e}H}/{}^{2}J_{H_{e}H}) = -0.09 F + 0.34 r^{2} = 0.969 / (3.60)$ Unlike, the plots of the Ratio against substituent electronegativity (EN) where the slope ($\delta R/\delta E_N$) increases . from -0.092 to -0.081 and then decreases to -0.098 for

from -0.092 to -0.081 and then decreases to -0.098 for the first, second, and third and fourth Row substituents respectively, the slopes of the plots ($\delta R/\delta F$) given by equations (3.58), e(3.59), and (3.60) increase from -0.16 to -0.11 to -0.09. Furthermore, for compounds with substituents in the second, third, and fourth Rows, the Ratios (${}^{2}J_{C,H}/{}^{2}J_{C,H}$) fall above the line defined by compounds with first Row substituents. This is in contrast to the plot of the Ratio against substituent



electronegativity where all points of the plot fall below the best fit straight line described by the first Row substituents.

3.5.2. Ethanoic Acid Derivatives- Variation of the Ratio $({}^{2}J_{COOH,H}/{}^{2}J_{H,H})$ with Substituent Electronegativity and Swain-Lupton Field Factors

The Ratio $({}^{2}J_{COOH,H}/{}^{2}J_{H,H})$ of the geminal carbonproton coupling constants for the ethanolic acid derivatives to the geminal proton-proton coupling constants for the analogous methyl derivatives are plotted against substituent electronegativity (E_N) in Figure 3.18. Equation (3.61) gives the best fit straight line for the points of the plot.

 $(^{2}J_{COOH,H}/^{2}J_{H,H}) = -0.075 E_{N} + 0.70 r^{2} = 0.599$ (3.61)

The value of the substituent electronegativity for the phenyl, cyano, and carboxyl substituents (Ph, CN, COOH) was taken as that for the methyl group $(CH_3)_{\alpha}$ i.e., 2.53. If the points for these three substituents are not used the best fit straight line is given by equation (3.62).

 $(^{2}J_{COOH,H}/^{2}J_{H,H}) = -0.082 E_{N} + 0.71 r^{2} = 0.637$ (3.62) The correlation coefficient does not improve

significantly over that found for equation (3.61).

If the Ratio of the coupling constants for the pairs of compounds with first Row substituents are considered,

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177 Plot of the Ratio of 2JCOOH, H for the 3.18. Figure ethanoic acid derivatives to $^{2}J_{\mathrm{H},\mathrm{H}}$ for the methyl derivatives against substituent NEM electronegativity. 0. 60 0, 56 O чų ტ 0, 52 ; 1 °30 √' ් ით ·RATIO Q 40 Ö ۳ 1.50 3.50 4.00 2.00 2.50 ELECTRONEGATIVI 3.00 (NEM∮ ΤY

the best fit straight line is given by equation (3.63). $({}^{2}J_{COOH,H}/{}^{2}J_{H,H}) = -0.13 E_{N} + 0.90 r^{2} = 0.972$ (3.63) Lack of coupling data for ethanoic acid derivatives with substituents from the second, third, and fourth Rows of the Period Table precludes the calculation of best fit straight lines for these groups of compounds. However, the larger intercept for the plot of R versus E_{N} for the compounds with first Row substituents suggests that points for the second, third, and fourth Row substituents would fall below this line in a manner similar to that found for the ethyl derivatives.

The Ratios $({}^{2}J_{COOH,H}/{}^{2}J_{H,H})$ of the geminal carbonproton coupling constants of the ethanoic acid compounds to the geminal proton-proton coupling constants for the methyl compounds are plotted against the Swain Lupton field factors (F) are Figure 3.19. The best fit straight line for the plot is given by equation (3.64). The correlation coefficient indicates that there is a considerable spread of data points.

 $({}^{2}J_{COOH,H}/{}^{2}J_{H,H}) = -0.13 + 0.55 r^{2} = 0.431$ (3.64) If the first Row substituents are considered, the correlation for the four points (CH₃, NHAC, OH, F) improves somewhat. However the point for the acetamido compounds falls off the straight line defined by the other three substituents. The best fit straight line for these four points is given by equation (3.65).

 $^{\circ}(^{2}J_{COOH,H}/^{2}J_{H,H}) = -0.16 F. + 0.53 r^{2} = 0.477 - (3.65)$

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Although the correlation coefficient has improved, there is still a considerable spread of data points and no usable correlation between the Ratio and F for the compounds with first Row substituents is found. 3.6.1. The Effect of Substituents on Vicinal Carbon-Proton $({}^{3}J_{C,H})$ and Vicinal Proton-Proton $({}^{3}J_{H,H})$ Coupling Constants for Structurally Sinilar Cyclopropanes

In the preceding sections, the effect of the electronegativity and the Swain-Lupton field factors of substituents on geminal carbon-proton and proton-proton coupling constants were discussed.

A similar approach is taken in this section for the cyclopropane derivatives. However, it must be noted that there are several differences between this section and the preceding sections of the discussion. The couplinga constants interest with ٥f the 2,2 diphenylmethylcyclopropane and cyclopropane derivatives are vicinal coupling constants. Instead of NEM electronegativities, Huggins electronegativities (E_n) of the substituents are used. Furthermore, the cyclic nature of these compounds gives rise to two measurable coupling constants, ³J^c and ³J^t. These coupling constants are shown in Figure 2.9 in section 2.5.1. Because of the well defined conformations of the coupled nuclei and the substituent with respect to the coupling path, both the electronic and orientational effects of the substituent must be considered.

The compounds of interest, the relevant vicinal

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coupling constants, substituent electronegativities and Swain-Lupton field factors are shown in Table 3.7.

3.6.2. Variation of the Vicinal Carbon-Proton Coupling Constants $({}^{3}J_{C,H}^{c} \cdot and {}^{3}J_{C,H}^{t})$ for the 2,2diphenylmethylcyclopropanes with Substituent Electronegativity.

The plots of the values of ${}^{3}J_{C,H}^{C}$ and ${}^{3}J_{C,H}^{L}$ for the 2,2-diphenylmethylcyclopropane derivatives against substituent electronegativity ($E_{\rm H}$) are shown in Figures 3.20 and 3.21 respectively. The best fit straight lines, calculated by linear regression analysis, for the plots shown in Figures 3.20 and 3.21 are given by equations (3.66) and (3.67).

 $^{3}J_{C_{\rho H}}^{2} = -1.49 E_{H} + 8.90 t^{2} = 0.935$ (3.66) $^{3}J_{C_{\rho H}}^{2} = -1.40 E_{H} + 6.18 t^{2} = 0.966$ (3.67)

The correlation coefficients are quite good and appear to indicate a reasonably linear dependence of the values of ${}^{3}J_{C,H}$ for the 2,2-diphenylmethylcyclopropane derivatives on the Huggins electronegativity of the substituent.

The substituents include both I and I type substituents as doned by Maciel, McIver, Ostlund and Pople (126, 127, 128, 129), i.e., D, I, Br, Cl, F, OCH₃ and NH₂ are'I substituents while CO₂CH₃, CN, and NC are I substituents. For the I substituents the

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Table 3.7. Vicinal Carbon-Próton and Proton-Proton Coupling Constants for the 2,2-Diphenylmethylcyclopropane Derivatives and the Analogous Cyclopropane Dorivatives. The Ratio of the Carbon-Proton and Proton-Proton Coupling Constants, Substituent Electronegativities (36), and Swain-Lupton Field Factors (117) are also shown.

¥ ',	с _{јс,н}	c _{j_{H,H}}	^t JC,H	^t J _{H,H}	Rat <u>cis</u> ,	io <u>trans</u>	°Ej	Ğ ,
4	* * * *		0			13 <i>4</i>	•	•
D.	5.91 ·	8.97	3.27	5.58	0.659	0.586	-2.20 [•]	0.00
I	4.94	7.55	2.57	4.37	0.654 -	o،588 ي	2.65	<u>م</u> 65 و
Br	4.49	7.16	1.98	3.82	0 .627	0.518 ′	2.95	· 0.72
ĊĨ	4.29,	7.02 .	1.72	3.59	0.611	0.479	3.15	0.72
P	^{3.20}	5.89	0.30	2.39	0.543	0.335	3.90 ั้	0.74
OCH3	3.7Q.	6.19	1.40	2,94	0.598	, 0.476	3.50	0,54
·MH2	4.41	6.63	1,84	3.55 ,	.0.665	0.518	3.05	⁶ 0.38
ĊN	5.17	8.40	2.34 *	5.09	0.616	0.460	Ź.60°	0.90
co ₂ Me	4.60	8 ,04	2.60	4.59	0.572	0.566	2.60	0.61
NC '	4.20	LI P	` 1.73	7.0		1	3.05	•

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i)Huggins Electronegativities ii) all coupling constants in Hertz .





electronegativity was taken as that for the atom of the group attached directly to the cyclopropane ring. If the I* substituents are considered separately, the best fit straight lines for the plots of the values of ${}^{3}_{J}C_{,H}$ and ${}^{3}_{J}C_{,H}$ against $E_{\rm H}$ are given by equation (3.6%) and (3.69). ${}^{3}_{J}C_{,H} = -1.56 E_{\rm H} + 9.20 r^{2} = 0.987$ (3.68)

 ${}^{3}J_{C_{\rho}H}^{2} = -1.43 E_{H}^{2} + 6.32 r^{2} = 0.985$ (3:69)

Although the correlation coefficients improve slightly for equations (3.68) and (3.69) compared to those for equations (3.66) and (3.67), (0.987 and 0.985 versus 0.935 and 0.966), the general trends for the plots are the same and very little difference in the slopes or intercepts are seen. The values of ${}^{3}J_{C_{0}H}^{C}$ and ${}^{3}J_{C_{0}H}^{L}$, decrease as the electronegativity of the substituent increases and the y-intercept for the plot of the <u>cis</u> coupling constant against $E_{\rm H}$ is larger than that for the trans coupling constant against $E_{\rm H}$ (approximately 9 versus 6).

In the absence of substituent effects, the <u>cis</u> coupling constant would be expected to be larger than the <u>trans</u> coupling constant on the basis of the dihedral angle (Φ) between the coupled nuclei. A Karplus type dependence predicts that the vicinal coupling constant should be larger for the <u>cis</u> coupling constant (dihedral angle of 0°) than for the <u>trans</u> coupling constant (dihedral angle of about 144°).
The slopes $(\delta^3 J_{C_{H}H}/\delta E_{H})$ of the plots are similar for both cis and trans coupling constants (-1.49 versus -1.40 for equations (3.66) and (3.67); -1.56 and -1.43 for equations (3.68) and (3.69))ⁿ although the value of the slope is larger for the trans coupling constants than that for the cis coupling constant. Here larger denotes less negative. This behavior is somewhat anomalous as the substituent is expected to exert its maximum effect when it is eclipsed with the coupling path, i.e., the . dihedral angle is 0°, or when it is antiperiplanar to the coupling path, i.e., the dihedral angle is 180°. For the cis coupling constants the substituent subtends a dihedral angle of 144° with respect to the coupled' proton, whereas for the trans coupling constants the substituent subtends a dihedral angle of 0° with respect to the coupled proton. These results appear to contradict the general substituent orientational 'effects proposed by Booth (42), (see. section 1.3.3), where the substituent exerted its maximum effect when it was antiperiplanar to or eclipsed with one of the coupled protons.

3.6.3. Correlations of the Vicinal Carbon-Proton Coupling Constants for 2,2-diphenylmethylcyclopropanes with $E_{\rm H}$ for Selected Groups of Substituents.

The <u>cis</u> and <u>trans</u> vicinal carbon-proton coupling constants for the 2,2-diphenylmethylcyclopropane derivatives correlate quite well with substituent electronegativity. However, there is a slight scatter of data points. Equations (3.70), (3.71), and (3.72) are the best fit straight lines for the plots of the values of ${}^{3}J_{C,H}^{c}$ for; the six compounds with first Row substituents (CO₂CH₃, CN, NH₂, NC, OCH₃, F); the three compounds with I⁺ first Row substituents, (NH₂, OCH₃, F); and the four compounds with halide substituents (F, Cl, Br, I) against substituent electronegativity (E_H).

 ${}^{3}J_{C,H}^{2} = -1.30 E_{H} + 8.27 r^{2} = 0.923$ (3.70) ${}^{3}J_{C,H}^{2} = -1.43 E_{H} + 8.74 r^{2} = 0.996$ (3.71) ${}^{3}J_{C,H}^{2} = -1.38 E_{H} + 8.61 r^{2} = 0.998$ (3.72)

The correlation for compounds with first Row substituents improves considerably when the I⁻ substituents (CO₂CH₃, CN, NC) are omitted from the plot, i.e., $r^2 = 0.923$ for I⁺ and I⁻ for the Row substituents and $r^2 = 0.996^\circ$ for the I⁺ first Row substituents. Furthermore, the correlation for equation (3.71) improves over that for all I⁺ substituents (see equation (3.68)).

. 188∙ Similarly the correlation for the plot of the values of <u>cis</u> vicinal carbon-proton coupling constants for the compounds with halide substituents improves over that for ail I⁺ substituents given by equation (3.68), i.e., $r^2 = 0.987$.

Similar results are found for the plots of the values of ${}^{3}J_{C,H}^{4}$ against substituent electronegativity for the compounds with first Row substituents, the compounds with first Row I⁺ substituents, and the compounds with halogen substituents. The best fit straight lines for these plots are given by equations (3.73), (3.74), and (3.75).

		•			r	<i>a</i>	
. ³ Jt,	7 9 800	-1.25	È _H	+ 5.68	\therefore $r^2 = 0.9$	69	(3.73)
з _J t,н		-1.22	E _H	+ 5.59	$r^2 = 0.9$	85	(3.74)
3Jt .H	8	-1.37	E _H	+ 6.11	$r^2 = 0.9$	86	(3.7,5)

The correlation coefficient for equation (3.74), (I⁺ substituents), improves slightly over that for equation (3.73), (I⁺ and I⁻ substituents), but the correlation does not improve over that for all I⁺ substituents given by equation (3.69). The slopes $(\delta^3 J_{C,H}/\delta E_H)$ and y-intercepts vary from -1.22 to -1.43 and from 5.59 to 6.32° in going from equation (3.74) to (3.69).

Even though slight improvements in the correlations between 'the value of ${}^{3}J_{C,H}$ and substituent electronegativity (E_H) are possible by choosing compounds with substituents in a particular Row or Group of the Periodic Table, the relationships shown in equations (3.66) through (3.69) describe in a general sense the overall dependence of ${}^{3}J_{C,H}$ for the 2,2- dipheny methylcyclopropanes on substituent electronegativity.

3.6.4. Variation of the Vicinal Proton-Proton Coupling Constants (${}^{3}J_{H,H}^{c}$ and ${}^{3}J_{H,H}^{t}$) for the Cyclopropane Derivatives with Substituent Electronegativity.

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The plots of the values of ${}^{3}J_{H,H}^{c}$ and ${}^{3}J_{H,H}^{t}$ for the nine cyclopropanes listed in Table 3.7 against substituent electronegativity (E_H) are shown in Figures 3.22 and 3.23. The best fit straight lines for these plots are given by equations (3.76) and (3.77) respectively.

 ${}^{3}J_{H,H}^{C} = -1.88 E_{H} + 12.88 r^{2} = 0.905$ (3.76) ${}^{3}J_{H,H}^{t} = -1.91 E_{H} + 9.66 r^{2} = 0.949$ (3.77) The correlation coefficients are reasonably good but there is some spread of data points. If the I substituents, (CO₂CH₃ and GN), are omitted, the best fit straight lines for the seven points are given by equations (3.78) and (3.79).

 ${}^{3}J_{H,H}^{c} = -1.76 E_{H} + 12.45 r^{2} = 0.913$ (3.78) ${}^{3}J_{H,H}^{t} = -1.83 E_{H} + 9.35 r^{2} = 0.972$ (3.79) The correlation coefficients for equations (3.78) and (3.79) improve slightly over those for equations (3.76) and (3.77), (0.913 versus 0.905 and 0.972 versus

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0.949).

As was found for the carbon-proton vicinal coupling constants of the 2,2-diphenylmethylcyclopropane derivatives, the values of ${}^{3}J_{H,H}^{c}$ and ${}^{3}J_{H,H}^{t}$ for the cyclopropane derivatives decrease with increasing substituent electronegativity. The slopes for the <u>cis</u> and <u>trans</u> vicinal proton-proton coupling constants are quite similar (-1.88 versus -1.91 for equations (3.76) and (3.77)) whereas the y-intercept for the <u>cis</u> coupling constant is considerably larger than that for the <u>trans</u> coupling constant (12.88 versus, 9.66 for equations (3.76) and (3.77)).

In contrast to the 2,2-diphenylmethylcyclopropane derivatives, where the absolute value of the slope $(\delta^3 J_{C,H}/\delta E_H)$ for the <u>cis</u> coupling constants was larger than that for the <u>trans</u> coupling constants, the absolute value of the slope of the plot of the <u>cis</u> proton-proton coupling constants against E_H is smaller than that for the <u>trans</u> coupling constants, i.e., $\delta^3 J_{C,H}^2/\delta E_H = -1.49$ versus $\delta^3 J_{C,H}^2/\delta E_H^2 = -1.40$, and $\delta^3 J_{H,H}^2/\delta E_H^2 = -1.88$ versus $\delta^3 J_{H,H}^3/\delta E_H^2 = -1.91$. Reference was made to the effect of the orientation of the substituent on the magnitude of the observed carbon-proton coupling constant of the 2,2diphenylmethylcyclopropane derivatives in section. 3.4.2. The change in the relative effect of the substituent in going from these compounds to the cyclopropanes, where the absolute value of the slope for the <u>trans</u> coupling constants is larger than that for the <u>cis</u> coupling constants, may be the result of two factors. The change may be due to a difference in the effect of substitutent orientation or could result from a change in the dihedral angle between the substituent and the coupled nuclei. The steric requirements of the methyl group of the monosubstituted 2,2-diphenylmethylcyclopropanes as opposed to a proton for the analogous cyclopropanes derivatives may cause a change in the dihedral angle between the coupled nuclei and result in the variation of the effect.

3.6.5. Variation of the Vicinal Proton-Proton Coupling Constants $({}^{3}J_{H,H}^{C})$ and ${}^{3}J_{H,H}^{L}$) for the Cyclopropane Derivatives with E_H for Selected Groupings of Substituents.

The best fit straight lines for the plot of the values of ${}^{3}J_{H,H}^{C}$ against E_{H} for the five compounds with first Row substituents (CO₂CH₃, CM, NH₂, OCH₃, F), the three compounds with I^{*} first Row substituents (NH₂, OCH₃, F) and the four compounds with halogen substituents are given by equations (3.80), (3.81), and (3.82).

3jg,₩	, E	-1,.86	E _{II}	÷	12.86	- r ²	8	0.889		. (3	3.80)
3 _{ЈС,Н}	8	-0.87	Ea	40	9.28	r ²	6	0.994		(3	3.81)
³ је, н	8	-1.33	E	ಟ್ಟೆ	. `` 11.12	r ²		0.992		, (3	3.82)
The co	ori	relati	on	im	oroves	cons	ide	rably	in	going	from

the plot for all first Row substituents to the plot for the three first Row I⁺ substituents, i.e., r^2 increases from 0.889 to 0.994. The correlation for the halides derivatives is excellent. For both equations (3.81) and (3:82) the correlations between ${}^{3}J_{H,H}^{C}$ and E_{H} improve over those for the general plot (equation (3.76)) and the plot of all I⁺ substituents (equation (3.78)).

3.7.1. Variation of the Vicinal Carbon-Proton Coupling Constants $({}^{3}J_{C,E})$ with Swain-Lupton Field Factors (F)

The plots of the values of ${}^{3}J_{C,H}^{c}$ and ${}^{3}J_{C,H}^{c}$ for the 2,2-diphenylmethylcyclopropane derivatives against the Swain-Lupton field factors (F) of the substituents are shown in Figures 3.24 and 3.25. The best fit straight lines for these plots are given by equations (3.83) and (3.84).

 ${}^{3}J_{C,H}^{2} = -1.38 F + 5.33 r^{2} = 0.209$ (3.83) ${}^{3}J_{C,H}^{2} = -1.36 F + 2.85 r^{2} = 0.238$ (3.84)

It is obvious that there is no general correlation between either the <u>cis</u> or the <u>trans</u> vicinal carbonproton coupling constants and the Swain-Lupton field factors of the substituents for these derivatives.

If we look at groups of substituents, such as the first Row substituents (C, N, O, F) or the halides (F, Cl, Br, I), the correlations between the <u>cis</u> and <u>trans</u> vicinal carbon-proton coupling constants and F improve in



Figure 3.25. Plot of ${}^{3}J_{C,H}^{t}$ for the 2,2diphenylmethylcyclopropane derivatives against the Swain-Lupton field factors (F) of the substituents.

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some cases. Equations (3.85), (3.86), and (3.87) are the best fit straight lines for the plots of the values of ³JC H for the compounds with first Row I substituents $(N_{\sigma} O_{\sigma}^{*} F)_{\sigma}$ the five compounds with first Row substituents, and the halides derivatives respectively against Swain-Lupton field factors. ${}^{3}_{JC_{2H}} = -3.32 \text{ F} + 5.61 \text{ r}^{2} = 0.999$ (3.85) $({}^{3}J_{C_{eH}}^{2} = 0.87 F + 3.66 r^{2} = 0.050$ · (3:86) ${}^{3}J^{C}_{C_{\mu}H} = -15.03 F + 14.87 r^{2} = 0.640$ (3, 87)Similar results are found for the plots of the values of $3_{J_{C,H}^c}$ against F for the same groupings of compounds as were used in equations (3.85), (3.86), and (3.87). The best fit straight lines are given by equations (3.88), (3.89) and (3.90). ${}^{3}_{J} = -3.89 F + 2.94$ $r^{2} = 0.999$. (3.88) ${}^{3}J_{C_{\alpha}H}^{2} = 0.29 F + 1.61$ $r^{2} = 0.006$ (3.89) $^{3}J_{C_{2}H}^{t} = -16.16 F \div 13.20 r^{2} = 0.750$ (3,90) Only the plots for compounde with first Row I* substituents (NH2, OCH3, F) show good correlations

between the vicinal carbon-proton coupling constant and the Swain Lupton field factors. The poor correlation for the halides can be attributed towthe similarity of the F values for these substituents and the fact that the coupling constants decrease in the order I>Br>C1>F.

. 3.8.1. Plots of ³J_{C/H} versus ³J_{B/H}

Figures 3.26 and 3.27 show plots of the <u>cis</u> vicinal carbon-proton coupling constants against the <u>cis</u> vicinal proton-proton coupling constants and the <u>trans</u> vicinal carbon-proton coupling constants against the <u>trans</u> vicinal proton-proton couplings constants for the 2,2diphenylmethylcŷclopropane derivatives and the analogous cyclopropane derivatives. The best fit straight lines for these plots, derived from linear regression analyses, are given by equations (3.91) and (3.92) respectively. ${}^{3}_{J}E_{cH} = 0.73 \; {}^{3}_{H_{cH}} = 0.82 \; r^{2} = 0.889 \; (3.91)$ ${}^{3}_{J}E_{cH} = 0.69 \; {}^{3}_{H_{cH}} = 0.69 \; r^{2} = 0.916 \; (3.92)$

The correlations coefficients are quite good, but if the I⁻ substituents, i.e., CO_2CH_3 and CN_7 are omitted the correlations improve considerably, from 0.889 to 0.953 for the <u>cis</u> coupling constants and from 0.910 to 0.985 for the <u>trans</u> coupling constants. The best fit straight lines for the seven I⁺ substituents are given by equation (3.93) and (3.94).

 ${}^{3}J_{C_{\rho H}}^{C} = 0.83 {}^{3}J_{H_{\rho H}}^{C} - 1.46 {}_{r}^{2} = 0.953$ (3.93) ${}^{3}J_{C_{\rho H}}^{L} = 0.77 {}^{3}J_{H_{\rho H}}^{L} - 0.95 {}_{r}^{2} = 0.985$ (3.94)

Equations (3.93) and (3.94) have larger slopes $(\delta^3 J_{C,H}/\delta^3 J_{H,H})$, and more negative y-intercepts han do equations (3.91) and (3.92); the slope increases from 0.73 to 0.83 for the <u>cis</u> coupling constants and from 0.69 to 0.77 for the <u>trans</u> coupling constants and the y-

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coupling constants and from -0.68 to -0.95 for the trans coupling constants. None of the plots pass through the origin. Whether or not the I⁻ substituents are included, equations (3.91) and (3.92) and (3.93) and (3.94) exhibit similar trends, i.e., the slope of the plot of the <u>cis</u> coupling constants is larger than that for the <u>trans</u> coupling constants, whereas the y-intercepts are more hegative for the <u>cis</u> than the <u>trans</u> coupling constants.

3.8.2. Correlations within the General Plot of ${}^{3}J_{C,H}$ Against ${}^{3}J_{H,H}$

Equations (3.95) and (3.96) give the best fit straight lines for the plots of the values of ${}^{3}J_{C,H}^{2}$ against ${}^{3}J_{H,H}^{2}$ and the values of ${}^{3}J_{C,H}^{2}$ against ${}^{3}J_{H,H}^{2}$ for the 2,2-diphenylmethylcyclopropane and cyclopropane derivatives with halogen substituents (F, CI, Br, T).

 ${}^{3}J_{C,H}^{C} = 1.03 \; {}^{3}J_{H,H}^{C} - 2.91 \; r^{2} = 0.997 \; (3.95)$ ${}^{3}J_{C,H}^{t} = 0.88 \; {}^{3}J_{H,H}^{t} - 1.34 \; r^{2} = 0.990 \; (3.96).$ The correlation coefficients are excellent and indicate that a linear relationship between carbon-proton and proton-proton coupling constants for these compounds exists. As was found for the more general plots, the slope of the plot for the cis coupling constants is larger than that for the trans coupling constants. A similar treatment of the cis and trans coupling constants for the compounds with first Row substituents $(CO_2CH_3, CN, NH_2, OCH_3, F)$ yields the best fit straight lines given by equations (3.97) and (3.98).

 ${}^{3}J_{C,H}^{c} = 0.63 \; {}^{3}J_{H,H}^{c} - 0.24 \; r^{2} = 0.850 \; (3.97)$ ${}^{3}J_{C,H}^{t} = 0.61 \; {}^{3}J_{H,H}^{t} - 0.47 \; r^{2} = 0.894 \; (3.98)$ The correlations improve considerably if the I⁻ substituents (CO₂CH₃ and CN) are omitted. The best fit straight lines for the three compounds with I⁺ the first Row substituents (NH₂, OCH₃, F) are given by equations (3.99) and (3.100).

> ${}^{3}J_{C,H}^{c} = 1.63 \; {}^{3}J_{H,H}^{c} - 6.42 \; r^{2} \neq 0.999 \quad (3.99)$ ${}^{3}J_{C,H}^{t} = 0.89 \; {}^{3}J_{H,H}^{t} - 1.30 \; r^{2} = 0.986 \quad (3.100)$

3.9. DEPENDENCE OF THE RATIO $({}^{3}J_{C,H} / {}^{3}J_{H,H})$ on substituent effects

3.9.1. Variation of the Ratio $({}^{3}J_{C,H}/{}^{3}J_{H,H})$ with Substituent Electronegativity (E_H)

Inspection of the ratios of the values of ${}^{3}J_{C,H}$, both <u>cis</u> and <u>trans</u>, for the 2,2-diphenylmethylcyclopropanes to the values of ${}^{3}J_{H,H}$ for the analogous cyclopropane derivatives shown in Table 3.7 indicates that no single ratio between carbon-proton and proton-proton coupling constants for these series of compounds exists. The ratios of both the <u>cis</u> and <u>trans</u> coupling constants vary as the substituent is changed. Figures 3.28 and 3.29 show plots of the Ratio (R) $({}^{3}J_{C,H}/{}^{3}J_{H,H})$ for the <u>cis</u> and <u>trans</u> coupling constants against substituent electronegativity (E_H). The best fit straight lines are given by equations (3.101) and (3.102).

 $R = {}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2} = -0.050 E_{H} + 0.76 r^{2} = 0.382 (3.101)$ $R = {}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2} = -0.13 E_{H} \neq 0.88 r^{2} = 0.692 (3.102)$

The correlation coefficients are poor for both plots but it is interesting to note that the Ratios for both the <u>cis</u> and <u>trans</u> coupling constants show a similar dependence on E_H , i.e., the Ratio decreases as the electronegativity of the substituent increases.

Much better correlations between the Ratios of ${}^{3}J_{C,H}$ and ${}^{3}J_{H,H}$ and substituent electronegativity (E_H) are found if pairs of compounds with substituents from the First Row or from Group VII of the Periodic Table are considered separately. Equations (3.103) and (3.104) give the best fit lines for the plots of the Ratios of the <u>cis</u> and <u>trans</u> coupling constants for the compounds with I⁺ first Row substituents (NH₂, OCH₃, F) against E_H. R = ${}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2} = -0.15 E_{H} + 1.11 r^{2} = 0.999$ (3.103) $\dot{R} = {}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2} = -0.20 E_{H} + 1.18 r^{2} = 0.891$ (3.104).

If the I⁻ substituents are included the correlations are much poorer. For the Ratio of <u>cis</u> coupling constants⁻ the correlation coefficient decreases from 0.999 to 0.185, while for the Ratio of the <u>trans</u> coupling constants the correlation coefficient decreases from 0.891 to 0.592.





The best fit straight lines for the plots of the Ratios of the <u>cis</u> carbon-proton to the <u>cis</u> proton-proton coupling constants and the Ratio of the <u>trans</u> carbonproton to the <u>trans</u> proton-proton coupling constants of the halide derivatives against substituent electronegativity ($E_{\rm H}$) are given by equations (3.105) and (3.106).

 $R = {}^{3}J_{C_{\mu}H}^{2}/{}^{3}J_{H_{\mu}H}^{3} = -0.091 E_{H} + 0.90 r^{2} = 0.999 \quad (3.105)$ $R = {}^{3}J_{C_{\mu}H}^{2}/{}^{3}J_{H_{\mu}H}^{4} = -0.20 E_{H} + 1.12 r^{2} = 0.999 \quad (3.106)$

The correlation coefficients are excellent for both equations and indicate a linear relationship between the ratio of the carbon-proton and proton-proton coupling constants for the halide derivatives of the 2,2diphenylmethylcyclopropanes and analogous cyclopropanes.

3.9.2. Variation of the Ratio $({}^{3}J_{C,H}/{}^{3}J_{H,H})$ With the Swain-Lupton Field Factor (F)

The plots of the Ratios (R) $({}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2})$ and $({}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2})$ against the Swain-Lupton field factors (F) of the substituents are shown in Figures 3.30 and 3.31. The best fit straight lines for these plots, calculated by a linear regression analysis, are given by equations (3.107) and (3.108) R = $({}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2}) = -0.08$ F +0.66 r² = 0.252 (3.107) R = $({}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2}) = -0.15$ F + 0.59 r² = 0.253 (3.108) \sim It is obvious from the poor correlation coefficients





for equations (3.107) and (3.108) that neither the <u>cis</u> nor <u>trans</u> Ratios correlate well with F.

However if only first Row I⁺ substituents are considered, the correlations for the plots of the <u>cis</u> and <u>trans</u> Ratios against F improve considerably. The best fit straight lines are given by equations (3.109) and (3.110).

 $R = ({}^{3}J_{C_{r}H}^{2}/{}^{3}J_{H_{r}H}^{2}) = -0.34 F + 0.79 r^{2} = 0.987$ (3.109) $R = ({}^{3}J_{C_{r}H}^{2}/{}^{3}J_{H_{r}H}^{2}) = -0.53 F + 0.74 r^{2} = 0.941$ (3.110) Inclusion of all first Row substituents, i.e., the I⁺ substituents, CN and CO₂CH₃, gives correlation coefficients that are much worse than those for the I⁺ substituents alone. For the <u>cis</u> Ratios the correlation coefficient decreases from 0.987 to 0.226 while for the <u>trans</u>. Ratios the correlation coefficient decreases from 0.941 to 0.218.

The best fit straight lines for the plots of the <u>cis</u> and <u>trans</u> Ratios for the halide derivatives against F are given by equation (3.111) and (3.112).

 $R = ({}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2}) = -0.98 F + 1.30 r^{2} = 0.631$ (3.111) $R = ({}^{3}J_{C,H}^{2}/{}^{3}J_{H,H}^{2}) = -2.27 F' + 2.068 r^{2} = 0.678$ (3.112) The correlation coefficients for both plots are poor and indicate that no correlation between the ratio of the carbon-proton and proton-proton coupling constants for the 2,2-diphenylmethylcyclopropyl halides and the cyclopropyl halides and the Swain-Lupton field factor of the substituents exists.

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3.10. THE 1-(1-deutero-4-t-butylcyclohezyl)methanol DERIVATIVES ,

3.10.1. The Vicinal Carbon-Proton Coupling Constants

As was noted in section 2.6.1., there are four distinct vicinal carbon-proton coupling constants for any pair of <u>cis</u> and <u>trans</u> isomers of a 1-(1-deutero-tbutylcyclohexyl) methanol derivative. The <u>cis</u> isomer, i.e., the isomer with the CH₂X group axial, gives rise to a <u>trans</u> (axial-axial) vicinal coupling constant, $({}^{t}J_{C_{r}H})$ and a <u>gauche</u> (CH₂X axial-H equatorial) vicinal coupling constant $({}^{g}J_{C_{r}H}^{HC})$, whereas the <u>trans</u> isomer, <u>i.e.</u>, the isomer with the CH₂X equatorial, gives rise to two <u>gauche</u> $(CH_{2}X$ equatorial, gives rise to two <u>gauche</u> $(CH_{2}X$ equatorial-H equatorial and CH₂X equatorial-H axial) vicinal coupling constants, ${}^{g}J_{C_{r}H}^{CC}$ and ${}^{g}J_{C_{r}H}^{CD}$.

The two vicinal coupling constants for the <u>cis</u> isomer, ${}^{t}J_{C,H}$ and ${}^{g}J_{C,H}^{HC}$, were measureable and are listed in Table 3.8. However, the two <u>gauche</u> coupling constants for the <u>trans</u> isomer, ${}^{g}J_{C,H}^{CC}$ and ${}^{g}J_{C,H}^{CD}$, could not be measured as the individual line positions of the coupled 'CH₂X carbon atom were not resolved. Both 20 megahertz and 100 megahertz spectra were run, but neither yielded spectra which allowed resolution of the triplet of triplets pattern resulting from the two coupling ^o constants. Instead line widths of CH₂X proton undecoupled carbon as listed in Table 3.8. \mathcal{D}

Table 3.8. The vicinal carbon-proton coupling constants, ${}^{t}J_{C_{\ell}H}$ and ${}^{g}J_{C_{\ell}H^{\ell}}^{H\ell}$ for the <u>cis-l-(l-deutero-4-t-butylcyclohexyl)</u>methane derivatives. The line widths (L.W.) of the proton undecoupled $CH_{2}K$ carbons for the <u>trans-l-(l-deutero-4-t-butylcyclohexyl)</u>methane derivatives are also listed.

•	3, ř	من ² +		٤.	
Substituent	E _H i	tjc,H	g _{jec} C, H (H2)	. LW.	
3 0	,	<u>c i</u> .	<u>s.</u>	trans	•
OH ·	3。50	8.60	3.10	7.27	
CL	· 3.15	10.50	3.60	7.60	
Br	2.95	10.62	3.90	7.80	
A.	2.65	10.99	4.00	8.03	
	• •	11-11-11 (20)		a Da	

i) Huggins electronegativity (36)

The inability to resolve the individual resonances of the fully coupled CH₂X carbon is not a digital resolution problem as both the 20 megahertz and 100 megahertz carbon spectrometers had digital resolutions of 0.125 Hz (20 megahertz, 8K data points sweep width 500 Hz) or less. The broadening of the line may be due to the twobond carbon-deuterium coupling constant, and the long range carbon-proton coupling constant (⁴J) possible for the <u>trans</u> isomer. The equatorial carbon and the equatorial protons four bonds removed are in a W configuration. Measurable carbon-proton coupling constants between nuclei through.four bonds have been observed (<u>vide infra</u>).

3.11.1. Variation of the Value of ${}^{t}J_{C,H}$ and ${}^{g}J_{C,H}^{HC}$ for the cis-1-(1-deutero-4-t-butylcyclohexyl)methanol Derivatives with Substituent Electronegativity (E_H)

Figures 3.32 and 3.33 shows plots of the values of the trans and gauche vicinal carbon-proton coupling constants for the cis-l-(l-deutero-4-tbutylcyclohexyl)methanol derivatives respectively against the Huggins electronegativity of the substituent $(E_{\rm H})$. The best fit straight lines for the plots shown in Figures 3.32 and 3.33 are given by equations (3.113) and (3.114).

 $t_{\rm J_{C,H}} = -2.68 \, {\rm S}_{\rm H} + 18.91 \, {\rm s}_{\rm r}^2 = 0.329 \, (3.113)$



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The correlations are not excellent, but the vicinal coupling constants, both trans and gauche, decrease with an increase in substituent electronegativity. The yintercept for the trans coupling is considerably larger than that for the gauche coupling, as one might predict from consideration of the dihedral angle between the coupled nuclei. However, the absolute value of the slope of equation (3.113); <u>i.e.</u>, $\delta^{t}J_{CH}/\delta E_{H}$ is larger than that for equation (3.114), $\delta^{g}J_{C,H}^{CH}/\delta E_{H}$.

In section 1.5.2., the effect of a substituent on the vicinal carbon-proton in a series of neopentyl derivatives (54) was discussed. As with the $l_{\tau}(1-\text{deutero-4-}$ t-butylcyclohexyl)methanol derivatives we are discussing here, the substituent was attached to the coupled carbon. The best fit straight line for the plot of the values of ${}^{3}J_{C,H}$ against substituent electronegativity for the iodo, bromo, chloro and hydroxy derivatives shown in Figure 3.34 is given by equation (3.115).

 ${}^{3}J_{C,H} = -1.77 E_{H} + 10.90$ $r^{2} = 0.846$ (3.115). The correlation is not excellent but the correlation coefficient is similar to those for the plots for ${}^{t}J_{C,H}$ and ${}^{g}J_{C,H}^{CH}$ against E_{H} .

Considering equations (3.113), (3.114), and (3.115), it appears the effect of a substituent that is directly attached to the coupled carbon, on vicinal carbon-proton coupling constants, is to cause a decrease in the



magnitude of ${}^{3}J_{C,H}$ as the electronegativity of the substituent increases. However, in a study of substituent effects on ${}^{3}J_{C,H}$ for a series of <u>n</u>-propyl derivatives where the first Row substituents (CH₃, NH₂, OH, F) were attached to the coupled carbon. Spoormaker and de Bie (55) have found that ${}^{3}J_{C,H}$ increases with increasing substituent electronegativity. The best fit straight line for the four derivatives is given by equation (3.116).

 ${}^{3}J_{C,H} = 0.83 \text{ E} + 3.10 \text{ r}^{2} = 0.991$ (3.116) The slope, $(\delta^{3}J_{C,H}/\delta \text{E})$, is positive unlike that for the halogen (C1, Br, I) and hydroxy substituents from equations (3.113), (3.114), and (3.115) where the slope is negative.

3.11.2. Variation of the linewidth of the CH_2X resonance of the <u>trans</u>-1-(1-deutero-4-<u>t</u>-butylcyclohexyl) methanol derivatives with substituent electronegativity.

The two vicinal carbon-proton coupling constants for the <u>trans</u>-1-(1-deutero-4-<u>t</u>-butylcyclohexyl)methanol derivatives, ${}^{g}J_{C,H}^{CC}$ and ${}^{g}J_{C,H}^{CD}$, could not be resolved. The proton undecoupled carbon spectra were run on both 20 and 100 Megahertz 13 C NMR spectrometers and neither gave a splitting pattern with sufficient resolution of peaks to afford measurement of the vicinal carbon-proton coupling constants. However, as the line widths of the proton - undecoupled carbon (CH₂X) resonances are related to the two <u>gauche</u> vicinal coupling constants, these were measured at one half height and are plotted against the electronegativity ($E_{\rm H}$) of the substituent in Figure 3.35. The best fit straight is given by equation (3.117).

L.W. = $10.44 - 0.90 E_{\rm H}$ $r^2 = 0.997$ (3.117) The correlation is excellent and as was found for the coupling constants for the <u>cis</u> compounds, the line width decreases as the substituent electronegativity increases.

3.12. The 1-methyl-4-phenyl-3,3',5,5'-tetradeuterocyclohexanols

The four carbon-proton coupling constants for the cis and trans 1-methyl-4-phenyl-3,3'5,5'-tetradeuterocyclohexanols and the analogous proton-proton coupling constants for the octadeuterocyclohexanols (130) are shown below.

coupled nuclei'

	C,H	. н,н	Ratio
tj	5.60 hz	11 . 11, °	. 0.51
g JHC	3.25	4.31	0.80 ⁰
g ¹ cc	2.20	3.29	<i>, ,</i> 0.67
. g _J CO	1.47	2.48	0.59

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The variation of the Ratio of the carbon-proton to proton-proton coupling constants can be attributed to

Figure 3.35. Plot of the line widths of the CH_2X resonances of the trans isomers against $E_{H^{\circ}}$



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three factors; the orientation of the coupled nuclei; the orientation of the substituent (OH) with respect to the coupling path; and the atoms antiperiplanar to the coupled nuclei.

The Ratio is 'smallest for the trans coupling constants, $t_{J_{\ell}}$ where the dihedral angle between the coupled nuclei is 180 degrees. The variation of the Ratios for the three gauche coupling constants, gJHC, g_{J}^{CC} and g_{J}^{CX} , is unlikely to be due to the dihedral angle between the coupled nuclei as the dihedral angle is approximately 60 degrees for all three couplings. The smallest ratio for the three gauche coupling constants is 0.59. The substituent (OH) is antiperiplanar to the coupling path for these coupling constants. For the gyCC and ^gJ^{HC} coupling constants, the Ratio increases from 0.67 to 0.80. Forrest (45) has developed an equation for predicting gauche proton-proton coupling constants which indicates that the magnitude of the coupling constant is dependent upon to the electronegativity of the atoms trans to the coupled nuclei. Such a dependence and the fact that the carbon-proton coupling constant is more sensitive to substituent electronegativity effects than the analogous proton-proton coupling constant would explain the increase in the Ratio from 0.59 to 0.67 to 0.80 for the g_{J}^{CX} , g_{J}^{CC} and g_{J}^{HC} doupling constants. A correlation of the ratio with electronegativity gives the following relationship.

Ratio = 0.77 – 0.15 E $r^2 = 0.88$ (3.118) It would appear that the vicinal carbon-proton. coupling constants in six-membered rings are affected by, the same parameters as vicinal proton-proton coupling constants. However, the carbon-proton coupling constant is more sensitive to substituent effects (electronegativity) that the analogous proton-proton coupling constants and the variation of the Ratio of these coupling constants reflects this fact.
CHAPTER FOUR

SUMMARY AND CONCLUSION

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4.1. Correlations of Carbon-Proton Coupling Constants with Substituent Electronegativity and Swain-Lupton Field Factors

The only series of compounds that gave a good correlation with Swain-Lupton field factors was that of the ethyl derivatives. The correlation with ${}^{1}J_{C,H}$ is shown in equation (4.1).

 $^{1}J_{CH}$, H = 126.13 + 35.54 F r^{2} = 0.920 (4.1) Swain-Lupton field factors did not give good correlations for other series of compounds even within restricted groups of substituents which were found to give good correlations with electronegativity values.

The best correlations were found with electronegativity values within Rows or Groups of the Periodic Table. A summary of the correlations within Rows and Groups is shown below by the equations (4.2) to (4.23).

 $J_{CN_{\gamma'}H}$ for the ethyl derivatives: $r^2 = 0.389$ all points J = 11.06 (1 + 0.089 E)(4.2 $J_{c} = 91.33 (1 + 0.181 E) r^{2} = 0.922$ (4.3) first Row $r^2 = 0.999$ second Row $\mathcal{J} \stackrel{!}{=} 73.03 (1 + 0.335 E)$ (4.4)third Row J = 84.71 (1 + 0.278, F) $r^2 = 0.997^{\circ}$ (4.5) $r^2 = 0.983$ fourth Row J =85.31 (1 + 0.303 E)(4.6)

 ${}^{2}J_{CH_{3},H}$ for the ethyl derivatives: all points $J = -6.71^{(1 - 0.185 E)}$ $r^{2} = 0.739$ (4.7)

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· · · · ·			o ar
first Row J = -8.19 (1 - 0.194)	E) $r^2 = 0.999$	(4.8)	, , , ,
second Row J = -8.44 (1 ~ 0.214	E) $r^2 = 0.990$	(4.9)	
third Row J'= -8.30 (1 - 0.248)	E) $r^2 = 0$,987	(4.10)	
fourth Row $J = -8.25 (1 - 0.273)$	E) $r^2 = 0.991$	(4.11)	< [*] (Γ , ∦s
² J _{COOH,A} for the ethanoic acid d	erivatives:	r N	ر م ر
all points $J = -11.00 (1 - 0.166)$	E) $r^2 = 0.467$	(4,12)	r
first Row $J = -13.31 (1 - 0.850)$	E) $r^2 = 0.973$	(4.13)°	۰ ۲
³ J ^C _{EH} for the diphenylmethylcy	clopropanes:	,	
(all cis)] = 8,90 (1 - 0.167 E)	$r_{1}^{2} = 0.935$	(4:14)	₹ ⁴
$\int_{-\infty}^{\infty} \frac{1}{1} \frac$) $r^{2} = 0.987$	(4.15)	
• first Row I $= 8.74 (1 - 0.169)$	E) $r^2 = 0.996$	(4.16)	· · · · ·
halides J = 8.61 (l - 0.160 E)	$r^2 = 0.998$	(4.17)	r +
· · · · · · · · · · · · · · · · · · ·		٩	+
JCH3,H for the diphenylmethyle	yclopropanes:	1	* ¢
• • all points $J = 6.18$ (1 = 0.227 E)) r ² = 0.966	(4.18)	,
1" <u>trans</u> J = 6.32 (1 - 0.226 E)) r ² = 0.985	(4.19)	
. first Row I J = 5.59 (1 - 0.218)	E) r ² = 0.985	(4.20)	° '
halides `J = 6.11 (1 - 0.224 E)) $r^{2} = 0.986$	(4.21)	
J _{CH X,H} for the <u>cis</u> -l-l-deutero	-4-t-butylcyclol	` nexyl)-`	5 1
methane derivatives:	• •	~	*
a, a $J = 18.91 (1 - 0.142 E)$	$r^2 = 0.829$	(4.22)	
a,e $J = 7.09 (1 - 0.156 \cdot E)$	$r^2 = 0.932$	(4.23)	. ~
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Several interesting trends emerge from these correlations. Increasing electronegativity decréases all coupling constants except for the one bond couplings. The general correlation of the one bond coupling constants with electronegativity is very poor (r^2 = 0.389), although correlations within Rows are very good. Another factor is clearly involved in influencing the value of these one bond couplings. This can easily be seen in the values for the ethyl halides, which in spite of the wide difference in substituent electronegativity have almost identical coupling constants. It'is interesting to note that the one bond coupling constants. provide the only series that correlates well with Swain-Lupton field factors.

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The general correlations for substituents in each series is not good, but it gets progressively better as the coupling path length increases, $(r^2 \text{ for }^1 \text{J} \cdot \text{of } \text{Q} \cdot 38,$ for $^2 \text{J}$ of 0.467 and 0.739, and for $^3 \text{J}$ of 0.935 and 0.966). In all cases the correlations improve very significantly when groups of substituents from the same Row of the Periodic Table are considered separately. A comparison of the effect of increasing electronegativity on $^2 \text{J}_{\text{C},\text{H}}$ in the ethyl derivatives shows that the coupling constant is more sensitive to electronegativity as one goes down the Periodic Table (c.f. equations 4.8- 4.11).

The effect of the orientation of the substituent

relative to the coupling pathway can be seen in values of ${}^{3}J_{C,H}$ of the cyclopropyl derivatives. The values of the trans coupling constants, where the substituent is eclipsing the coupled proton, are more sensitive to substituent electronegativity than are the values of the <u>cis</u> coupling constants, where the substituent subtends an angle of about 144° to the coupled proton (c.f. equations 4.14 to 4.17 and 4.18 to 4.21).

Comparison of equations 4.8 and 4.13 indicates that the effect of substituent electronegativity on sp^3 and sp^2 hybridized carbons, is the similar, with a slightly higher factor for the sp^3 hybridized carbon.

Although a number of useful correlations between carbon-proton coupling constants and substituent electronegativity have been found, these correlations are sensitive to other factors such as the length of the coupling pathway, the Row of the Periodic Table to which the substituent belongs, the orientation of the coupled nuclei, substituent orientation with respect to the coupling path, and the hybridization of the coupled carbon.

4.2 Correlations of Carbon-Proton and Proton-Proton Coupling Constants

The correlations for the geminal and vicinal coupling constants are summarized below.

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Ethyl derivatives:

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first Row
$${}^{2}J_{C,H} = 0.71 \; {}^{2}J_{H,H} + 4.91 \; r^{2} = 0.936 \; (4.24)$$

first Row, $-N \; {}^{2}J_{C,H} = 0.77 \; {}^{2}J_{H,H} + 5.46 \; r^{2} = 0.999$
(4.25)
second Row ${}^{2}J_{C,H} = 0.72 \; {}^{2}J_{E,H} + 4.90 \; r^{2} = 0.994 \; (4.26)$
Ethanoic acid.derivatives:
allpoints ${}^{2}J_{COOH,H} = 0.62 \; {}^{2}J_{H,H} + 1.57 \; r^{2} = 0.851 \; (4.27)$
first Row ${}^{2}J_{COOH,H} = 0.62 \; {}^{2}J_{H,H} + 7.57 \; r^{2} = 0.988 \; (4.28)$
Diphenylmethylcyclopropane derivatives:
all points ${}^{3}J_{C,H}^{c} = 0.73 \; {}^{3}J_{H,H}^{c} - 0.82 \; r^{2} = 0.689 \; (4.27)$
I + ${}^{3}J_{C,H}^{c} = 0.83 \; {}^{3}J_{H,H}^{c} - 1.46 \; r^{2} = 0.9953 \; (4.30)$
I + first Row ${}^{3}J_{C,H}^{c} = 1.63 \; {}^{3}J_{H,H}^{c} - 2.91 \; r^{2} = 0.999 \; (4.31)$
halides ${}^{3}J_{C,H}^{c} = 1.03 \; {}^{3}J_{H,H}^{c} - 2.91 \; r^{2} = 0.997 \; (4.32)$
all points ${}^{3}J_{C,H}^{c} = 0.69 \; {}^{3}J_{H,H}^{c} - 0.69 \; r^{2} = 0.985 \; (4.33)$
I + ${}^{3}J_{C,H}^{c} = 0.89 \; {}^{3}J_{H,H}^{c} - 1.30 \; r^{2} = 0.986 \; (4.34)$
I + first Row ${}^{3}J_{C,H}^{c} = 0.89 \; {}^{3}J_{H,H}^{c} - 1.30 \; r^{2} = 0.986 \; (4.35)$
halides ${}^{3}J_{C,H}^{c} = 0.88 \; {}^{3}J_{H,H}^{c} - 1.34 \; r^{2} = 0.990 \; (4.36)$

As was found for the plots of ${}^{2}J$ against E, the usefullness of the correlations of ${}^{2}J$ and ${}^{2}J$ are generally restricted to limited sets of data points. If values of ${}^{2}J_{C,H}$ are to be predicted using values of ${}^{2}J_{H,H}$ for structurally similar compounds, the Row to which the subsrituent belongs should be taken into account. The hature of the substituent and the orientation of the coupled nuclei must also be considered when predicting ${}^{3}J_{C,H}$ from ${}^{3}J_{H,H}$ for cyclopropanes.

4.3 Ratio of Carbon-Proton to Proton-Proton Coupling Constants

For the purpose of predicting carbon-proton coupling constants from proton-proton coupling constants in similar situations it would be most convenient if a single factor could be used to convert $J_{H,H}$ to $J_{C,H}$. The desirability of this convenience has proven tempting and has lead to such a factor being promoted for use in spite of the fact that such a factor is guite inapplicable.

Quite clearly it is useful to have such a ratio, but as the ratio is dependent on several factors no single ratio is valid.

The results of this investigation show that ratios for particular situations can be useful if substituent effects are taken into consideration. A summary of equations for determining such ratios is given below:

÷ .

²J_{CH2},H ^{*} all points $R = 0.51 (1 - 0.153 E) r^2 = 0.925 (4.37)$ first Row R = 0.56 (1 - 0.164 E) $r^{2_0} = 0.987$ (4.38) second Row R = 0.52 (1 - 0.156 E) $r^2 = 0.991$ (4.39) $R = 0.53 (1 - 0.185 E) r^2 = 0.999$ third, fourth Rows (4.40)²J_{COOH,H} : all points R = 0.71 (1 - 0.115 E). $r^2 = 0.637 (4.41)$ first Row R = 0.90 (1 - 0.144 E) $r^2 = 0.972 (4.42)$ ³J_{CH2,H} <u>cis</u> in cyclop⁹opanes all points $\vec{R} = 0.76 (1 - 0.066 E) r^2 = 0.382 (4.43)$ first Row $I^+ R = 1.11 (1 - 0.135 E) r^2 = 0.999$ (4.44) $R = 0.88 (1 - 0.103 E) r^2 = 0.999$ halides (4.45)³J_{CH2},H trans in cyclopropanes:

all goints R = 0.88 (1 - 0.148 E) $r^2 = 0.691$ (4.46) first Row I⁺ R = 1.18 (1 - 0.178E) $r^2 = 0.891$ (4.47) halides R = 1.11 (1 - 0.182 E) $r^2 = 0.998$ (4.48)

 ${}^{3}J_{CH_{2}X,H}$ a,a in cyclohexanes: all points R = 1.45 (1 - 0.147 E) $r^{2} = 0.832$ (4.49)

³J_{CH X,H} a,e in cyclohexanes:

all points

 \Diamond

R = 1.94 (1 - 0.156 E)

= 0.932 (4.50)

4.4. Variation of the Ratio with Dihedral Angle and Substituent Orientation

The effect of the dihedral angle and substituent orientation on the ratio can be seen from the ratios of oxygen substituted cyclohexanes and cyclopropanes. (Table 4.1). The ratios vary with both substituent orientation with respect to the coupled nuclei and the relative orientation of the coupled nuclei.

The values of the <u>gauche</u> ratios are very sensitive to the electronegativity of the substituents <u>anti</u> to the coupled nucleii. The changing ratios reflect the greater sensitivity of the carbon-proton coupling constant to the electronegativity of the <u>anti</u> substituent.

The ratio for ${}^{g}J_{C,H}^{HO}$ is calculated from the other three listed gauche ratios. In changing from a proton opposite the coupled carbon to a carbon opposite the coupled carbon, the gauche ratio changes from 0.67 to 0.80. From the ${}^{g}J_{C,H}^{CO}/{}^{g}J_{H,H}^{CO}$ ratio of 0.59, the fatio for a proton opposite the coupled carbon instead of a carbon would be 0.59 * (0.80/0.67) = 0.70, i.e., ${}^{g}J_{C,H}^{HO}/{}^{g}J_{C,H}^{HO}$ = 0.70. The validity of this calculation is supported by independent ratios from another set of Table 4.1. The variation of the Ratio of the vicinal carbon-proton to the vicinal proton-proton coupling constant as the dihedral angle between the coupled nuclei (Φ) and the orientation of the substituent with respect to the coupling pathway (Θ) are changed in cyclic compounds with oxygen substituents. The carbon-proton coupling constants are from the 1-methyl-4-phenyl-3,3',5,5'-tetradeuterocyclohexanols and the 1-methoxy-2,2-diphenylmethylcyclopropanes while the proton-proton coupling constants are from the analogous octadeuterocyclohexanols and cyclopropanols.

Coupling	Φ.	θ	Ratio (C,H/H,H)
tJ	Ì 180	60	0.51
g ¹ CO	. 60 .	' · 180`	0.59
g ¹ CC	. 60	60	0.67
,gJHC	60	60.	0.80
д _Ĵ но	60	180,	0.70*
3 _Ј с	0	.144	0.60
з _{jt}	- 144	0	0.48

Superscripts after J refer to the atoms anti to the coupled nuclei.

* Calculated from Ratios of J^{CO} , J^{HC} , J^{HC} . Ratio, J^{HO} = 0.59 * 0.80 / 0.67

coupling constants. For the <u>t</u>-butyl and isopropyl alcohols, the ratio of ${}^{3}J_{C,H}$ to ${}^{3}J_{H,H}$ is found to be 0.66 (54). Using the ratios above, the expected value of the ratio of the carbon-proton to proton-proton coupling constants is the average of the ratios of the conformers, i.e.,

 $t_{JC,H}^{t} t_{JH,H} = 0.51$ $g_{JC,H}^{HC} g_{JH,H}^{HC} = 0.80$ $g_{JC,H}^{HO} g_{JH,H}^{HO} = 0.70$

and the expected Ratio = 0.51/3 + 0.80/3 + 0.70/3 = 0.67, which is in excellent agreement with the observed value.

EXPERIMENTAL

CHAPTER FIVE

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All solvents used were reagent grade unless noted below. Reference to petroleum ether implies the low boiling fraction $(35 - 60^\circ)$ unless noted in the text. Dry diethyl ether was obtained from Fisher Scientific (anhydrous) and used without further preparation. Drydimethylformamide was obtained from Fisher Scientific and used without further purification.

All chemicals were obtained commercially and used , without further purification.

5.1. Preparation of the 2,2-diphenylmethylcyclopropane derivatives

The synthetic pathways utilized to obtain the methyl-2,2-diphenyl cyclopropanes are shown in Scheme's 1, 2 and All syntheses of the cyclopropane ring involved the - 3. addition of a diphenyl carbene (Ph2C:) across the double substituted acrylic or 2-methyFacrylic acid bond of an ester. The synthesis of the ovarious compounds are described below. The numerals refer to the compounds in schemes 1, 2 and 3. Compounds not synthesized by the author were provided by Professor H. M. Walborsky, of the Florida State University and his generosity is greatly appreciated. Dr. Walborsky provided the isonitrile, cyano, aldehyde, and acetamido derivatives of 2,2diphenyl methylcyclopropane, i.e., X = NC, CN, CHO, and The syntheses of these compounds are NHCO2C2HE described in the literature (131, 132, 133, 134, 135).

5.1.1. Preparation of Benzophenone Hydrazone 1

Benzophenone (42.0 g, 0.23 mol); 10% ethanolic potassium hydroxide (360 mL) and 95 percent hydrazine hydrate (80 mL) we're added to a one-liter, round bottomed flask. The magnetically stirred solution was refluxed over a steam bath for two and one half hours and cooled. The yellow white crystals which formed upon cooling were







collected and recrystallized from a minimum amount of hot ethanol to yield 1, 35 g (77%), m.p. 94-97°, lit. 95-98° (136).

5.1.2. Preparation of Diphenyldiazomethane 2

Benzophenone hydrazone 1 (13.0 g, 0.067 mol), yellow mercuric oxide (35.0 g, 0.16 mol), saturated ethanolic potassium hydroxide (5 mL) and anhydrous sodium sulfate (15.0 g) were added to diethyl ether (200 mL) in a 500-mL pressure flask. The flask was corked and wired shut, and the solution stirred for 3 h at room temperature. The deep red solution was filtered (elemental mercury was produced) and concentrated to yield diphenyldiazomethane 2, as a red oil, 10.0 g (78%). The diphenyldiazomethane was immediately taken up in petroleum ether and refrigerated.

5.1.3. Preparation of methyl α -bromoacrylate <u>3c</u> and methyl 1-bromo-2,2-diphenylcyclopropanecarboxylate <u>4</u>

A 250 mL-round bottomed flask was charged with methyl acrylate (40.0 g, 0.47 mol), methanol (20 mL) and a trace of hydroquinone. Bromine (26 mL, 78.0 g, 0.49 mol) was added with stirring at a rate that kept the solution temperature below 40 °. When the elemental bromine had been consumed (as evidenced by the disappearance of the red color), the solution was distilled under reduced pressure (20 mm Eg) to yield methyl α, β - dibromopropionate.

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The methyl α, β -dibromopropionate (65.0 g, 0.27 mol) and quinoline (35.0 g, 0.27 mol) were distilled with stirring in a Claisen apparatus. The resulting clear distillate was collected in an acid- washed flask. As the distillation progressed the residue in the Claisen apparatus turned a brownish orange color. The crude methyl α -bromoacrylate 3c was used without further purification.

The methyl α -bromoacrylate <u>3c</u> was dissolved in petroleum ether (80 mL) and heated to reflux. Diphenyldiazomethane (20 g, 0.10 mol) in petroleum ether (100 mL) was added until the red color of the diazo compound was retained. Concentration of the solution yielded a yellow oil that crystallized with cooling and scratching. The crude methyl l-bromo-2,2diphenylcyclopropane carboxylate <u>4c</u> was recrystallized from methanol to yield colorless plates , 12.0 g (36%), m.p. .84-85 $^{\circ}$.(135)

5.1.4. Preparation of the methyl 1-cyano and methyl 1chloro-2,2-diphenylcyclopropanecarboxylates (<u>4a</u> and <u>4b</u>).

The cyano and chloro derivatives of methyl 2,2-

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diphenylcyclopropanecarboxylate, compounds 4a and 4brespectively, were prepared in a manner similar to that for the bromo derivative from the cyano and chloro methyl acrylates, compounds 3a and 3b.

The steps in the reduction of the methylesters, compounds <u>4a</u>, <u>4b</u>, and <u>4c</u>, are essentially the same for the cyano, chloro, bromo, fluoro <u>10</u> and methoxy <u>14</u> compounds. This reduction is discussed in detail in the preparation of 1-methoxy-2,2-diphenylmethylcyclopropane <u>14</u>.

5.1.5. Preparation of 1-iodo-2,2-diphenylmethylcyclopropane 7d

The bromide 4c (3.4 g, 0.012 mol) was dissolved in benzene-petroleum ether (1:1) (100 mL) and the resulting solution cooled to 5°. A solution of n-butyllithium in dry diethyl ether (0.10m, 100 mL) was added to the solution in such a manner as to keep the temperature of the mixture below 6° (complete addition took approximately 30 minutes). Following the addition, the solution was stirred at 5° for 20 minutes and iodine added to decompose the lithium compound. The solution was washed with H₂O (2 x 20 mL), dried over anhydrous sodium sulfate, filtered and concentrated to yield 2.0 g (50%) of 7d.

 δ 1.88, δ 1.63, dd, 2H, ²J = 6.3 Hz . 5.1.6. Preparation of 1-deutero-2,2-diphenylmethylcyclopropane <u>7e</u>

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A solution of <u>n</u>-butyllithium in dry ether (0.10m, 100 mL) was added slowly to a solution of the bromide <u>7c</u> (3.4 g, 0.012 mol) in 100 mL of benzene-petroleum ether (1:1) which had been cooled to 5° in such a manner as to keep the temperature of the resulting solution below 6°. After stirring for 20 minutes at 5°, deuterated methanol (CH₃OD) was added to decompose the 1 ithium compound. The solution was then washed with water (2 x 20 mL), dried over anhydrous sodium sulfate, filtered and concentrated to yield 1.8 g (72%) of <u>7e</u>. N.M.R (CBCT₃) - δ 7.50 - 7.00, bm, 10H; δ 1.24, 1.11, dd, 2H, ²J = 4.5 Hz; δ 0.91, s, 3H.

5.1.7. Preparation of ethyl 1-fluoro-2,2-diphenylcyclopropanecarboxylate 2 via ethyl α -fluoroacrylate 8

Ethyl oxalate (20.7 g, 0.14 mol) and one drop of ethanol were added to a 56 % dispersion of podium hydride in oil (5.58 mL, 0.13 mol), dissolved in benzene (100 mL), and ethyl fluoroacetate (12.4 g, 0.13 mol) added dropwise. During the course of the addition, which took one hour, the temperature of the reaction mixture was kept between 40° and 60° . The ethanol was distilled off and after the solution had been cooled to 40° , trioxymethylene (3.87 g, 0.13 mol) was added. The mixture was stirred for 15 minutes and the resulting solution of ethyl -fluoroacrylate <u>8</u> used without purification.

Diphenyldiazomethane (3.92 g) in 90 mL of petroleum ether was then added to the refluxing ethy $\Delta \alpha$ fluoroacrylate solution. After refluxing overnight, the solution was cooled, filtered and concentrated. The crude product was taken up in benzene (50 mL), washed successively with concentrated sulfuric acid (2 x 10 mL), water (2 x 15 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to yield 2.0 g (15%) of 9 (131).

The ester was reduced to the methyl fluoro derivative 10 in the same manner as the methoxy compound 14. See section 5.1.11.

N.M.R. $(CDCl_3)^{\circ} - \delta 7.50 - 7.00$, bm, 10H; $\delta 1.75$, $\delta 1.13$, 2H (ABX), ${}^{2}J_{A,B} = 6.0$ Hz, ${}^{3}J_{H,F} = 3.60$, 22.90 Hz; $\delta 1.30$, d, 3H, ${}^{3}J_{F,H} = 17.5$ Hz, m.p. 173 - 175°, 1it. 174 -175° (131).

5.1.8. Preparation of Methyl α, β -Dibromopropionate 11

Bromine (26 mL) was added to a solution of methyl acrylate (40.0 g, 0.47 mol), 20 mL of methanol and a trace of hydroquinone in a 250 mL round bottomed flask at a

rate that kept the solution temperature below 40 C°. The solution was stirred overnight at room temperature and then distilled under reduced pressure (approximately 20 mm Hg). The first fraction (10 mL) was discarded. The second fraction yielded 86g (92%) of methyl $\alpha_{,}\beta_{-}$ dibromopropionate 11.

5.1.9. Preparation of Methyl α -Methoxyacrylate 12

5.0 g of sodium metal was dissolved in methanol (80 mL) and added dropwise to a stirred solution of methyl α , β -dibromopropionate (20.0 g, 0.081 mol). Following the addition the solution was left to stir at room température for 5 days. The reaction was quenched with dry ice (CO₂) (20 g) and the solution filtered. The filtrate was washed with methanol (20 mL) and the organic layer hydrolysed with water (30 mL). Chloroform (40 mL) was added, and the aqueous layer separated and washed with chloroform (40 mL). The organic layers were combined , washed with H₂O (2 x 10 mL) dried over, anhydrous magnesium sulfate and concentrated to yield 8.67 g (93%) of a reddish colored oil 12 (134).

5.1.10. Preparation of methyl 1-methoxy-2,2-diphenyl cyclopropanecarboxylate 13

Methyl Q-methoxyacrylate 12 (8.0 g, 0.08 mol) was

dissolved in cyclohexane (50 mL) and diphenyldiazomethane (20.0 g, 0.10 mol) in cyclohexane (70 mL) added over twenty minutes to the stirred solution. The solution was heated to reflux and the refluxing continued overnight. After cooling, the solution was concentrated to yield 18.67 g of the crude carboxylate <u>13</u>.

The crude product was dissolved in benzene (100 mL), washed with cold concentrated sulfuric acid (2 x 3 mL), H_2O (3 x 10 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to give a yellow liquid that crystallized on standing to yield 8.4 g (368) of 13.

5.1.11. Reduction of the methyl 2,2-diphenylcyclopropanecarboxylate derivatives to 2,2-diphenylmethylcyclopropane derivatives

The reduction of the methyl ester of the cyclopropane carboxylic acid to the methyl cyclopropane is described below for the methoxy derivative. The same procedure was used for the chloro, bromo, cyano, and fluoro derivatives.

Was dissolved in dry diethyl ether (75 mL) and added dropwise to a stirred solution of lithium aluminum hydride (1.90 g, 0.050 mol) in dry diethyl ether (25 mL) cooled to 0°. After the addition was complete (approximately 45 minutes), the solution was refluxed for one hour, cooled and saturated ammonium chloride solution (35 mL) added slowly to quench the excess lithium aluminum hydride. The mixture was filtered, the aqueous layer discarded and the organic layer dried over anhydrous sodium sulfate and concentrated to yield 4.96 g (72%) of the alcohol 5 where $X = OCH_3$, m.p. 80 - 81°, lit. 82 - 83° (131).

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5.1.12. Tosylation of <u>l-methoxy-2,2-diphenyl-</u> cyclopropane methanol <u>5</u>

The crude alcohol (4.96 g, 0.18 mol) was dissolved in pyridine (S0 mL), cooled in an ice-water bath, and paratoluenesulfonyl chloride (5.4 g, 0.03 mol) added. The solution was stirred for one and one half hours at 0° , refrigerated overnight, then poured into an ice water mixture (75.0 g). The aqueous mixture was extracted with diethyl ether (3 x 80 mL), the ether extracts combined and washed with 1N hydrochloric acid (3 x 60 mL) and saturated copper sulfate solution to remove the pyridine. The ether solution was dried over anhydrous sodium sulfate, filtered and concentrated to give 3.4 g (40%) of the tosylated alcohol. 5.1.13. Reduction of the tosylate of 1-methoxy-2,2diphenylcyclopropane methanol

The tosylate (3.1 g, 0.000 mol) was dissolved in dry diethyl ether and added rapidly to a stirred solution of lithium aluminum hydride (0.6 g, 0.016 mol) in dry diethyl ether (60 mL). After stirring for three and one half hours, dry tetrahydrofuran (20 mL) was added and the solution stirred overnight. The excess lithium aluminum hydride was quenched by cautious addition of saturated ammonium chloride solution (20 mL), the solution filtered and the aqueous layer discarded. The organic layer was dried over anhydroug sodium sulfate and concentrated to yiold 1.8 g of the crude product.

To purify the desired product 14, a silica gel column was used. Petroleum ether $(30-60 \ \circ \ \text{Fraction})$ benzene (9:1) were used as the eluant. The desired product was a white crystalline solid, melting point 70-73. °.

N.M.R (CDCl₃) - δ 7.50 - 7.00, bm, 10H; δ 3.13, s, 3H; δ 1.66, δ 1.26, dd, 2H; ²J = 6.03 Hz. The proton chemical shift and coupling constant data for the cyano, chloro, and bromo 2, 2, 2diphenylmethylcyclopropane derivatives, compounds 7a, 7b, and 7c respectively are listed below. CN - N.M.R. (CDCl₃) - δ 7.50 - 7.00; bm, 10H; δ 1.93,

δ1.55, dd, 2H, ²J = 4.8 Hz; δ1.22, s, 3H.,

Cl = N.M.E: $(CDCl_{3}) = \delta7.50 = 7.00$, bm, lOH; $\delta1.85$, $\delta1.65$, dd, 2H; $^{2}J = 6.3$ Hz; $\delta1.54$, s; 3H,

m.p. $66 - 68^\circ$ Br - N.M.R. (CDC1'₃) - δ 7.50- 7.00, bm, 10H; δ 1.95, δ 1.69, dd, 2H, ²J = 6.4 Hz; δ 1.72, s, 3H, m.p. 84 - 85°,

5.1.14. Preparation of methyl 2,2-diphenylmethyl .

To a refluxing solution of methyl methacrylate (15.0 g, 0.15 mol) in petroleum ether (30 -60 C^O ffaction) (45 mL), diphenyldiazomethane (29.1 g, 0.15 mol) in petroleum ether (80 mL) was added until the solution retained the red color of the unreacted diphenyldiazomethane. The solution was cooled and concentrated to yield a yellow '

The crude product was recrystallized from a minimum amount of bot methanol to yield 12.3 g (318) of the desired compound 15, N.M.R. (CDCL3) - δ 7.50- 7.00, bm; 10H; δ 2.28, δ 1.45, dd, 2H, 2J = 4.8 Hz; δ L.20, s; 3H, m.p. 56 - 59°. 5.1.15. Preparation of 2,2-diphenylmethylcyclopropanecarboxylic acid 16

The methyl ester 15 (9.5 g, 0.036 möl) was refluxed in a solution of 25 percent aqueous potassium hydroxide (50 mL) and methanol (70 mL) overnight. The solution was cooled, acidified with 2N hydrochloric acid, and the solid collected by filtration and air died to yield 7.8 g-(883) of the acid 16.

N.M.R. $(CDCl_3) = \delta7.50 - 7.00$, bm, 10H; $\delta2.20$, $\delta1.47$, dd, 2H, 2J = 4.7 Hz; $\delta1.13$, s, 3H, m.p. 175 - 179

5.1.16. Preparation of 1-amino-2,2-diphenylmethylcyclopropane 20

A solution of ethyl chloroformate (1.25 mL, 0.012 mol) in acetone (3 mL) was added to a mixture of the acid (16) (2.53 g, 0.010 mol), triethylamine (1.75 mL, 0.012 mol) and acetone (40 mL) cooled to -10 C^O in a salt-ice bath. After stirring the resulting solution for two hours, a mixture of sodium azide (1.25 g, 0.012 mol) and water (10 mL) was added dropwise and stifring continued for a further four hours. The solution was taken up in pentane (100 mL), and the pentane layer washed successively with in hydrochloric acid (2 x 10 mL) and saturated sodium carbonate (2 x 15 mL), dried over anhydrous sodium sulfate, filtered and concentrated. The crude azide $\frac{17}{12}$ was left in a vacuum desicator overnight.

The crude azide 17 was refluxed in benzene (100 mL) for six hours under a nitrogen atmosphere, then left to cool. The solvent was removed under feduced pressure and the residue 18 dissolved in a (2:1) water hydrochloric acid mixture (45 mL) and refluxed overnight.

After cooling, a brownish solid formed in the solution. The solid was collected by filtration and washed with acetone to leave a white crystalline solid. Recrystallization of this white solid gave 1.0 g (40%) of the hydrochloride salt 19 of the desired amino derivative, m.p. 130 - 135.(132)

As the free amine is unstable, it is generated in situ in deuterated chloroform (CDCl₃) when NMR spectra. are acquired. The generation of 20 from 19 involves adding saturated aqueous sodium carbonate solution to a mixture of the salt in CDCl₃. With stirring the free amine 20 is liberated and dissolves in the chloroform. N.M.R. (CDCl₃) - δ 7.55- δ 7.00, bm, 10H; δ 1.47, δ 1.30, dd, ²J = 4.0 Hz; δ 1.28, s, 3H

5.2 ¹H NMR and Mass Spectral data for the 2,2-diphenylmethylcylcopropane derivatives

The relevant proton (1H) data for the 2,2-diphenylmethylcyglopropane derivatives were obtained at Dalhousie University on a Varian T-60 or a Varian CFT-20 NMR spectrometer. The mass spectra were obtained on a DuPont-CEC model 21-104 spectrometer using an ionization voltage of 70 electron volts. The mass spectra data are listed in Table 5.1. TABLE 5.1 Mass Spectral Data for the 2,2-Diphenyl methyl cyclopropanes

'NHAR	NegCl	έ.Ε	· C1	CIV	. 002012E5	I	Ø Ø	•	
MV 295	261,259	225	244,242	, 233 .	230 .	324 .	236		
. 29(100)	⁻ 223(100)	206(100)	207(100)	233(100)	· 207(100)	127(100)	235(109)		
42(100)	146(93)	226(79)	129(79)	295(63)	206(81) .	254(83)	207(100)	, ¹ 6	
-205(73)	- 42(60)	191(66)	-2¢5(24) ··	165(63)	129(63)	. ⁴ 2 123(25) –	129(95)	, ,	4
105(32)	36(56)	165(56)	191(66)	232(44)	105(55)	63.5(11)	165(90)	٠	
77 (19)	208(49)	211(36)	165(51)	. 218(32)	205(45)	129(10)	221(76)	۲	
.207(17)	- 165(47)	205(26)	91(39)	⁷⁷ 191(28)	• 91(43)	43(9).	91(75)	4 4	-
205(27)	44(40) ¹	`133(26) ·	242(34)	, 51 ⁽²³⁾	77(43)	45(8)	115(67)	*	
.165(16)	43(33)	207(21)·	243(8)	178(19)	165(38)	28(8)	51(52)	,	
.43(16)	· 77(31)	189(19)	128(28)	91(15)	· 29(30)	77(8)	77(48)	•	•
191(15)	222(27)	. 225(18)	. 205(25)	89(15)	51(28)	91(8)	- 39(45)	• ·	
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5.3. Preparation of the 1-(1-deutero-4-1butylcyclohexyl)methane Derivatives

The synthetic pathways for the preparation of the 1-(1-deutero-4-t-butylcyc sohexy I) methanol derivatives are shown in Scheme 4. The syntheses of the compounds shown in Scheme 4 are described in detail below.

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5.3.1. Preparation of 4-t-butylmethylenecyclohexane

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Fifteen milliliters of a solution of bromobenzene' (26.0'g, 0.17 mol) in dry diethylether (75 mL) were added to lithium shavings (2.7 g, 0.17 mol) contained in a flamed, nitrogen-flushed 500 mL-flask. When the reaction was noticed to start (as evidenced by the production of heat) the remaining bromobenzene solution was added at a that maintained the reflux of the solution. Complete addition took approximately one hour. The grayish solution was stirred for one half hour, diethyl ether (30 mL) was added and the solution decanted from the excess lithium into a clean, flamed, nitrogenflushed, 500 mL7flask. Triphenylmethylphosphonium bromide (53.0 g, 0.17 mol) was added over fifteen minutes and resulting solution "stirred at room temperature for four hours. The preparation of triphenylmethylphosphonium bromide is described following the completion of the



description of this Wittig reaction.

A solution of 4-t-butylcyclohexanone (23.0 g, 0.15 mol) in dry diethyl ether (30 mL) was added to the mixture and the mixture refluxed overnight. Following hydrolysis of the excess phenyllithium with water (25 mL), the solution was filtered, the filtrate washed with diethyl ether and the ether layers combined, dried over anhydrous sodium sulfate and concentrated.

The crude product (16.5 g) was distilled under reduced pressure (20 mm Hg) to yield 8.0 g (35%) of a light yellow oil, which was essentially pure product <u>21</u>.

N.M.R. (CDC1₃) - δ4.52, s, 2H; δ2.60 - 1.00, bm, 9H; δ0.87,. s, 9H.

The yield for this Wittig reaction appears to be dependent upon the efficient mixing of the phosphorus yild and the ketone. Much better yields were realized when the reaction was carried out on a smaller scale and efficient magnetic stirring was possible.

5.3.2. Preparation of Triphenylmethylphosphonium Bromide

Methylbromide (15.0 g, 0.10 mol) was added to a cooled (10°) solution of triphenylphosphine (34.0 g, 0.13 mol) in dry toluene (30 mL) contained in a flask. The flask was sealed with a rubber bung secured by wire and left for twenty four hours at room temperature.

The solution was cooled in an ice-salt bath (-10°)

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and yellow white crystals were noticed to form. The crystals were collected by filtration, dried at 115° for twenty four hours and stored over phosphorus pentoxide in a vacuum desiccator. The yield was quantative. (137)

5.3.3. Preparationof 1-(1-deutero-4-t-butylcyclohexyl), methanol 22

Sodium-borodeuteride (6.42 g, 0.010 mol) was added over a period of two minutes to a solution of 4-t-butylmethylenecyclohexane (5.0 g, 0.033 mol) in dry tetrahydrofuran (20 mL) contained in a flamed, nitrogenflushed 125-mL flask. To this stirred solution, a solution of boron trifluoride etherate (1.9 g, 0.33 mol) in dry tetrahydrofuran (5 mL) was added slowly over a one hour period. The solution was then stirred for one and one half hours at room temperature, made alkali by the addition of 3N sodium hydroxide (3.5 mL), and 30% hydrogen peroxide (3.5 mL) was added slowly over a one hour period.

The mixture was washed with water (2 x 30 mL) and the aqueous washes extracted with diethyl ether (2 x 30 mL). The tetrahydrofuran layer and ether washes were combined, dried over anhydrous magnesium sulfate and concentrated to yield 4.4 g (78%) of 1-(1-deutero-4-t-butylcyclohexyl) methanol 22.(138)

» N.M.R. (CDC1₃) - δ 3.60, δ 3.40, s, 2H; δ 2.00- 0.90, bm,

9H; δ0.83, s, 9H.

(The product contained both <u>cis</u> and <u>trans</u>-1-(1deutero-4-<u>t</u>-butylcyclohexyl)methanol. <u>Cis</u> and <u>trans</u> refer to the orientation of the <u>t</u>-butyl and CH₂OH groups with respect to each other on the cyclohexane ring. The bulky <u>t</u>-butyl group favors the equatorial position over the axial position on the ring but the CH₂OH can assume both the equatorial and axial positions giving the <u>trans</u> " and <u>cis</u> compounds respectively. No effort wa's made to separate these isomeric alcohols prior to preparation of the halide derivatives via the tosylates of these alcohols.

5.3.4. Preparation of the tosylate of the 1-(1-deutero-4-t-butylcyclohexyl)methanol 23

The cyclohexylmethanol $\underline{22a}$ (3.3 g, 0.019 mol) was dissolved in pyridine (25 mL), cooled to 0°, and paratoluenesulfonyl chloride (5.6 g, 0.029 mol) added over one half hour. Following the addition the solution was stirred vigorously for three hours, refrigerated for seventy two hours, then poured into ice water (100 g). The aqueous solution was extracted with diethyl ether (3 x 70 mL) and the ether extracts washed with dilute hydrochloric acid (4 x 30 mL), saturated copper sulfate solution (3 x 5 mL), dried over anhydrous sodium sulfate and concentrated. The yield was 3.7 g (59%) of 23. N:M.R. (CDCl₃) - δ 7.80- δ 7.20, AB doublet, 4H, ${}^{3}J_{AB}$ 8.0
Hz; δ4.20, s, 2H; Φδ2.40, s, 3H; δ2.00-1.20, bm, 9H, δ0.73, s, 9H.

5.3.5. Preparation of 1-(chloromethyl)-1-deutero-4-t-

The tosylate 23 (0.80 g, 2.45 x 10^{-3} mol) was added to a stirred mixture of lithium chloride (0.13 g, 3.06 x 10^{-3} mol) in dry dimethylformamide (20 mL) and the solution heated at 90° for five hours. The solution was removed from the water bath and left overnight at room temperature. Water (30 mL) was added, the organic phase extracted with diethyl ether (3. x 30 mL) and the ether extracts washed with water (4, x 25 mL) to remove any traces of dimethylformamide. The ether extracts were dried over anhydrous magnesium sulfate, filtered and concentrated to yield 0.35 g (76%) of the chloro derivative 22 b.

N.M.R. $(CDCl_3) - \delta 3.57, \delta 3.36, s, 2H; \delta 2.00 - 1.20, bm, 9H; \delta 0.87, s, 9H.$

5.3.6. Preparation of 1-(bromomethy1)-1-deutero-4-tbutylcyclohexane 22 c

The tosylate 22 (0.85 g, 2.60 x 10^{-3} mol) was added to a stirred mixture of lithium bromide (0.26 g, 2.98 x 10^{-3} o mol) in dry dimethylformamide (20 mL). After heating the

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solution for two hours at 90°, it was removed from the heat and left at room temperature overnight. The solution was hydrolysed with water (25 mL) and extracted with diethyl ether (3 x 50 mL). The ether extracts were washed with water (4 x 25 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated to yield 0.5 c (82%) of the bromo derivative 22 c. N.M.R. (CDCl₃) - δ 3.48, δ 3.26, s, 2H; δ 2.00 - 1.20, bm, 9H, δ 0.87, s, 9H.

5.3.7. Preparation of 1-(iodomethyl)-1-deutero-4-t-butyl cyclohexane 22 d

The tosylate 23 (0.80 g, 2.45 x 10^{-3} mol) was added to a stirred solution of lithium iodide (0.29 g, 2.45 x 10^{-3} mol) in dry dimethylformamide (20 mL). After heating the solution for twelve hours at 90°, it was left at room temperature overnight. The solution was hydrolysed with water (25 mL), extracted with diethyl. ether (3 x 50 mL) and the three extracts washed with water, (5 x 25 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to yield 0.40 g (58%) of the iodo derivative 22 d: N.M.R. (CDCl₃)- δ 3.30, δ 3.10, s, 2H; δ 2.00- 1.20, bm, 9H; δ 0.87, s, 9H. 5.4. Preparation of the 1-methy1-3,3',5,5'-tetradeutero-4-phenylcyclohexane derivatives

The preparation of this series of compounds, the 1hydroxy, 1-chloro, 1-bromo, and 1-iodo-1-methyl-3,3',5,5'-tetradeutero-4-phenylcyclohexanes respectively, is shown diagramatically in Scheme 5. As is shown in Scheme 5, the substituent can assume both <u>cis</u> and <u>frans</u> orientations relative to the phenyl group. The phenyl group was incorporated into the molecule to lock the cyclohexane ring in a particular conformation, <u>i.e.</u>, that with the phenyl group in the equatorial position, and allow formation of the <u>cis</u> and <u>trans</u> isomers. The 1chloro, 1-bromo, and 1-iodo derivatives in the <u>trans</u> orientation, <u>e.g.</u>, the chloro equatorial-phenyl equatorial compound, could not be synthesized in '

5.4.1. Preparation of 1,4-cyclohexanedione 24

1,4-cyclohexanediol (15.0 g, 0.13 mol) was dissolved in acetone (300 mL) and Jones reagent (125 mL) added to the cooled (15-20°); magnetically stirred solution over a three hour period. When the addition was complete the solution was concentrated and the green residue taken up in a minimum amount of warm water. The aqueous layer was



extracted with warm ethyl acetate (5 x 60 mL) and the ethyl acetate extracts concentrated to leave a brownish solid which was recrystallized from isopropyl etherisopropyl alcohol to yield 755 g of the $l_{c}4$ -(cyclohexanedione 24. (139)

5.4.2. Preparation of 1,4,9,12-tetraoxadispifo[4.2.4.2]

N.M.R. $(CDCl_3) = \delta 2.77 \sigma s_{\sigma} 8H_{\circ}$

Ethylene glycol (12 mL, 0.093 mol) and a catalytic -amount of p-toluenesulfor c acid (0.05 g) were added to a solution of 1,4 cyclohexandione (10.4 g; 0.093 mol) in benzène (200 mL); The magnetically stirred mixture was refluxed for four hours using a Dean Stark trap to remove the H₂O produced by the reaction. After the theoretical amount of H₂O had been collected, the solution was allowed to cool. The solution was washed with saturated NaHCO₃ (2 x 30 mL) and H₂O (2 x 20 mL), dried over anhydrous sodium carbonate and concentrated. The resulting white solid was recrystallized from hot isopropyl alcohol yield 25, 13.0 g (70%). (140) N:M.R. (CDCL₃) - δ 3.93, s, 8H; δ 1.77, s, 8H.

5.4.3 Preparation of 1,4-dioxaspiro[4.5]decan-8-one 26

The diketal 25 (13.0 g, 0.065 mol), 1.4-

cyclohezanedrone (7.3 g, 0.065 mol) and g-toluenesulfonic acid (0,25,g) were dissolved in benzene (125 mL) and refluxed for four hours: The solution was removed from the heat and pyridine (3 drops) added. The cooled solution was washed successively with saturated sodium bicarbonate solution (2 x 8 mL) and saturated sodium chloffde solution (2 x-8 mL) and finally extracted with water (2 x 15 mL) to remove dry 1,4-cyclohexahedio w that .. remained.' The benzene layer was dried over anhydrous sodium carbonate and concentrated. The white residue was distilled under reduced pressure (0.13 mm Hg) through a Vigreux column and the fraction coming off at 78 - 80° . collected to yield 26, 7.0 g (70%). (140) N.M.R. $(CDCl_3) = \delta 4.03$, s, $4H_2 \cdot \delta 2.50$, bt, $4H_2 = 7.0$ Hz; δ2.00; bt, 4H, 3J = 7.0 Hz.

5.4.4. Preparation of 7,7',9,9'-tetradeutero-1,4dioxaspiro[4.5]decan-8-one 22

The monoketal <u>26</u> (5.0 g, 0.032 mol) was stirred in D₂O (35 mL) and sodium metal (1.5 g, 0.060 mol) was added. After 24 hours the aqueous (D₂O), layer was extracted with diethyl ether (3 x 30 mL) and the ether extracts dried over anhydrous sodium sulfate and concentrated to yield <u>27</u>, 3.5 g (698). 5.4.5. Preparation of 7,7',9,9'-tetradeutero-8-hydroxy-8-

5

Magnes fum metal. (1.5 g, 0.062 mol) was placed in a 3neck round bottom flask equipped with a dropping funnel and a condenser with a drying tube. The apparatus was flamed to remove any traces of moisture and allowed to 'cool. A part (7 mL) of a solution of bromobenzene (9.0 g) in diethyl ether (30 mL) was run from the dropping funnel onto the magnesium. After the reaction had started, the remaining bromobenzene solution was diluted with diethyl ether (20 mL) and added to the reaction mixture at a rate which maintained a steady reflux. The solution was refluxed for 30 minutes after the addition was complete.

To the cooled Grignard reagent a solution of 7,7',9,9'-tetra deutero-1,4-dioxaspiro [4.5] decan-8-one (9.0 g, 0.058 mol) in diethyl ether (25 mL) was added in a rapid succession of drops with constant shaking.

The mixture was refluxed for 15 minutes and then poured into a mixture of ice (75 g) and water (75 mL). Following the addition ammonium chloride (5 g), the organic and aqueous layers were separated. The aqueous layer was washed with diethyl ether (2 x 30 mL) and the ether extracts combined with the organic layer. The organic layer was washed with 5% sodium bicarbonate (60 mL) and saturated sodium chloride solution (50 mL) and / dried over anhydrous potassium carbonate. The solution was concentrated to gield 28, 8.0 g (58%), N.M.R. (CDCl₃) - δ 7.4 7.0, bm, 58; δ 3.73, s, 48; δ 2.23, δ 1.37, AB doublet, 48; ²J = -12.5 Hz.

5.4.6. Preparation of 7,7',9,9'-tetradeutero-8-phenyl-1,4-dioxaspiro [4.5] decane 22

7,7:,9,9'-tetradeutero-8-hydroxy-8-phenyl-1,4-dioxaspiro [4.5] decane (1.1 g, 0.0045 mol) was dissolved in 3 glacial acetic acid (30 mL) in a 500 mL-pressure bottle and 10% palladium on charcoal (0.15 g) added. The solution was heated to 50° and mechanically shaken under a hydrogen atmosphere (30 psi) for four hours. The solution was filtered to remove the Pd/C catalyst, poured into water (20 mL) and diethyl ether (50 mL) added. The ether layer was separated washed with saturated sodium bicarbonate (3 x 20° mL) and concentrated to yield 29, 0.8 g (80%).(141)

N.M.R. $(CDCl_3) = \delta 7.20$, bs, 5H; $\delta 3.93$, s, 4H; $\delta 1.75$, bs, 4H.

5.4.7. Preparation, of 3,3',5,5'-tetradeutero-4-pheny'l cyclohexanone 30

7,7',9,9'-tétradeutero-8-phenyl-1,4-dioxaspiro[4.5] decane 29 (1.0 g, 0.0044 mol) was dissolved in 95% ethanol Ľ

(10 mL) and 2N hydrochloric acid (15 mL) added. After refluxing overnight, the solution was cooled, water added and the solution extracted with diethyl ether (4 x 30, mL). The ether extracts were dried over, anhydrous potassium carbonate and concentrated to yield 30, 0.7 g

N.M.R. (CDC1₃) - δ7,20, s, 5H; δ2.83; s, 1H; δ2.43, bs,
 4H.

5.4.8. Preparation of the Isomeric Alcohols <u>31</u>

Magnesium (0.63 g, 0.026 mol) was added to a 3-necked round bottom flask (500 mL) with a reflux condenser and drop funnel attached. The apparatus was flamed to remove any traces of H_2O and a drying tube attached to the condenser. After the glassware had cooled, 10 mL of a solution of methyl iodide. (3.7 g, 0.026 mol) in diethyl ether (35 mL) was added.

When the reaction had started the remaining ether solution was diluted with diethyl ether (20 mL) and added to the reaction mixture so as to maintain reflux (complete addition took only five minutes). The solution was then refluxed for thirty minutes, cooled in an ice bath, and the ketone <u>30</u> (4.0 g, 0.023 mol) in diethyl ether (30 mL) added in a rapid succession of drops with efficient stirring.

A yellow solid was noticed to precipitate out. The

solution was refluxed for a further 20 min., then poured.
into an ice-water-ammonium chloride solution. Diethyl
ether. (100 mL) was added and the aqueous and organic layers separated. The aqueous layer was extracted with diethyl ether (400 mL) and the ether layers combined,
dried over anhydrous magnesium sulfate and concentrated to yield a viscous, yellow oil. The pure compound. crystallized out_upon cooling. Yield 87% of 31.
N.M.R. (CDCl₃)- δ7.50-.7.00, bm, 5H; δ2.47, 1H; δ2.00-δ1.55, bm, 4H; δ1.33, δ1.27, s, 3H.

References.

1.

- E. D. Becker, High Resolution NMR-Theory and Chemical Applications; Academic Press, 2nd ed., Toromto (1980).
- 2. G. J. Karabatsos, J. Am. Chem. Soc., <u>88</u>, 1230
- 3. ⁶G. J. Karabatsos, J. D. Graham and F. M. Våne, J. Am. Chem. Soc., <u>84</u>, 37 (1962).
 - R. M. Lyden-Bell and N. Sheppard, Proc. Roy. Soc. A., <u>269</u>, 385 (1962).
- 5. G. J. Karabatsos and E. E. Orzech Jr., J. Am. Chem. Soc., <u>87</u>, 560 (1965).
- δ. J. L. Marshall and D. E. Miiller, J. Ams Chem. Soc.,
 <u>95</u>, 8305 (1973).
- 7. O. Yamamoto, M. Watabe, and O. Kekuchi, Mol. Phys., 17, 249 (1969).
- 8. N. Muller, J. Chem. Phys., <u>37</u>, 2727, 1980.

9. R. Freeman and W. A. Anderson, J. Chem. Phys., <u>39</u>,
806 (1963).

- 10. R. Freeman, J. Chem. Phys., <u>40</u>, 3751 (1964).
- 11. R. Freeman, J. Chem. Phys., 43, 3087 (1965).
- 12. V. D. Ziessow and E. Lippert, Ber. Bunsengesellschaft Phys. Chem., <u>74</u>, 335 (1970).
- 13. V. D. Ziessow and E. Lippert, Ber. Bunsengesellschaft Phys. Chem., 74, 568 (1970).
- 14. J. L. Marshall, D. E. Miiler, S. A. Conn, R. Seiwell and M. Irhig, Acc. of Chem. Research, 7, 333 (1974).

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	15.	U. Vogeli and W. von Phillipsborn, Org. Magn.	· · · · · ·
	-	Reson., Z, 617 (1975).	
	16.,	J. L. Marshall and R. Seiwell, Org. Magn. Reson. 8,	
	4.4 A	*419 (1976).	ہ ۲۰۰۰
L	17.	T. P. Forrest and S. Sukumat, Can. J. Chem., 55,	4
		3689 (1977).	
	18.	P. Ayras, Acta, Chen. Scan. B., <u>31</u> , 325 (1977).	
	19.	P. Ayras, Org. Magn. Reson., 2, 663 (1977).	, n , 4
þ	.20.	H. S. Gutowsky and D. W. McCall, Phys. Rev., <u>82</u> , 748	,
67	•	(1951).	u.
	21.	H. S. Gutowsky, D. W. McCall and C. P. Slickter;	
		Phys. Rev., <u>84</u> ; 589 (1951).	• •
•. •	22.`	E. L. Hahn and D. E. Maxwell, Phys. Rev., 84, 1246	ż
•		(1951).	۰ ۲
,	23°.	E. L. Hahn and D. E. Maxwell, Phys. Rev., 88, 1070	् ५ १ छ १
4	24		
	4/te.,	N. F. Kamsey and L. M. Purcett, Phys. Rev., <u>02</u> , 145, "	• ب
,	•		-
۰ ·	25.	N. F. Ramsey, Phys. Rev., <u>91</u> , 303 (1953).	B
	26.	J. Kowalewski, Progress in NMR Spectroscopy, 11, 1	• • 57
		(1977).	
	27.	H. M. McConnell, J. Chem. Phys., <u>24</u> , 460 (1956).	•••
ø	28 [#] •	J. A. Pople and D. P. Santry, Mol. Phys., 8, 1	
t	, ° \	· (1964) .	Q
et u	29.	I. Ando and G. A. Webb brg. Magn. Reson., <u>15</u> , 111	• • •
4		(1981).	· · ·
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271	8
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(30. R. U. Lemieux, R. K. Kullhnig, H. J. Berstein and W.	•
G. Schneider, J. Am. Chem. Soc., <u>80</u> , 6098 (1958).	• '
31. M. Karplus, J. Com, Phys., 30, 6098 (1959).	8
32. K. L. Williamson; J. Am. Chem., Soc:, 85, 516 (1963).	3
33. P. Laszlo and P. von R. Schleyer, J. Am. Chem. Soc.,	<i></i>
85, 2018 (1963).	ı
34. O. L. Chapman, J. Am. Chem. Soc., 85, 2014 (1963).	l •*7
35. R. E. Glick and A. A. Bothner-By, J. Chem. Phys.	~~~
<u>65,</u> 1871 (1956).	, ,
36. M. Huggins, J. Am. Chem. Soc., <u>75</u> , 4123 (1953).	۷ - ۲
37. J. S. Waugh and S. Costeblano, J. Chem. Phys., 35,	,
1900 (1961).	``) •
38. C. N. Banwell and N. Sheppard, Disc. Farad Soc., No.	, t
34, 115 (1962). (1962).	ъ с
39. G. E. Maciel, J. W. McIver, N, S. Ostland and J. A.	
Pople, J. Am. Chem. Soc., 4497 (1970).	, o
40. A. J. Abraham and K. G. R. Pachler, Mol. Phys., Z.	٦
165 (1964).	1.,
41. D. H. Williams and N. S. Bhacca, J. Amer. Chem.	
Soc., <u>86</u> , 2742 (1964).	•
42., H. Booth, Tetrahedron Letters, 411 (1965).	٢
43. K. G. R. Pachlar, Tetrahedron, 27, 187 (1971).	
• 44. "R. J. Abraham and G. Gatti, J. Chem. Soc. (B), 961	k
(1969).	5
45. T. P. Forrest, Org. Magn. Reson., 6, 355 (1974).	
46. H., R. Buys, Recl. Trav. Chim. Pays - Bas, 88, 1003	۲ •
47. J. B. Lambert, J. Am. Chem. Soc., <u>89</u> , 1836 (1964).	ı
	*
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	۰.	
	•	
•	48_	T. P. Forrest, J. Am. Chem. Soc., <u>97</u> , 2028 (1975).
•	, ⁴⁹ .	R. U. Lemieux, T. L. Nagabhushan, and B. Paul, Can. J.
•	· ·	Chem., <u>50</u> , 773 (1972).
•	50.	A. S. Perlin and B. Casu, Tetrahedron Letters, 34,
		2921 (1969).
۱	51.	R. E. Wasylishen and T. Schaefer, Can. J. Chem., 50, 5
°		2710 (1972):
•	52	M. E. Rennekamp and C. A. Kingsbury, J. Org, Chem.,
,	·	38, 3959 (1973).
, ***	53.	J. A. Schwarcz and A. S. Perlin, Can. J. Chem., 50,
b - £		3667 (1972).
	54;	J. Karabatsos and C. E. Orzech Jr., J. Am. Chem.
5	- 5 NC	Soc., <u>86</u> , 3574 (1964).
	55.	T. Spoormaker and M. J. A. de Bie, Recl. Travl.
		.Chim. Pays-Bas, <u>98</u> , 380 (1979).
`	56.	S. Sukumar, Masters Thesis, Dalhousie University,
0	•	1977.
0	57.	J. A. Pople and A. A. Bothner-By, J. Chem. Phys.,
<u>،</u>	, r ·	<u>42</u> , 1339 (1965).
-	58.	M. Barfield and D. M. Grant, J. Am. Chem. Soc., <u>85</u> ,
all	an 479 - ¹⁶⁴⁷ 14	.1899 (1963).
r r	59.	M. Anteunis, G. Swaelens, R. Anteunis-De Ketelaere,
•	Þ	and P. Direnck, Bull. Soc. Chim. Belg. <u>80</u> , 409
-	5	(1971).
ł	60.	R. C. Cookson and T. A. Crabb, Tetrahedron, <u>24</u> , 2385
		· (1968).

ė,

f.

ø

C63.

272

- 61. R. Davies and J. Hudek, J. Chem. Soc., Perkin II, 1395 (1975).
- 62. R. Davies, J. Chem.-Soc., Perkin II,,1400. (1975).
- 63. M. J. Lacéy, C. G. MacDonald, A. Press, J. S.
 Shannon; and S. Sternhell, Aust. J. Chem., 23, 1421 (1970).
- 64. T. Spoormaker and M. J. A. de Bie, Recl. Trav. Chim.Pays-Bas, <u>99</u>, 194 (1980).
- 65. R. E. Wasylishen, K. Chum, and J. Bukata, Org. Magn. Reson., 2, 473 (1977).
- 66. S. Braun, J. Kinkeldei and L. Walther, Org. Magn. Réson., <u>14</u>, 466 (1980).
- 67. S. Braun, U. Eichenauer, Z. Naturforsch, <u>35B</u>, 1572 (1980).

68. R. Aydin, H. Gunther, J. Runsink, H. Schmickler, and J. Seel, Org. Magn. Reson., <u>13</u>, 210 (1980).

69. A. W. Douglas, Org. Magn. Reson., 9, 69 (1977).

70. A. Bax, R. Freeman, and S. P. Kempsell, J. Am. Chem. Soc., <u>102</u>, 4849 (1980)

71. S. Berger, Org. Magn. Reson., 22, 47 (1984)

72. S.: Berger, Org. Magn. Reson., <u>14</u>, 65 (1980)

-73. S. Berger, Tetrahedron; <u>36</u>, 1891 (1980)

•74. R. Jacquesý, C. Narbonne, W. E. Hull, A. Neszemelyi, and G. Lucas, J. Chem. Soc., Chem. Commun., 409

(1982).

`273

75. A. Neszemelyi and G. Lucas, J. Am. Chem. Soc. 104, 5342 (1982) 76. W. Ammann, R. Richarz, T. Wirthlin, and D. Wendisch, Org. Magn. Reson., 20, 260 (1982) 77. M. Barfield, S. A. Conn, J. L. Marshall, and D. E., Miiller, J. Am. Chem: Soc., 98, 6253 (1976) 78. P. E. Hansen, Org. Magn. Reson., 11, 215. (1978) M. Barfield, J. Am. Chem. Soc., <u>102</u>, 1 (1980) 79. V. Wray, Prog. Nucl. Magn. Reson. Spectrosc., 13, 80. 177 (1980) E. E. Hansen, Annual Reprorts NMR Spectroscopy, 11A, 81. (1981) 66 V. Wray and P. E. Hansen, ibid., 11A, 99 (1981) 82. 83. L. H.Cox and L. A.Levy, Org. Magn.' Reson., 21, 73 (1983)84. M. K. Klessinger and M. Stocker; Org. Magn. Reson., 17,, 97 (1981) K. Kamienska-Trela, Z. Biedrzycka, R. Machinek, B. 85. Rnieriem, and W. Luttke, Magn. · Réson., Org. $22, 317 (1984)^{4}$. 86. J. L. Marshall, Carbon-Carbon / and Carbon-Proton Couplings: Applications to Organic Stereochemistry and Conformational Analysis, Verlag Chemie, 4983. S. Watanabe and I. Ando, Bull. Chem. Soc. Jpn., 53, 87. 1257 (1980).

88. ¹P. Laszlo, Progress in NMR Spectroscopy, Vol. 3, 231, Perganon Press, Oxford (1967). 89. M. D. Johnson and M. Barfield, J. Chem. Phys. <u>54</u>,

3083 (1971).

90. N. D. Johnston and M. Barfield, J. Chem., Phys., <u>55</u>, 3483 (1971).

91. M. Kondor, S. Watanabe and I. Ando, Mol. Phys., <u>37</u>, 1521 (1979).

92. S. Castellano and A. A. Bothner-By, J. Chem. Phys., <u>41</u>, 3863 (1964).

93. C: W. Haigh, Ann. Reports in NMR Spectrosc., <u>4</u>, 311

- 94. P. Diehl, R. R. Harris and R. G. Jones, Progress in NMR Spectroscopy, Vol. 3, Pg. 1, Pergamon Press, Oxford (1967).
- 95: R. R. Fraser, M. A. Petit, and M. Miskow, J. Am. Chem. Soc., <u>94</u>, 3253 (1972).

96. D. Dougherty, K. Mislow, J. F. Blount, J. B. Wooten and J. Jacobus, J. Am. Chem. Soc., <u>99</u>, 6149 (1977).

97. J. P. Bloxsidge, J. A. Elvidge, J. R. Jonés, R. B. Mane, and M. Saljoughian, Org. Magn. Reson., <u>12</u>, 574 (1979).

98, J. M. A. Al-Rawi, J. A. Elvidge, and J. R. Jones, J. Chem. Soc., Perkin II, 449 (1975).

99. K. M. Crecely, V. S. Watts and J. H. Goldstein, J. Molec. Spec., <u>30</u>, 184 (1969).

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. `	` 100.	K. B. Wiberg, I). E. Barth'and	H. Schlerter, J	•
۵ ^۰ ۰ ^۰ .		Org. Chem., <u>38</u> ,	378 (1973). [*]	۰	
• • •	• 101 .	P. A. Scherr an	d J. P. Oliver	, J. Mol. Spec	ap <u>30</u> p
		184 (1969).		ı Y	· 、、、
· · · ·	402 。	Ç. A. G. Haasno	E, F. A. A. M. d	e Leeuw and C.	y,
``a```,	, *e ,	Altona, Tetrahe	dron, 2783, <u>36</u>	(1980).	
· .) .	· 103。1	R. R. Harris, 'N	iclear Magnet	ic Resonance	I
	. (Spectroscopy, Cop	op Clark Pittman	, Toronto (1983))。
•	· 104.	L. Pauling, The	Nature of the C	hemical Bond, 3	rd
		Ed., pg. 88, Cor	néll University	Press, Ithaca,	N. Y.
, č		(1960)。			**
	. 105.	R. Mulliken, J.	Chem. Phys., 2,	782 (1934)。	7
α ,	106.	J. St. John and	A. N. Block, Ph	y's. Rev. Letter	s, <u>33</u> ,
	. /	1095 (1974).	•	۰ ۱	
	107:	A. L. Allred an	d E. G. Rochow,	J. Inorg. Nucl.	
٠.		Chem., <u>5</u> , 264 (1958). 🖓		
°, °	108.	J. R. Cavanaugh	and B. P. Daile	ey, J. Chem. Phy	S.,
		34, 1099 (1961)	o ^p	• •	
•	109.	R. T. Sanderson	, J. Chem. Educ.	, <u>22</u> , 539 (1952)。
	, IIO.	G. Simons, M. E.	Zandler, and I	E. R. Tąlaty, J.	Am.
	•	Chem. Soc., <u>98</u> ,	7869 (1976).	• / •.	
	· 111.	J. C. Phillips,	Phys. Rev. Lett	erș, <u>20</u> , 550 (1	968).
••••	112.	C. Mande, P. Des	skmukh and P. De	skmukh, Atomic I	Moléc.
	-]	Phys., <u>10</u> , 2293	(1977). ⁾		
°	° 113.	R. J. Boyd and	G. E. Markus, J.	. Chem. Phys., 7	5, .
•	. !	5385 (1981). É	× ~ ~ ~		5, () ()
• ح	114.	I. Batsanov, Ru	ss. Chem. Rev.,	37, 332 (2968).	,
•			•	. .	8
ь sl	l	, .		- ,	
-	Sar.	* . •	Fi 4 1		۲.

i.

115. T. Spoormaker and M. J. A. de Bie, Recl. Travl. Chim. Pays-Bas, <u>97</u>, 138 (1978).
116. C. G. Swain and E. C. Lupton, J. Am. Chem. Soc., <u>90</u>, 4328 (1968).
117. G. Swain, J. Am. Chem. Soc., <u>105</u>, 492 (1983)
118. M. Charton, Prog. in Phys. Org. Chem., <u>13</u>, 119 1981).
119. W. F. Reynolds and R. D. Topsom, J. Org. Chem., <u>49</u>, 1989 (1984)

120. A. J. Hoefnagel, W. Oosterbeek, and B. M. Wepster, J. Org. Chem., <u>49</u>, 1993 (1984)

- 121. M. Charton, J. Org. Chem, <u>49</u>, 1997 (1984)
- 122. G. Śwain, J. Org. Chem_r, <u>49</u>, 2005 (1984),

125. N. H. Werstiuk, R. Taillefer, A. Bell, and B. Sayer, Can. J. Chem., <u>51</u>, 3010, (1973).

123. A. W. Douglas, J. Chem. Phys., <u>45</u>, 3465 (1966).

124.G. K. Hamer, I. R. Peat and W. F. Reynolds, Can. J. Chem., <u>51</u>, 897 (1973).

126. G. E. Maciel, J. W. McIver, N. S. Östlund and J. A. Pople, J. Am. Chem. Soc., <u>92</u>, 1 (1970).

127. G. E. Maciel, J. W. McIver, N. S. Ostlund and J. A. Pople, J. Am. Chem. Soc., <u>92</u>, 11 (1970).

128. G. E. Maciel, J. W. McIver, N. S. Ostlund and J. A. Pople, J. Am. Chem. Soc., <u>92</u>, 4151 (1970).

129. G. E. Maciel, J. W. McIver, N. S. Ostlund and J. A. ' Pople, J. Am. Chem. Soc., <u>92</u>, 4506 (1970). 130. D. Hottner, S. Lesko, and G. Bunsch, Org. Magn. Reson., <u>11</u>, 179 (1978).

131. H. M. Walbrosky, L. E. Allen; H. J. Traenckher, and J. Power, J. Org. Chem., <u>36</u>, 2937 (1971).

132. H. M. Walborsky, P. E. Ronman, J. Org. Chem., <u>38</u>, 4213 (1973).

133. H. M. Walbrosky and G. E. Niznik, J. Org. Chem., <u>37</u>, 187 (1972).

134. N. Ogata, S. Nazakwa and S. Murakashi, Bull. Chem. Soc. Japan, <u>43</u>, 2987 (1970).

135. H. M. Walborsky and F. J. Impastato, J. Am. Chem. Soc., <u>81</u>, 5836 (1959).

136. Org. Syn., 24, 53 (1944).

137. A. I. Vogel, A Textbook of Practical Organic Chemistry, John Wiley and Sons, New York, N.Y., 1956.

138. H. C. Brown and G. Zweifel, J. Am. Chem. Soc., <u>82</u>, 3222, 3223, 4708 (1960).

b 139. D. J. Pasto and C. R. Johnson, Organic Structure Determination, Prentice-Hall Inc., Englewood Cliffs, New Jersey (1969).

140. P. Mussini, F. Orsini and F. Pellizoni, Syn. Comm.

141. J. C. Fisher, Carbohy. Res., 59, 459 (1977).