

SPIN ECHOES AND CHEMICAL EXCHANGE

by

EARL KRAKOWER

B.Sc., McGill University, 1960

M.Sc., University of British Columbia, 1963

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF
THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

in the Department

of

Chemistry

We accept this thesis as conforming to the
required standard

THE UNIVERSITY OF BRITISH COLUMBIA

August, 1966.

In presenting this thesis in partial fulfillment of the requirements for an advanced degree at the University of British Columbia, I agree that the Library shall make it freely available for reference and study. I further agree that permission for extensive copying of this thesis for scholarly purposes may be granted by the Head of my Department or by his representatives. It is understood that copying or publication of this thesis for financial gain shall not be allowed without my written permission.

Department of Chemistry

The University of British Columbia
Vancouver 8, Canada.

Date August 25, 1966

The University of British Columbia

FACULTY OF GRADUATE STUDIES

PROGRAMME OF THE

FINAL ORAL EXAMINATION

FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

of

EARL KRAKOWER

B.Sc., McGill University, 1960

M.Sc., The University of British Columbia, 1963

TUESDAY, AUGUST 23, 1966 AT 3:30 P.M.

IN ROOM 261, CHEMISTRY BUILDING

COMMITTEE IN CHARGE

Chairman: Sydney M. Friedman

C. Froese

R. E. Pincock

D. C. Frost

L. W. Reeves

C. A. McDowell

R. C. Thompson

External Examiner: J. D. Baldeschweiler

Department of Chemistry

Stanford University

Palo Alto, California

Research Supervisor: L. W. Reeves

SPIN ECHOES AND CHEMICAL EXCHANGE

ABSTRACT

The performance of a spin echo spectrometer which is suitable for chemical exchange studies is described. Using the Carr-Purcell sequence of pulses, proton T_2 values were obtained from two experiments differing only in their method of eliminating accumulated error in the width of the 180° pulses. The Meiboom-Gill method of phase shifting the r.f. in the first pulse is more flexible in the range of pulse intervals.

Following the theory of Bloom, Reeves and Wells, rate constants describing the exchange process in two molecules were measured from the dependence of T_2 upon the pulse interval. The values of the rate constants for the hindered internal rotation about the N-N bond in N,N-dimethylnitrosamine agree with previous high resolution studies.

A similar spin echo study has been conducted in order to measure the rates of internal rotation about the C-N bond in N,N-dimethylcarbonyl chloride. The values for the entropy of activation are consistently low. The possibility of systematic errors in the spin echo method has been investigated.

It is concluded that reported values of rate constants in magnetic resonance should be the result of a spin echo investigation extending over as wide a temperature range as possible in addition to a high resolution study which involves a complete theoretical line shape fit to the experimental data.

GRADUATE STUDIES

Field of Study: Physical Chemistry

Topics in Physical Chemistry	J. A. R. Coope A. Bree
Topics in Inorganic Chemistry	N. Bartlett W. R. Cullen H. C. Clark
Topics in Organic Chemistry	J. P. Kutney D. E. McGreer R. E. Pincock
Crystal Structure	J. Trotter
Seminar	W. A. Bryce
Spectroscopy	L. W. Reeves E. J. Wells C. Reid K. B. Harvey
Chemical Physics	W. C. Lin D. C. Frost B. A. Dunell

Related Courses

Differential Equations	Dean Gage
Linear Algebra	R. C. Thompson
Physics	M. Bloom

PUBLICATIONS

1. E. Krakower, L. W. Reeves and E. J. Wells.
Disc. Far. Soc. 34, 199 (1962).
2. E. Krakower and L. W. Reeves.
Trans. Far. Soc. 59, 2528 (1963).
3. E. Krakower and L. W. Reeves.
Spectrochimica Acta, 20, 71 (1964).
4. K. H. Abramson, P. T. Inglefield, E. Krakower
and L. W. Reeves. Can. J. Chem. 44, 1685
(1966).

Supervisor: L.W. Reeves.

i

ABSTRACT

The performance of a spin echo spectrometer which is suitable for chemical exchange studies is described. Using the Carr-Purcell sequence of pulses, proton T_2 values were obtained from two experiments differing only in their method of eliminating accumulated error in the width of the 180° pulses. The Meiboom-Gill method of phase shifting the r.f. in the first pulse is more flexible in the range of pulse intervals.

Following the theory of Bloom, Reeves and Wells, rate constants describing the exchange process in two molecules were measured from the dependence of T_2 upon the pulse interval. The values of the rate constants for the hindered internal rotation about the N-N bond in N,N-dimethylnitrosamine agree with previous high resolution studies.

A similar spin echo study has been conducted in order to measure the rates of internal rotation about the C-N bond in N,N-dimethylcarbonyl chloride. The values for the entropy of activation are consistently low. The possibility of systematic errors in the spin echo method has been investigated.

It is concluded that reported values of rate constants in magnetic resonance should be the result of a spin echo investigation extending over as wide a temperature range as possible in addition to a high resolution study which includes a complete theoretical line shape fit to the experimental data.

Table of Contents

CHAPTER		PAGE
I	<u>INTRODUCTION</u>	
	A. Rotating Co-ordinates	1
	B. Nuclear Relaxation Processes and Diffusion Effects	2
	C. Chemical Exchange Theory in Nuclear Magnetic Resonance	9
	D. Hindered Internal Rotation and Molecular Conformation	16
II	<u>EXPERIMENTAL</u>	
	A. Preparation of Compounds	21
	B. The Spin Echo Spectrometer	22
	C. Magnet Systems	25
	D. Measurement and Reliability	28
	E. Computer Programs	28
III	<u>EXPERIMENTAL RESULTS</u>	31
	A. N,N-Dimethylnitrosamine	31
	(i) Free Induction Tail Experiments	32
	(ii) Carr-Purcell Trains	33
	(iii) Limiting Cases - Off and On Resonance	34
	(iv) Calculation of ' r_1 '	38
	(v) Activation Parameters	40
	B. N,N-Dimethylcarbonyl Chloride	42
	(i) Calculation of ' r_1 '	43
	(ii) Limiting Cases	46
	(iii) T_2^O , T_1 , Data	48
	(iv) Activation Parameters	50

CHAPTER		PAGE
IV	<u>DISCUSSION</u>	53
	A. Experimental Consideration	53
	B. Sensitivity of the Rate Constant and Activation Parameters to Systematic Errors	56
	C. Comments on the Spin Echo Method	65
V	<u>BIBLIOGRAPHY</u>	68

List of Illustrations

Figure		To follow page
I	Transverse Components of the Magnetic Moment Referred to Fixed Axes and Axes Rotating with the R.F. Field.	2
II	The Formation of an Echo after Successive 90 and 180° Pulses.	6
III	Schematic Relationship of the Magnetization Observed in a $\frac{\pi}{2}, \pi, \pi, \dots$ Pulse Sequence.	11
IV	Transmitter Circuit	22
V	Block Diagram of Receiver Circuit	23
VI	Receiver Circuit	23
VII	Generation of the Carr-Purcell Sequence	23
VIII	Reference Signal Amplifier, Multiplier, Phaser and Attenuator	25
IX	Waveforms Resulting from Frequency Multiplication Showing Respective Amplitudes	25
X	Free Induction Decay for DMNA	32
XI	Carr-Purcell Trains of the Protons in DMNA	33
XII	Short τ Limit Plot for DMNA-off Resonance	35
XIII	Short τ Limit Plot for DMNA-on Resonance	35
XIV	Dependence of $T_2(C.p)$ upon the Pulse Interval for DMNA	38
XV	Activation Energy Determination for DMNA	40
XVI	Dependence of T_2 upon the Pulse Interval for DMCC	43
XVII	Short τ Limit Plot for DMCC	46

Figure	To follow page
XVIII Temperature Dependence of T_2^0 , T_1	49
XIX Activation Energy Determination for DMCC	50

List of Tables

Table		Page
I	Dimethylnitrosamine-Rate Constants from $r_1 \approx k \mp k \pm \frac{2}{3} k (\omega \zeta)^2$	37
II	Dimethylnitrosamine-Rate Constants from $r_1 = k - (\frac{1}{2\zeta}) \sinh^{-1} F$	39
III	Dimethylnitrosamine-Comparison of Rate Constants.	40
IV	Dimethylnitrosamine-Comparison of Activation Parameters.	42
V	Dimethylnitrosamine-"Besfit" to $r_1 = k - (\frac{1}{2\zeta}) \sinh^{-1} F$	45
VI	Rate Constant Data for Dimethylcarbamyl Chloride.	47
VII	Dimethylcarbamyl chloride-Temperature Dependence of T_2^O .	50
VIII	Dimethylcarbamyl chloride-Activation Parameters.	51

ACKNOWLEDGMENTS

The Spin Echo method in Nuclear Magnetic Resonance represents a relatively new and interesting approach to the study of Chemical Exchange. In this regard I wish to thank Dr. L. W. Reeves for his helpful direction and sincere dedication to this research program. His advice has been deeply appreciated.

I am grateful to Mr. P. T. Inglefield for advice and discussion regarding the construction of apparatus. The quality of this thesis has been enhanced by discussion with Mr. Inglefield who has made available to me results on similar systems.

I am grateful to Dr. C. A. McDowell, for allowing me to work in the Chemistry Department and gain the experience that I now have in undergraduate teaching.

Acknowledgments are accorded to Mr. K. H. Abramson and to Mr. E. Fisher for their work on the spin echo spectrometer. I am grateful to Mr. R. Wolfe and to Dr. J. Herring for help with the computer programs.

INTRODUCTION

CHAPTER I

A) Rotating Co-Ordinates:

An insight into the nature of nuclear induction (1) experiments is obtained from a consideration of the magnetic moment components referred to a rotating set of co-ordinates (2).

In a field \underline{H} , a macroscopic nuclear magnetic moment \underline{M} per unit volume experiences a torque ($\underline{M} \times \underline{H}$) which is equal to the rate of change $\gamma \hbar \frac{d\underline{I}}{dt}$ of its angular momentum. The equation of motion of a system in the stationary co-ordinate system is:

$$\hbar \left(\frac{d\underline{I}}{dt} \right) = \gamma \hbar [\underline{I} \times \underline{H}] = \gamma \underline{M} \times \underline{H} \quad (1)$$

where γ is the gyromagnetic ratio.

In order to solve equation (1), it is useful to transform to a frame of reference rotating with an angular velocity $\underline{\omega}$ with respect to the stationary frame. Then:

$$\frac{d\underline{I}}{dt} = \frac{\partial \underline{I}}{\partial t} + [\underline{\omega} \times \underline{I}] \quad (2)$$

where $\frac{\partial \underline{I}}{\partial t}$ represents the time dependent measurement of \underline{I} by an observer in the rotating reference frame. Combining equations (1) and (2), the motion of the magnetic moment in the rotating frame is given by:

$$\hbar \frac{\partial \underline{I}}{\partial t} = \gamma \hbar \underline{I} \times \left(\underline{H} + \frac{\underline{\omega}}{\gamma} \right) \quad (3)$$

Now the magnetic field \underline{H} is replaced by an effective field

$$\underline{H}_{\text{eff}} = \left(\underline{H} + \frac{\omega}{\gamma} \right).$$

For a magnetic field \underline{H}_0 which is constant in time, $H_{\text{eff}} = 0$ when observed from a frame of reference rotating with $\underline{\omega}_0 = -\gamma \underline{H}_0$. With respect to the stationary reference frame the magnetic moment vector precesses with an angular velocity $\underline{\omega}_0 = -\gamma \underline{H}_0$. This is the Larmor precession frequency of the spin in an applied magnetic field \underline{H}_0 (3).

B) Nuclear Relaxation Processes and Diffusion Effects:

Consider a set of nuclei placed in a fixed magnetic field \underline{H}_0 acting in the z direction and also subjected to a radio frequency field \underline{H}_1 applied orthogonally to \underline{H}_0 . The components of the \underline{H}_1 field rotating with an angular frequency ω are:

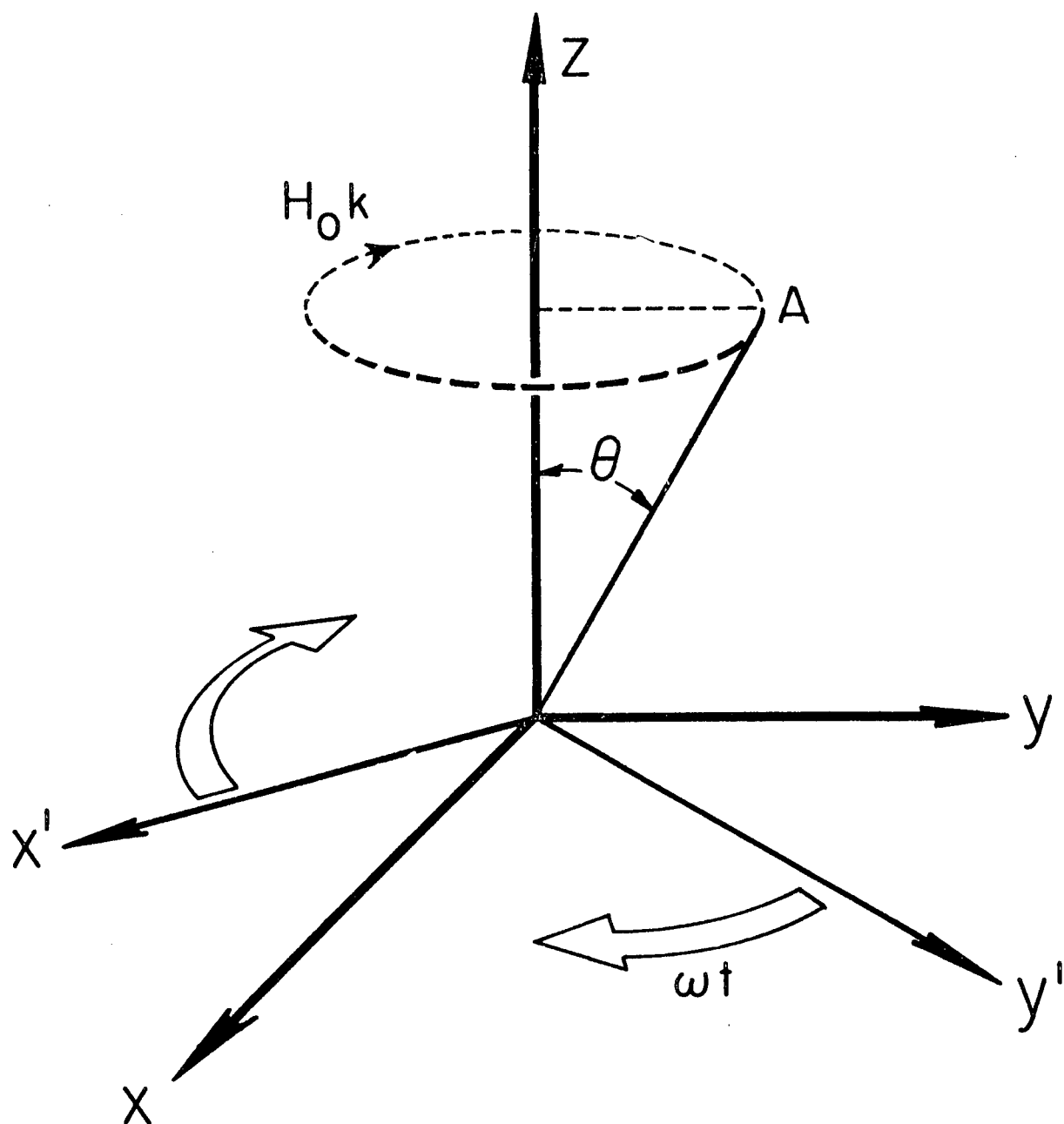
$$\begin{aligned} (H_1)_x &= H_1 \cos \omega t \\ (H_1)_y &= -H_1 \sin \omega t \end{aligned} \tag{4}$$

The Bloch equations(1) are now referred to a set of axes rotating with the \underline{H}_1 field. If u and v are the components of \underline{M} directed along and perpendicular to the direction of the \underline{H}_1 field, then:

$$\begin{aligned} u &= M_x \cos \omega t - M_y \sin \omega t \\ v &= -M_x \sin \omega t - M_y \cos \omega t \end{aligned} \tag{5}$$

The transverse components of magnetization in the stationary and rotating set of co-ordinates are illustrated in figure I.

The Bloch equations(1) referred to the rotating axes are:



$$\frac{du}{dt} + \frac{u}{T_2} + (\omega_0 - \omega)v = 0 \quad (6)$$

$$\frac{dv}{dt} + \frac{v}{T_2} - (\omega_0 - \omega)u + \gamma H_1 M_z = 0 \quad (7)$$

$$\frac{dM_z}{dt} + \frac{M_z - M_0}{T_1} - \gamma H_1 v = 0 \quad (8)$$

The time constants T_1 and T_2 describe relaxation mechanisms which involve transitions brought about by nuclei exchanging energy with their environments and with themselves.

With the application of a steady H_0 field to a set of nuclei, at equilibrium, the population of the $(2I + 1)$ Zeeman levels (for protons, spin $I = 1/2$) is governed by the Boltzmann factor, $\exp(2\mu H_0/kT)$, with the excess number in the lower states. The system is subjected to the H_1 field and the previously attained equilibrium state is now disturbed. The process of spin lattice relaxation re-establishes the Boltzmann excess of nuclei in the lower state (4). T_1 then is the time constant for the system to reach equilibrium. Essentially it is the time required for M_z , the component of nuclear magnetization in the direction of H_0 , to decay back to the equilibrium magnetization M_0 . This is described by:

$$M_z = M_0 (1 - 2e^{-t/T_1}) \quad (9)$$

where t is the time in which M_z is sampled.

In the introduction to his paper, Bloch(1) suggested the possibility of observing a nuclear induction signal in the absence of the r.f. field by subjecting the system to a pulse of r.f. energy. Torrey(5)

considered the solutions to the Bloch equations when the r.f. field is suddenly applied. Methods of measuring T_1 and T_2 are presented(5).

The experimental effects of the free nuclear precession about a static magnetic field after the r.f. field is removed was first reported by E.L. Hahn(6). In 1950 Hahn(7) published his classic paper on the measurement of nuclear relaxation times by employing a pulsed \underline{H}_1 field rather than a continuous radio frequency field.

The effect of the rotating field \underline{H}_1 at the resonance frequency is to alter the direction of the bulk nuclear magnetization vector \underline{M} . At equilibrium, \underline{M} is parallel to the direction of \underline{H}_0 . When the \underline{H}_1 field is applied, \underline{M} will change its direction depending upon the duration of the pulse, and will precess about the static field at the Larmor frequency. Hahn(7) referred to this signal as the FREE INDUCTION DECAY.

An r.f. pulse of amplitude H_1 and duration t_w will rotate the magnetization vector \underline{M} from the z direction with an angular velocity of γH_1 . Adjusting H_1 and t_w such that $\gamma H_1 t_w = \frac{\pi}{2}$ the magnetization vector \underline{M} will be rotated into the x-y plane. The pulses are referred to as 90° pulses and immediately after the pulse, \underline{M} will be in the y direction. The component of magnetization in the x-y plane perpendicular to \underline{H}_0 precesses about the z direction and its amplitude decays exponentially. The induction signal decays with a rate e^{-t/T_2^*} , where T_2^* involves the width of the line due to magnetic field inhomogeneities and includes the natural relaxation time, T_2^0 .

The effects of magnetic field inhomogeneities will result in a

distribution of the Larmor frequencies ω_0 usually assumed to be Gaussian. Hahn (7) has considered the behaviour of the magnetization vector \underline{M} at different times in the decay process. The spin vectors--called spin isochromats--are rotated into the x-y plane by a 90° pulse. If the pulse is applied along the x' axis in the rotating co-ordinate system, then after the removal of the $\frac{\pi}{2}$ pulse the spin vectors are parallel to the y' axis.

Since there is a distribution in the Larmor frequencies, the vectors of the spin isochromats fan out in the x'-y' plane. Considering a magnetization vector in a region where its Larmor precession frequency is greater than the mean by $\Delta\omega_0$, the magnitude of the spin isochromat is reduced by e^{-t/T_2^*} and the vector is at an angle of $(\Delta\omega_0)t$ from the mean vector. In this case t is the time measured after the removal of the 90° pulse. The resultant is proportional to

$$e^{-t/T_2^*} \int_{-\infty}^{\infty} g(\Delta\omega_0) \cos(\Delta\omega_0 t) d(\Delta\omega_0).$$

$g(\Delta\omega_0)$ represents a Gaussian distribution of the Larmor frequencies and

$$g(\Delta\omega_0) = (2\pi)^{-1/2} T_2^* \exp\left[-(\Delta\omega_0 T_2^*)^2 / 2\right]. \quad (10)$$

At a later time τ after the 90° pulse the sample is subjected to a second pulse of r.f. energy. This π pulse, applied for twice the duration of the $\frac{\pi}{2}$ pulse, rotates the magnetization vectors in the plane by 180° . The relative phase angle between two magnetization vectors

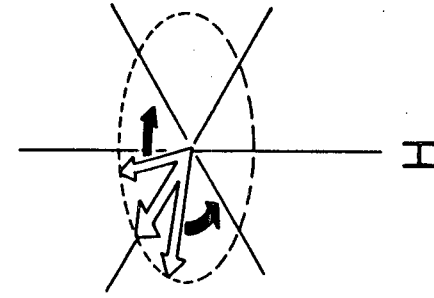
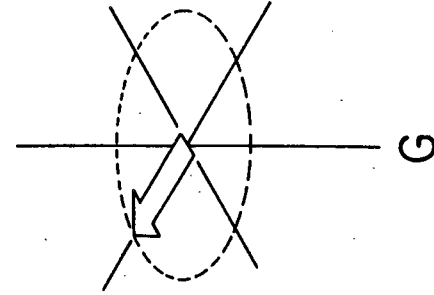
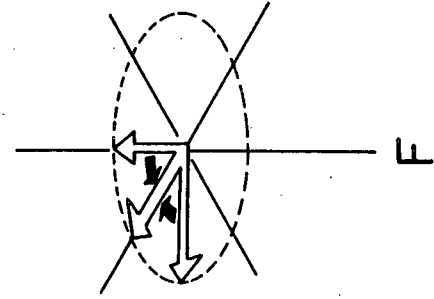
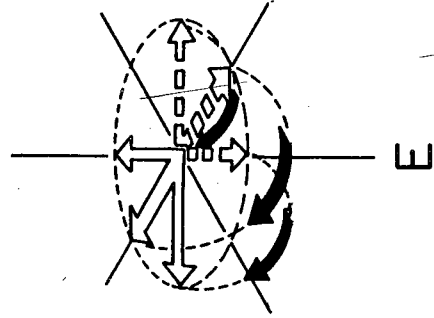
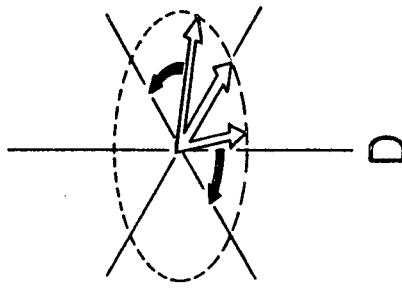
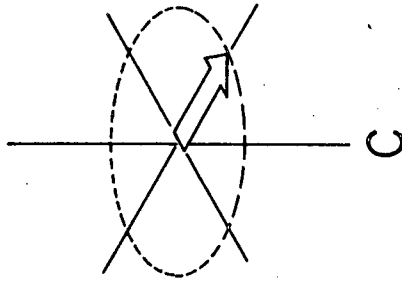
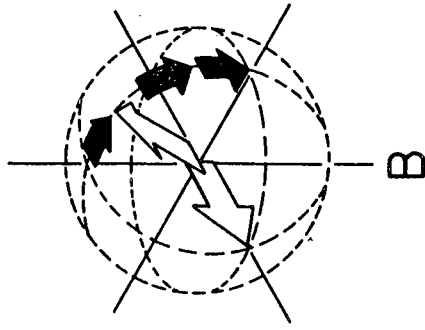
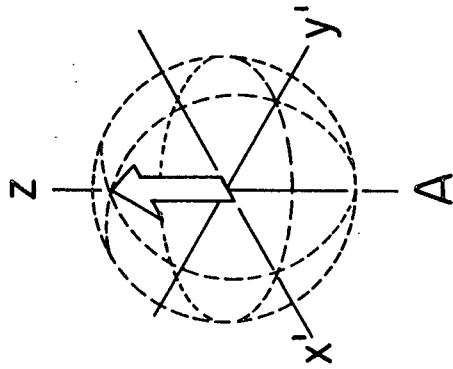
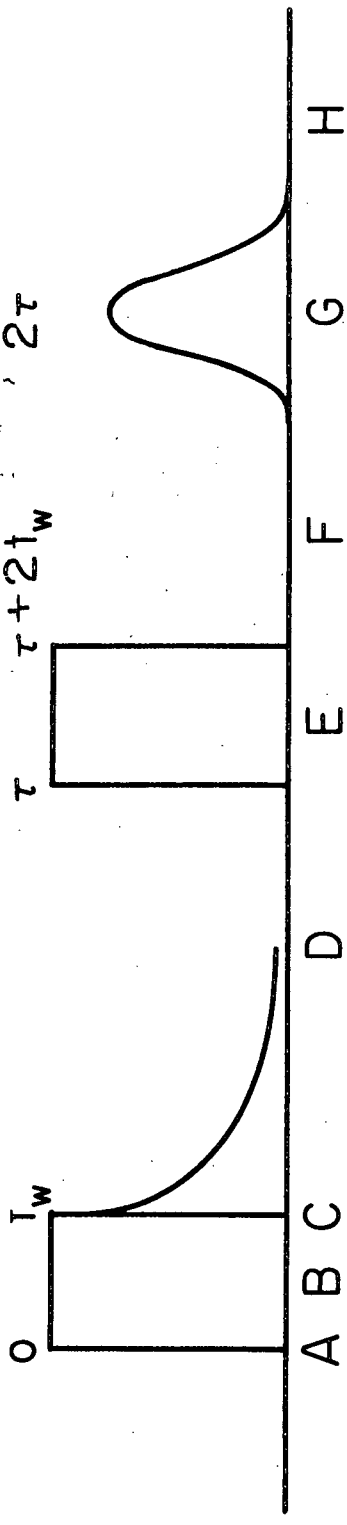
which had been increasing after the pulse now decreases. Assuming that the precession frequency of the magnetization vectors is constant, the effect of the pulse is to cause the vectors to constructively interfere giving rise to a signal at a time 2τ . This induced nuclear signal is referred to as the SPIN ECHO. (Figure II).

Hahn(7) directly measured T_2 by plotting the logarithm of the maximum echo amplitude versus arbitrary values of 2τ . Hahn's T_2 values for protons in an aqueous solution of Fe^{+3} ions was in good agreement with results obtained by Bloembergen(4).

In liquids diffusion processes are not always negligible. Some of the vectors change their rate of fanning out when the molecules move in an inhomogeneous field. As a result diffusion processes attenuate the amplitude of the spin echo since the number of nuclei rephased at a time 2τ is reduced.

Hahn noted and developed the theory of the "stimulated echo" which appears in company with other echoes when a third pulse is applied at a time T such that $2\tau < T < T_2$. If $k\tau^2 T \ll T/T_1$ then a plot of the logarithm of the amplitude of the stimulated echo versus T gives a measure of T_1 , the spin-lattice relaxation time. Bloom and Muller(8) have calculated the effect of diffusion on the stimulated echo.

Carr and Purcell(9) successfully extended the work of Hahn(7) by developing a more reliable method of measuring T_2 and at the same time minimizing the effects of molecular diffusion. Their procedure



involved the application of a single $\frac{\pi}{2}$ pulse followed by a series of n/π pulses applied at times $\tau, 3\tau, 5\tau, \dots$. After each π pulse an echo appears and the exponential decay of the echo amplitudes is a measure of the time constant T_2 . The expression for the transverse magnetization, M_y' , as observed from a frame of reference rotating with the Larmor frequency is given as:

$$M_y'(t) = M_0 \exp \left[(-t/T_2) + (-\gamma^2 G^2 D t^3 / 12 n^2) \right] \quad (11)$$

where: M_0 is the equilibrium magnetization.

t is the time corresponding to a given echo amplitude.

G is the magnitude, in gauss/cm, of the magnetic field gradient.

D is the molecular self-diffusion constant in cm^2/sec .

n is the number of π pulses applied after the initial $\frac{\pi}{2}$ pulse.

It is seen from equation (11) that diffusion effects can be minimized in a Carr-Purcell experiment by applying a large number of π pulses in a $\frac{\pi}{2}, \pi, \pi, \dots$ sequence. Carr and Purcell (9) clearly illustrated this by comparing the values of T_2 for water given by the Hahn method in a two pulse multiple exposure sequence (Method I) with the $\frac{\pi}{2}, \pi, \pi, \dots$ series (Method II). Method I gave a value of 0.2 seconds compared with the Carr and Purcell measurement of 2.0 seconds.

Carr and Purcell(9) have described a method for measuring T_1 , the spin-lattice relaxation time. The effect of an initial π pulse is to invert the magnetization vector 180° into the $-z$ direction. T_1 relaxation processes begin to return the z - component to its original value.

$\frac{\pi}{2}$ pulses applied at various times τ nutates the total magnetic moment vector into the equatorial plane. A free induction decay signal appears after the 90° pulse. The signal amplitudes increase algebraically in an apparatus provided with r.f. phase detection and provide a measure of T_1 . For one value of τ i.e. τ_{null} there is no tail. T_1 at this point is calculated approximately from:

$$\tau_{\text{NULL}} = T_1 \ln 2 \quad (12)$$

The null method of measuring T_1 can only be used if the pulse duration is very accurately set.

Douglas and McCall (10) have used the spin echo method to measure self diffusion coefficients of a series of paraffin hydrocarbons and obtained linear plots of $\ln D$ vs $1/T$. Diffusion coefficients of CH_4 , CF_4 and mixtures of the two in argon have been measured by Rugheimer and Hubbard (11) from T_1 pulse data. Woessner (12) has calculated the effects of diffusion for a three and four pulse sequence. He has measured diffusion coefficients (13) from the proton T_1 values of n-paraffins in CCl_4 solutions and considered (14) the movement of molecules undergoing restricted diffusion. A publication by Stejskal and Tanner (15) investigated the effect of a controlled magnetic field gradient on the spin echo experiment. By keeping the field gradient small during the application of the pulse and during the time of the echo, they were able to observe the effects of smaller diffusion constants from the change in amplitude of the broadened echo and to overcome the requirement that

$\gamma_{H1} \gg (\Delta\omega)_{1/2}$ in very inhomogeneous fields needed for certain diffusion studies.

C) Chemical Exchange Theory in Nuclear Magnetic Resonance:

A nucleus with spin $I > 0$ which exchanges between two or more chemically distinct environments precesses at a different Larmor frequency in each of the sites. The exchange mechanism represents a time dependent process which will influence the shapes and widths of the resonance signals (3). Neglecting the effects of spin-spin coupling and considering the sites to be equally populated, the N.M.R. spectrum shows two signals of equal amplitude and line width when $k < \omega$. In the region of rapid exchange-- $k > \omega$ and $\omega = p_a \omega_a + p_b \omega_b$ -- the two signals collapse to a single peak. (k = rate constant, ω = chemical shift.)

The theory of nuclear transfer effects in magnetic resonance was originally developed by Gutowsky, McCall and Slichter (16) who modified the Bloch (1) equations for chemical exchange between two equally populated sites. Subsequent investigations considered exchange between unequally populated sites (17) and the effects of chemical exchange with nuclear spin-spin coupling (18). Hahn and Maxwell (19) and McConnell (20) generalized the modified (16) Bloch (1) equations and McConnell (20) considered a nucleus being transferred between two sites having different relaxation properties. Alexander (21,22,23) has further developed the exchange theory of nuclear spins in magnetic resonance using spin density matrices. His work represented a quantum mechanical

extension of the classical theory developed by Piette and Anderson (24). An interesting review article discussing the use of steady state N.M.R. techniques to the study of chemical exchange rates has been written by Loewenstein and Conner (25).

The investigation into the use of pulse methods to study chemical exchange began in 1961. At that time Woessner (26) considered the mechanism of nuclear transfer in magnetic resonance as being somewhat analagous to the diffusion process. In this regard, chemical exchange effects are a function of the τ pulse repetition frequency in the Carr-Purcell (9) experiment (equation (11)).

Luz and Meiboom (27) have calculated the spin echo decay rate in the presence of chemical exchange. They have derived the following theoretical equation for the dependence of T_2 upon the pulse repetition frequency in the region of rapid exchange:

$$\frac{1}{T_2} = \frac{1}{T_2^0} + P_a P_b (\delta\omega)^2 \tau \left[1 - (2\tau/t_{C.P.}) \tanh(t_{C.P.}/2\tau) \right] \quad (13)$$

where: T_2^0 is the natural relaxation time.

P_a, P_b are the nuclear populations in sites A and B.

$\delta\omega$ is the chemical shift.

$t_{C.P.}$ is the pulse repetition frequency.

2τ is the mean exchange lifetime.

The contents of the results reported in this thesis are based upon a theoretical study of spin echoes and chemical exchange developed

by Bloom, Reeves and Wells (28). The theory to date has been confined to the case of exchange between two sites in the absence of spin-spin coupling.

In order to develop equations describing the nuclear magnetization, probability theory is used to compute the phase angle distribution function $P(\phi, t)$ of the nuclear spins in the $x'-y'$ plane allowing any number of site transfers and r.f. pulses in a time t .

Consider individual nuclei with spin $I > 0$ which can exchange between two sites A and B in a molecular system. In the absence of transfer between the two sites, nuclei located in A and B will precess in their respective sites with an angular frequency of ω_a and ω_b . The expression for the nuclear magnetization is given by:

$$M(t) = \left[(P_a \cos \omega_a t + P_b \cos \omega_b t) \underline{i} + (P_a \sin \omega_a t + P_b \sin \omega_b t) \underline{j} \right] G(t) \quad (14)$$

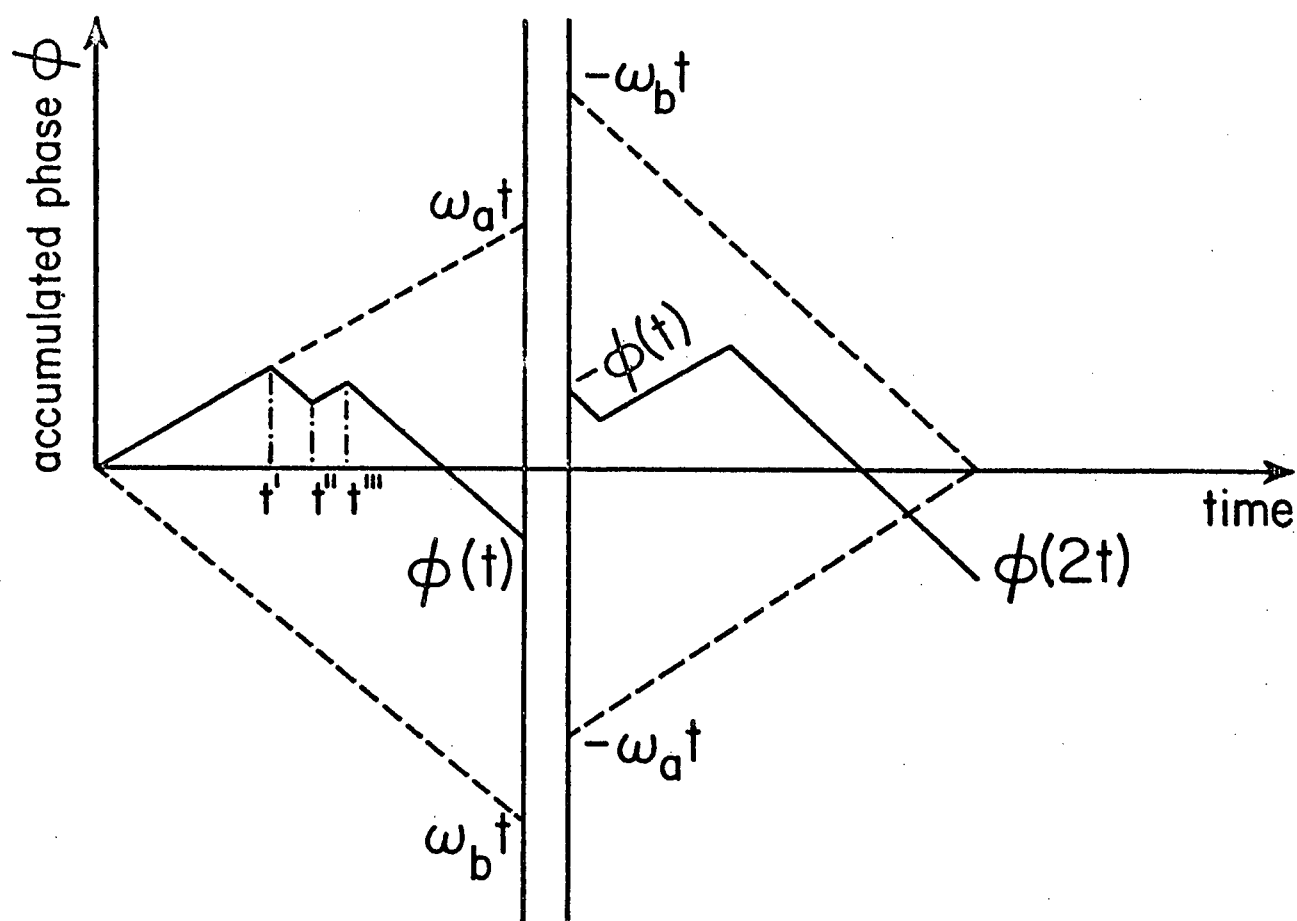
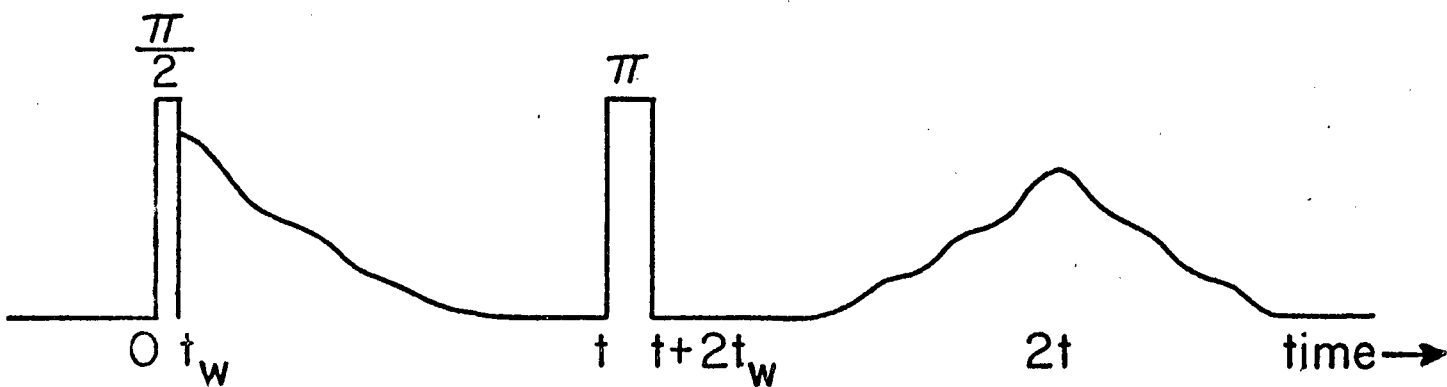
where: P_a, P_b are the fractional populations in sites A and B.

$G(t)$ is a relaxation function describing the decay of $M_x(t)$ and $M_y(t)$ and in this treatment $G(t) = 1$.

The accumulated phase can be written as:

$$\phi(t) = \int_0^t \omega(t') dt' \quad (15)$$

The application of a π pulse at a time τ after the first $\frac{\pi}{2}$ pulse transforms the phase $\phi(\tau)$ into $2\phi_0 - \phi(\tau)$ where ϕ_0 is the phase of the H_1 field in the rotating co-ordinate system. For simplicity, $\phi_0 = 0$. The phase collected by a nucleus as it exchanges between A and B during a two pulse-echo sequence is illustrated in figure III.



Using recursion formulae in order to follow the accumulated phase of a nucleus performing "n" jumps in a time "t", the BRW theory derived the following expressions for the nuclear spin magnetization

$M_a(t)$ and $M_b(t)$:

$$M_a(t) = f_a e^{i\phi_a} \langle e^{i\phi(t)} \rangle_{aa} + f_b e^{i\phi_b} \langle e^{i\phi(t)} \rangle_{ba} \quad (16a)$$

$$M_b(t) = f_b e^{i\phi_b} \langle e^{i\phi(t)} \rangle_{bb} + f_a e^{i\phi_a} \langle e^{i\phi(t)} \rangle_{ab} \quad (16b)$$

where: f_a, f_b are the a priori lengths of the magnetization vectors in A and B.

ϕ_a, ϕ_b are the initial phases.

ϕ_o , the phase of the r.f. field in the rotating co-ordinate system is assumed to be zero. For each 180° pulse $M_a(t)$ and $M_b(t)$ must be multiplied by $e^{-2i\phi_o}$.

Equations (16a) and (16b) are solutions to the equations for $M_a(t)$ and $M_b(t)$ derived by Hahn and Maxwell (19) and McConnell (20).

A matrix operator \underline{E} having as a matrix element

$$E_{ij} = \sum_k \langle e^{i\phi(\tau)} \rangle_{ik} \langle e^{i\phi(\tau)} \rangle_{kj}, \quad \tau = \frac{t}{2} \quad (17)$$

has been used to evaluate the amplitude of the spin echo at a time

2τ . The magnetization $M(2\tau)$ is expressed in matrix form as:

$$\begin{pmatrix} M_a(2\tau) \\ M_b(2\tau) \end{pmatrix} = \begin{pmatrix} E_{aa} & E_{ab} \\ E_{ba} & E_{bb} \end{pmatrix} \begin{pmatrix} M_a^*(0) \\ M_b^*(0) \end{pmatrix} \quad (18)$$

In the Carr-Purcell (9) experiment, π pulses are applied at $(2n+1)\tau$, $n=0,1,2,\dots$ and the theory has developed the relationship of the magnetization at the $2n^{\text{th}}$ echo to the initial magnetization $M(0)$ as:

$$M(4n\tau) = (\underline{E}\underline{E}^*)^n M(0) \quad n \text{ even} \quad (19)$$

For the case of chemical exchange between sites, they (28) have shown that the echo envelope is in fact a superposition of two exponentials and as such:

$$M(4n\tau) = A_1 e^{-r_1 4n\tau} + A_2 e^{-r_2 4n\tau} \quad (20)$$

where: r_1, r_2 are the time constants which are independent of the initial conditions.

A_1, A_2 are the amplitudes which depend upon the initial conditions.

The eigenvalue equation involving the matrix operator is given as:

$$(\underline{E}\underline{E}^*)\underline{\mu}_i = \lambda_i e^{-4k\tau} \underline{\mu}_i \quad \underline{\mu}_i = \frac{\mu_{ia}}{\mu_{ib}} \quad (21)$$

where: $\underline{\mu}_i$ are the eigenfunctions.

λ_i are the eigenvalues.

Substituting in equation (12) the generalized expression for the time constants is:

$$r_i = k - (\ln \lambda_i / 4\tau) \quad (22)$$

Spin echo results reported in this thesis were obtained using diode detection where the signal is proportional to the magnitude of the nuclear magnetization in the x-y plane and is independent of ω_0 . This is a more convenient method experimentally as the resonance condition does not have to be so precisely defined as it would be using phase sensitive detection. Theoretically however, using diode detection, the echo envelope is more complicated because of cross terms introduced between the eigenfunctions μ_1 and μ_2 . However for a two site exchange both methods of detection will give an exponential envelope decay which corresponds to the larger of the two time constants r_1^{-1} and r_2^{-1} . Results reported here measure r_1 . Although theoretically predicted, r_2 has not as yet been experimentally observed.

For the case of equal populations, the eigenvalues are always real. The time constant for the decay of the echo amplitudes in a Carr-Purcell sequence is given by:

$$r_1 = k - \frac{1}{2\tau} \sinh^{-1} F \quad (23)$$

F has been computed for the exchange regions as:

$$\omega > k: F = \frac{k}{(\omega^2 - k^2)^{1/2}} \sinh 2\tau(\omega^2 - k^2)^{1/2} \quad (24)$$

$$\omega < k: F = \frac{k}{(k^2 - \omega^2)^{1/2}} \sinh 2\tau(k^2 - \omega^2)^{1/2} \quad (25)$$

$$\omega = k: F = 2k\tau \quad (26)$$

$$r_1 = \frac{1}{T_2} - \frac{1}{T_2^0} \quad \text{incorporates the effect of exchange and the natural relaxation time.}$$

$1/T_2$ c.p. is the observed time constant.

T_2^0 is the natural relaxation time which

is obtained in nonviscous liquids from

a measure of T_1 .

k is the mean rate constant for the exchange $= \frac{k_a + k_b}{2}$.

ω is half the chemical shift $= \frac{\omega_a - \omega_b}{2}$.

τ is the $\frac{\pi}{2}, \pi$ pulse interval.

Some limiting cases for r computed in BRW theory and amenable to experimental verification are:

	EQUATION	CONDITIONS
SHORT τ LIMIT	$r_1 = \frac{2}{3} k (\omega \tau)^2$ (27)	$k \tau \ll 1, \omega \tau \ll 1, \omega < k$ or $k < \omega$
LONG τ LIMIT	$r_1 = \omega^2 / 2k$ (28)	$\sinh 2\tau(k^2 - \omega^2) \gg 1, \omega \ll k$

In this thesis an attempt has been made to verify experimentally the BRW theory using two molecules each of which involves nuclear transfer between two equally populated sites.

Allerhand and Gutowsky (29) have used Woessner's equations (26) to derive an expression similar to the Meiboom equation (27). However the equation leads to inaccuracies in the slow exchange region for systems with two sites separated by a large chemical shift. As a result Allerhand and Gutowsky (30) derived closed form expressions for the decay of the echo amplitudes in the Carr-Purcell sequence. Their expression is the same as equation (23) derived in the Bloom, Reeves and Wells theory (28).

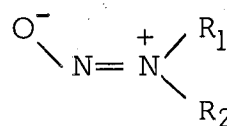
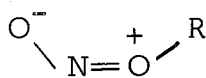
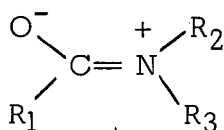
Powles and Strange (31) have theoretically considered the modulation of the echo amplitude for a two site exchange system with nuclear spin-spin coupling. They have investigated the effect of amplitude modulation for the hydroxyl proton exchange in methyl alcohol. Gutowsky, Vold and Wells (32) have formulated a general theory of chemical exchange effects in N.M.R. Assuming equal relaxation in the sites, in the Carr-Purcell sequence they have used density matrices to indicate that both exchange and J coupling effects could be removed in the limit of rapid pulsing. Further, in the region of very fast exchange, the modulation of spin echoes due to spin-spin coupling is removed. Allerhand (33) has derived general equations which describe the effect of homonuclear coupling on the Carr-Purcell experiment.

Since chemical exchange may be incorporated as a relaxation mechanism into basic relaxation theories (4), it is amenable to study by pulse double resonance experiments. This technique for the study of relaxation processes in liquids has been developed by Baldeschwieler (52). Though the technique has not as yet been used to derive kinetic data for chemical exchange the obvious application exists.

D) Hindered Internal Rotation and Molecular Conformation:

Experiments in nuclear magnetic resonance have contributed significantly to the study of structural isomerism. Many amides and nitrites have potential energy barriers which are due to the partial

double bond character of the C-N, O-N and N-N bonds (25). These bonds assume their partial double bond character from resonance forms of the type:



If the barrier to conversion from one isomer to another is relatively high, then the exchange will be sufficiently slow to resolve two separate signals in the N.M.R. spectrum. This occurs in the region where the rate constant is less than the chemical shift.

Many publications have considered the application of N.M.R. to the study of hindered internal rotation (25). Variations in the method of experimentation and evaluation of data have led to discrepancies among independent workers who report different activation parameters for the same chemical system.

Pertinent to our investigations in this laboratory, Rogers and Woodbrey (34) have studied hindered internal rotation in a series of substituted N,N-dimethylamides. They have measured the mean lifetime of a nucleus exchanging between two sites as a function of temperature by calculating the ratio of the maximum to minimum signal intensities (35). In N,N-dimethyltrichloroacetamide and N,N-dimethylcarbamylochloride the activation parameters were not in agreement with the spin echo measurements of Gutowsky (29). Carr-Purcell measurements made in this laboratory (36) have reported a higher value compared with Rogers and

Woodbrey (34) for the activation energy of N,N-dimethyltrifluoroacetamide. Since this compound has a small chemical shift, it was proposed that the spin echo method provided a better estimation of the true rate constants. The spin echo method has the advantage of more easily taking into account variations with temperature of T_2^0 and the chemical shift.

Phillips (37) has conducted a variable temperature study of N,N-dimethylnitrosamine. The room temperature N.M.R. spectrum consisted of two peaks chemically shifted by 26 c.s. He has reported a barrier height for the exchange of the methyl groups of 23 Kcal./mole. Brown and Hollis (38) have questioned the previous assignments of the N.M.R. spectra of alkyl nitrites and nitrosamines. They felt that other mechanisms apart from hindered internal rotation should be considered for the interconversion. Blears (39) has studied the N.M.R. spectrum of dimethylnitrosamine up to 190°C. His reported activation energy, obtained from the ratio of I_{\min}/I_{\max} , of 25 Kcal/mole is in good agreement with the value obtained by Phillips (37).

Solvent effects on the energy barrier have been reported for the hindered internal rotation in some molecules. Woodbrey and Rogers (40) have found a strong dependence of the barrier height upon the nature and concentration of the solvent. They resolved their results by considering the more polar of the two possible resonance forms in some di-substituted amides is stabilized to a higher degree in more polar solvents. Large solvent effects interpreted in terms of dipolar

association have been found between dimethylformamide and solvent (41). Blears (39,42) has considered the effect of solvents in dimethylnitrosamine, and in the complexing of boron halides with dimethylformamide, variations in the activation energy are attributed to changes in the π character of the C-N bond when one of the resonance forms is stabilized by the formation of the complex.

Nuclear magnetic resonance rate studies of the ring inversion in saturated six-membered ring systems have been investigated in cyclohexane, substituted cyclohexanes, piperazine and dioxane.

Since cyclohexane is an A_6B_6 system, the rate of inversion has been studied using cyclohexane- d_{11} . Bovey et al (43) studied conformational isomerism in $C_6D_{11}H$ from -75° to -47° . Any line broadening arising from H-D coupling was eliminated by double resonance. Anet, Ahmad and Hall (44) obtained an activation energy of 11.3 Kcals/mole for $C_6D_{11}H$ studied from -94° to $-32^\circ C$. However in a second publication (45) discussing ring inversion in cyclohexane, Anet indicated that his earlier work contained an arithmetical error in the rate constant calculation. His corrected value of E_a is 10.9 Kcal/mole. Allerhand, Chen and Gutowsky (46) have used the spin echo method to study conformational isomerism of C_6H_{12} and $C_6D_{11}H$. In the limits of slow and fast exchange regions, the exchange contribution is comparable to instrumental capabilities of measuring the total linewidth. Rapid pulsing in the Carr-Purcell experiment eliminates instrumental line broadening effects. In

cyclohexane- d_{11} , T_2^O , the natural relaxation time, increased from 10 to 85 seconds over a 100° temperature range. Using the spin echo method Gutowsky measured the exchange rate over five orders of magnitude. The activation energy and frequency factor for cyclohexane and cyclohexane- d_{11} were given as 9.5 Kcal/mole and $4.5 \times 10^{11} \text{ sec.}^{-1}$

Spin echo studies of intramolecular exchange in the coupled AB system 1,1-difluorocyclohexane (47) and the chair to chair isomerization of perfluorocyclohexane (48) have also been reported.

EXPERIMENTAL

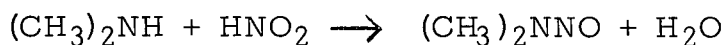
CHAPTER II

A) Preparation of Compounds

(i) N,N-Dimethylnitrosamine:

Secondary amines upon treatment with nitrous acid yield nitrosamines which are stable yellow liquids or low melting point solids. N,N-dimethylnitrosamine was prepared by the reaction of dimethylamine hydrochloride and sodium nitrite in acid solution. The mixture was distilled rapidly to dryness and the distillate was treated with an excess of potassium carbonate. The nitrosamine appeared as a yellow oil which was further treated with more solid potassium carbonate in order to remove the water. The dimethylnitrosamine was transferred to a small distilling flask and the liquid was dried over fresh anhydrous potassium carbonate. The pure compound, boiling point 150-151°C, was collected after two successive distillations under a nitrogen atmosphere.

The overall reaction is given as:



(ii) N,N-Dimethylcarbamyl Chloride:

The sample of N,N-dimethylcarbamyl chloride was obtained from K & K Laboratories Co. Ltd. with an indicated boiling point of 165-167°C. It was further purified by double distillation under a nitrogen atmosphere.

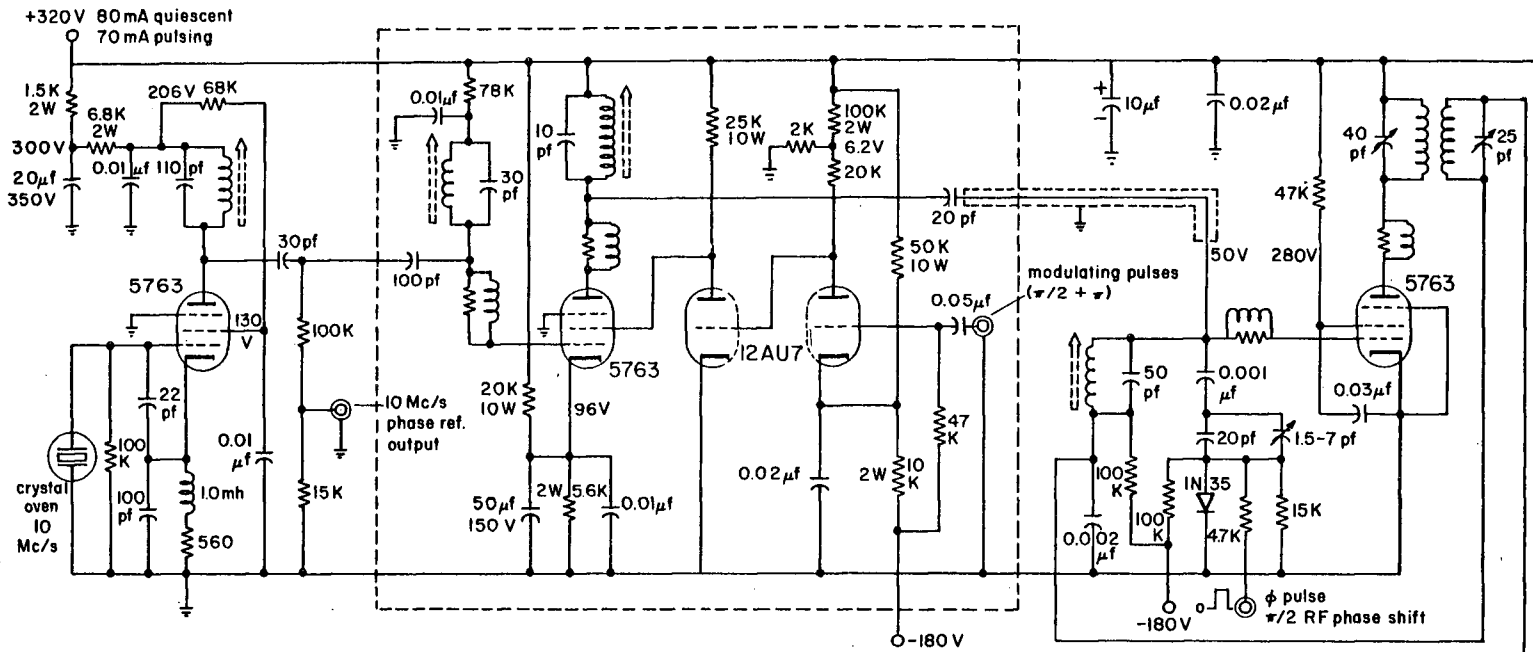
The samples used in this investigation were prepared for analysis in five millimeter outer diameter tubes which had been rounded off at one end. The tube containing the sample was mounted on a high vacuum system and the sample was thoroughly degassed by freezing with liquid nitrogen and allowing it to warm to room temperature under vacuum. This freeze-pump-thaw procedure was repeated several times and the tube was then sealed off.

The compounds were checked for purity spectroscopically using a Varian A-60 N.M.R. spectrometer.

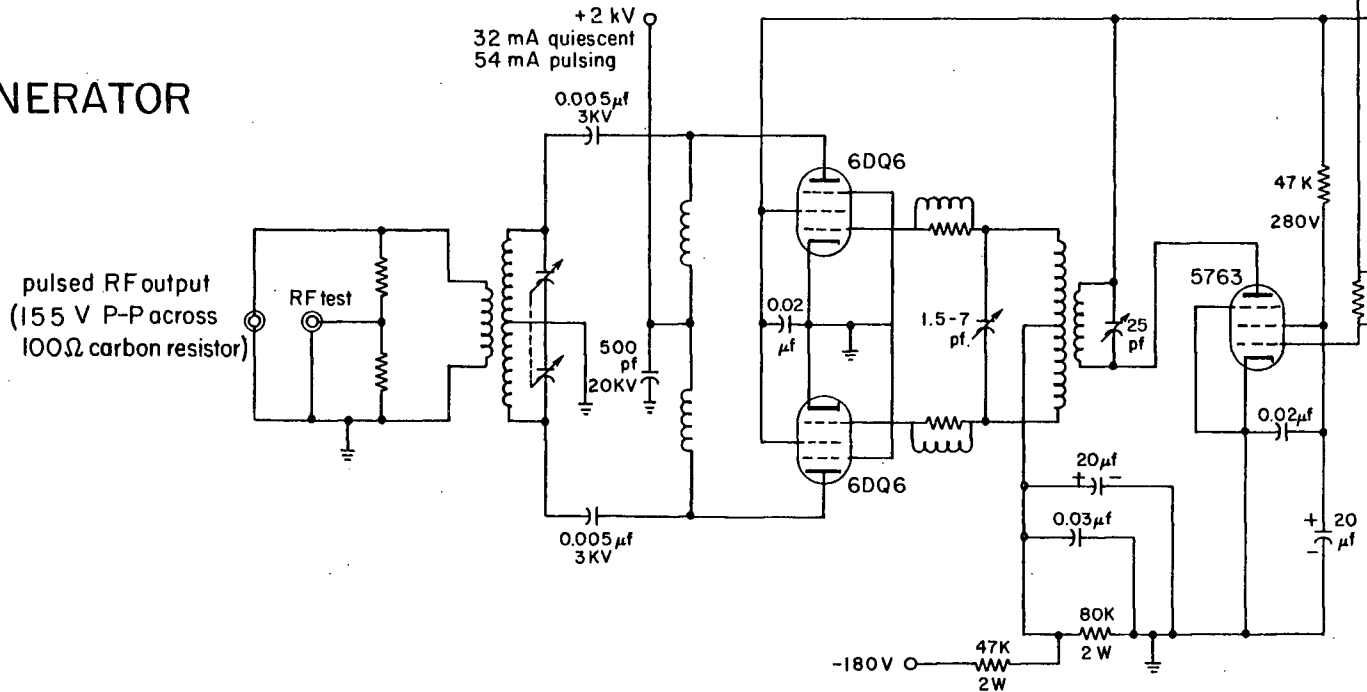
B) The Spin Echo Spectrometer:

The spin echo spectrometer described below was constructed in our own laboratories.* The apparatus is a further development of one constructed several years ago and is designed for nuclear magnetic resonance work in liquids. The major features of the apparatus include: (a) a radio frequency generator (Figure IV) consisting of a highly stable 10 Mc./s. crystal oscillator, a pulse modulator stage, two frequency doublers, a 40 Mc./s. driver stage and a push-pull final amplifier stage; (b) a Tektronix 545A oscilloscope, a Tektronix 162 waveform generator and three type 163 pulse generators in order to synthesize the modulating pulse train; (c) a Varian crossed-coil probe modified by appropriate changes of capacitors in the transmitter coil circuit to facilitate

* Acknowledgements are accorded to Mr. K. H. Abramson and to Mr. E. Fisher for their work on the pulse machine.



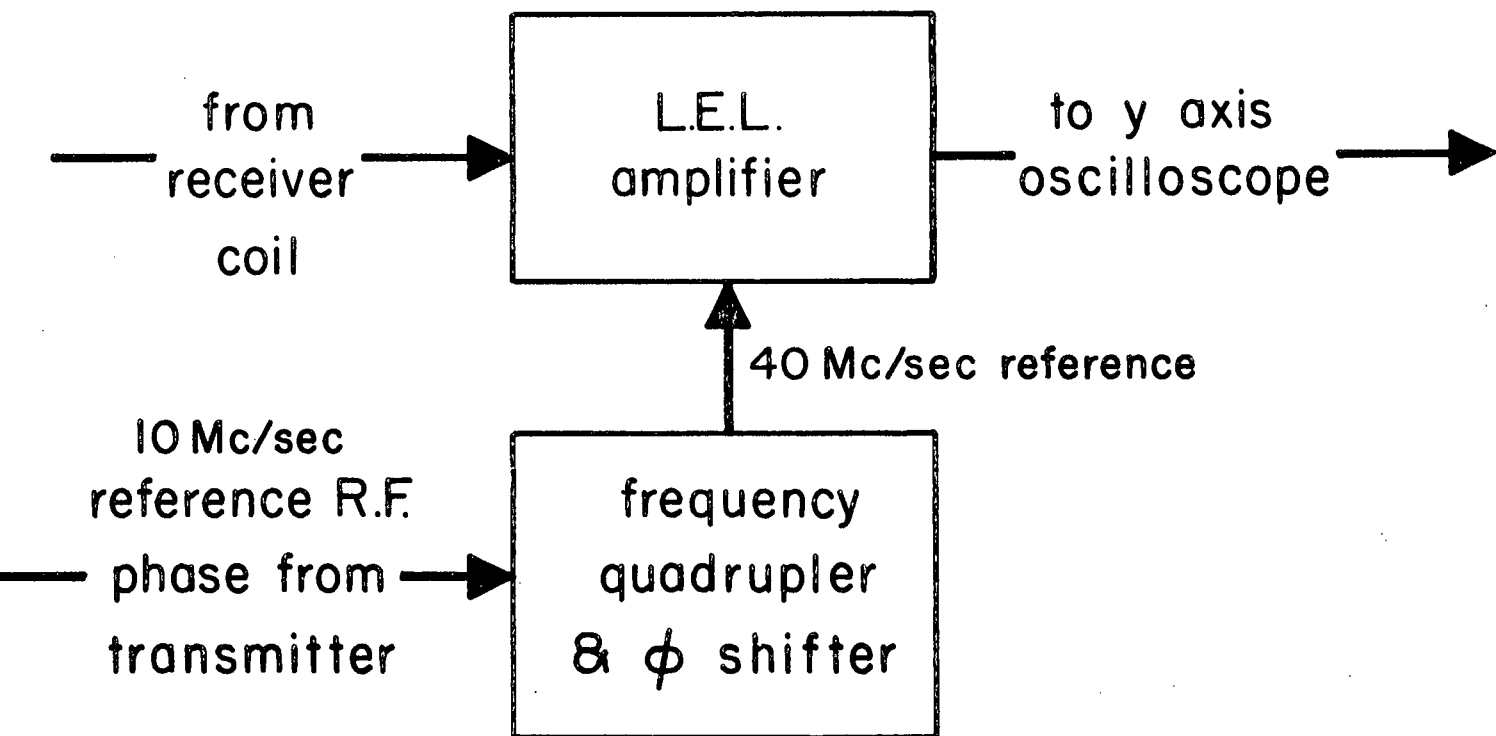
RF GENERATOR



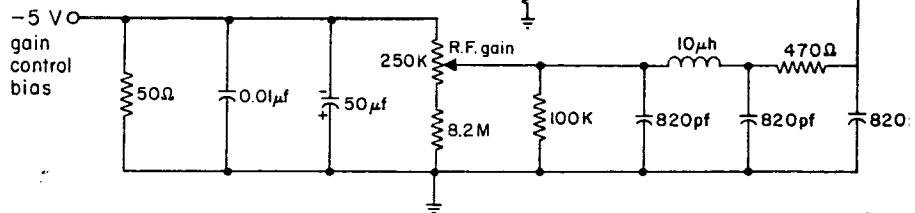
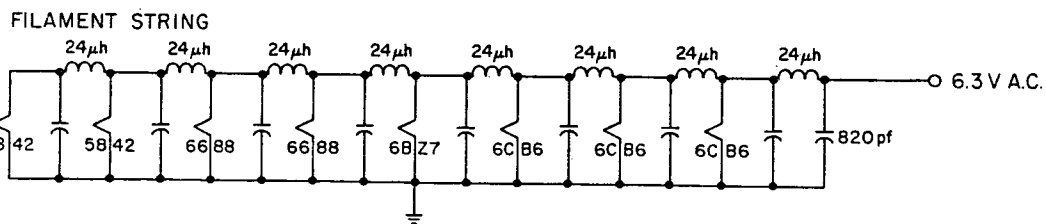
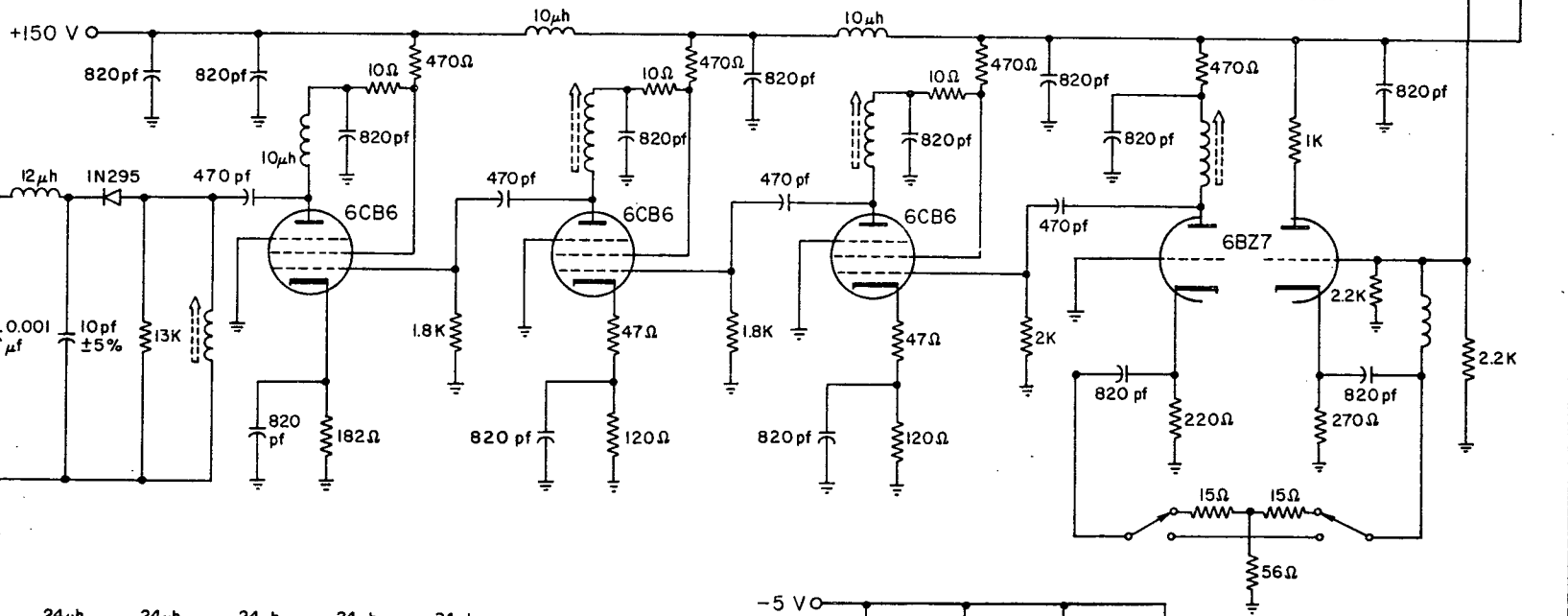
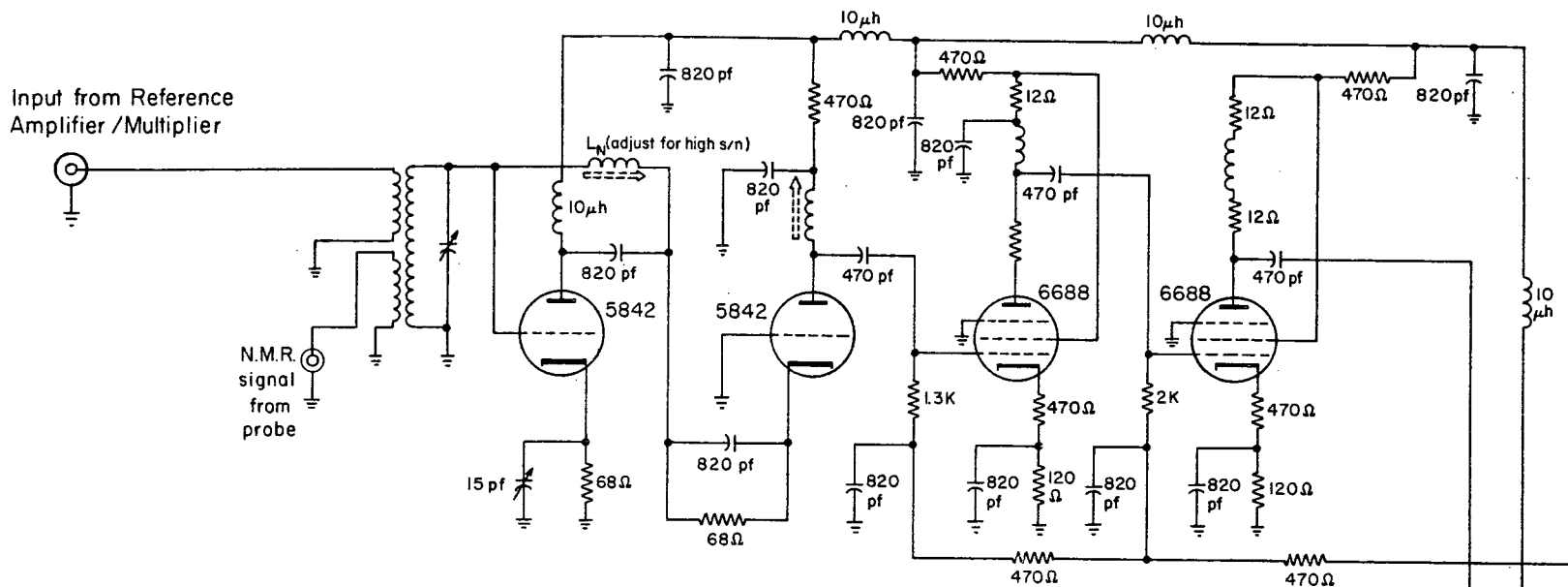
impedance matching. The probe was used for both high resolution and spin echo experiments; (d) a L.E.L.-I.F. amplifier which was used as a broadband receiver. (Figures V, VI).

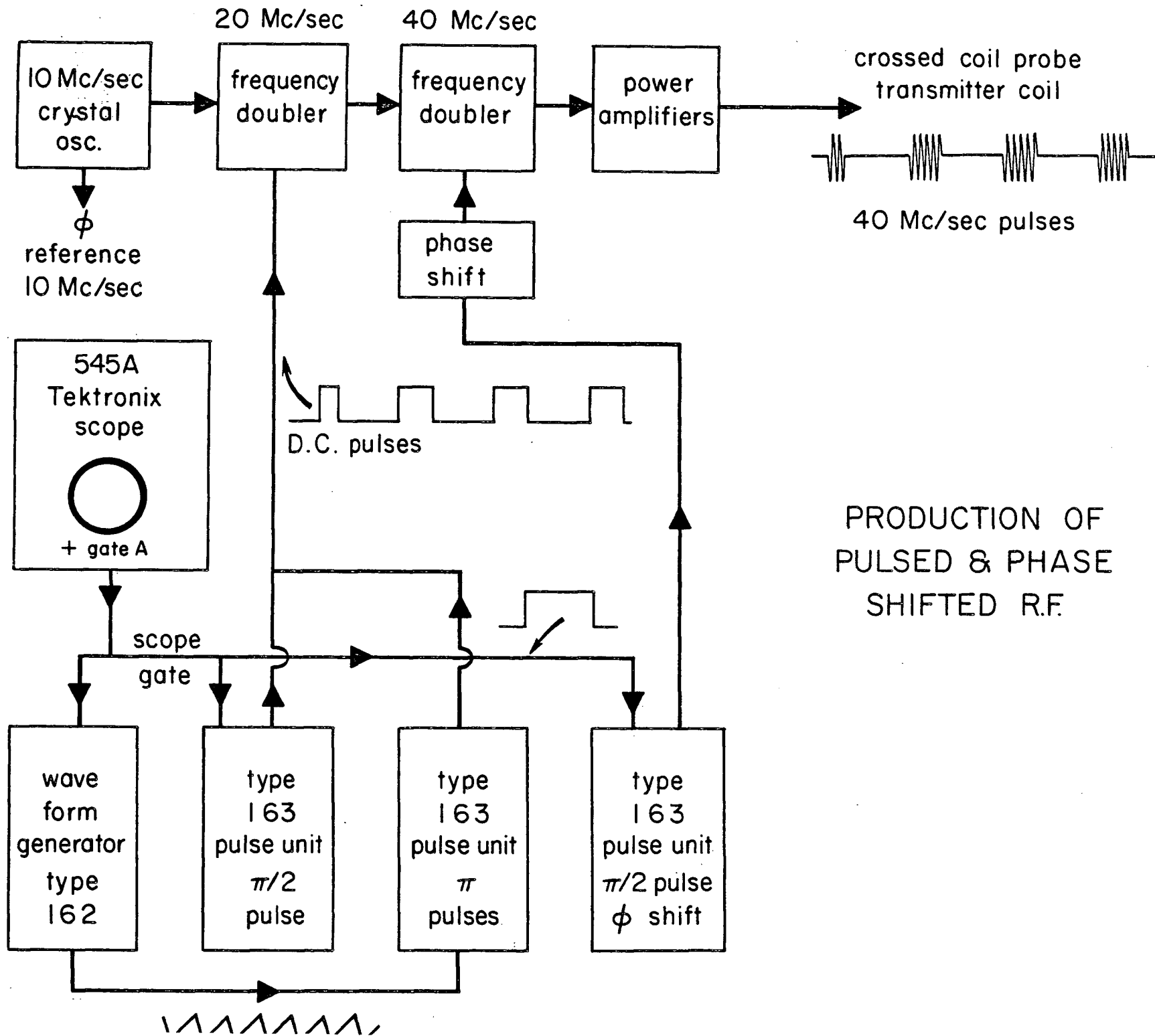
The generation of the Carr-Purcell pulse sequence is illustrated in figure VII. The 10 Mc./s. crystal was thermostatically maintained at 85°C in a crystal oven. Phase coherent 40 Mc./s. R.F. pulses were obtained by allowing the 10 Mc./s. oscillator to run continuously while pulse modulating the first doubler stage. Leakage of 40 Mc./s. during the "pulse-off" period was eliminated by careful interstage shielding. The Meiboom-Gill method (49) of phase shifting the $\frac{\pi}{2}$ pulse by 90° with respect to the π pulse was accomplished in the second doubler grid circuit. To achieve this, a pulse, identical to the $\frac{\pi}{2}$ pulse, switches a back-biased semi-conductor diode into its conductive state so that effectively a phase-changing capacitor is placed across the tuned circuit for the duration of the $\frac{\pi}{2}$ pulse. This 90° phase change minimizes the effect of accumulative error which might occur in the width of the pulses during a $\frac{\pi}{2}, \pi, \pi, \dots$ (Carr-Purcell (9)) pulse series. The R.F. output power of the transmitter was approximately 250 watts corresponding to a $\frac{\pi}{2}$ rotation of the magnetization vectors in 15-20 microseconds.

In order to initiate a pulse train, a positive gate voltage was fed from the "+ GATE A" terminal of the oscilloscope to the trigger inputs of two type 163 pulse generators one of which produced the single $\frac{\pi}{2}$ pulse and the other the 90° phase shifting pulse (49). In this manner



RECEIVER CIRCUITS





the initiation of the $\frac{\tau}{2}$ pulse and phase shifting pulses coincided with the commencement of the oscilloscope trace. The production of pulses at times $\tau, 3\tau, 5\tau \dots$ was achieved by employing the same "+ GATE A" from the oscilloscope to gate a type 162 waveform generator which produced a saw-tooth train of variable frequency. The negative-going saw-tooth was then used to trigger another type 163 pulse generator resulting in a train of τ pulses. The series of τ pulses were delayed from the $\frac{\tau}{2}$ pulse by adjustment of the "OUTPUT PULSE DELAY" control on the pulse generator. In the same manner the time between τ pulses- the pulse repetition period- was adjusted by the "PULSE INTERVAL" control on the waveform generator and measured with a Hewlett-Packard 522B electronic counter.

Receiver coil orthogonality and the leakage paddles on the Varian crossed-coil probe were adjusted in order to obtain excellent isolation between the transmitting and receiving coils. This adjustment was made such that the central portion of the R.F. pulse was negligible and only the high frequency components- the leading and trailing edge of the pulse- were detected as two small spikes. Optimizing these adjustments in this manner resulted in quick receiver recovery times and avoided inducing into the receiver coil large "ringing currents" which could distort the overall H_1 from the transmitter coils.

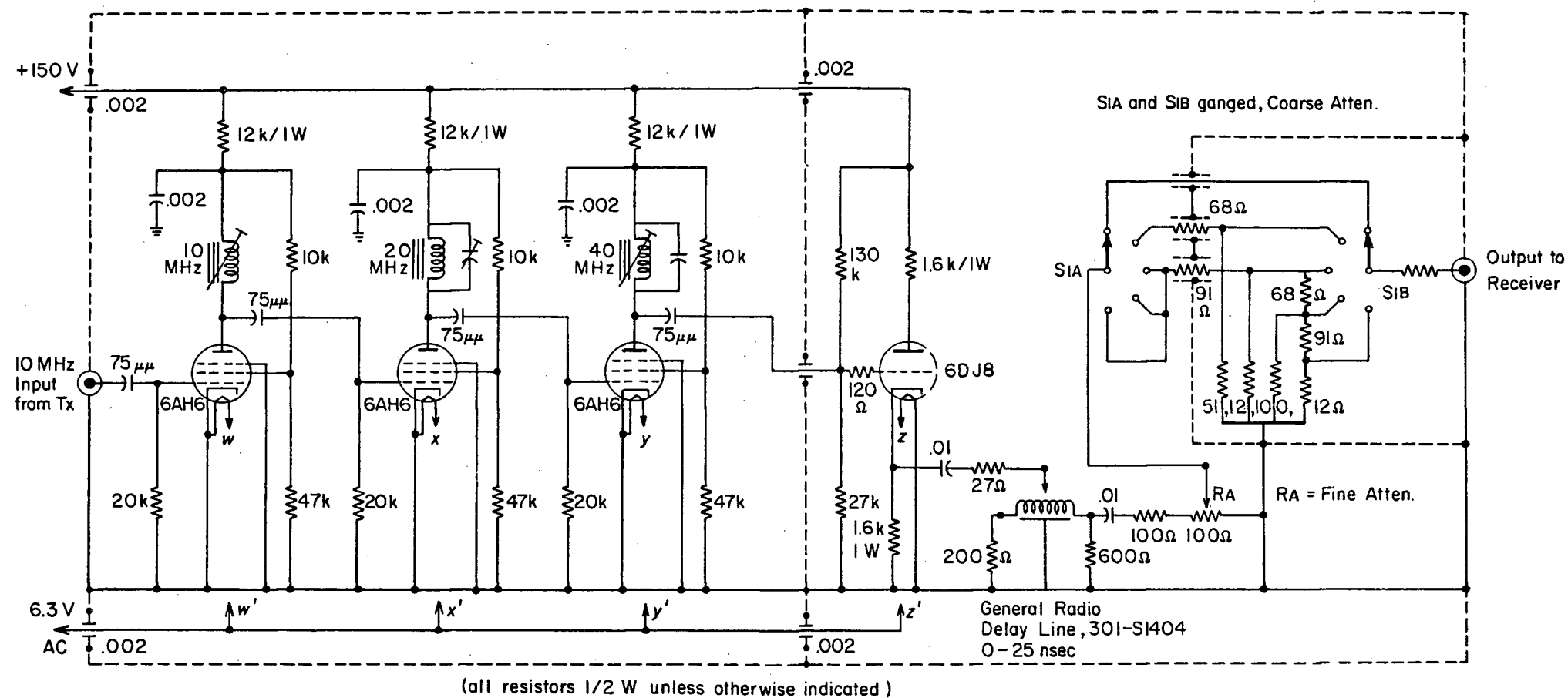
The modified L.E.L.-I.F. amplifier used as a receiver, maximum receiver gain of 2×10^5 with a bandwidth of 3 Mc./s., provided

both diode and phase sensitive signal detection.

Originally, in the phase sensitive detection mode, the receiver was supplied with a 10 Mc./s., 3 volt signal from the crystal oscillator of the transmitter. The signal was fed to a frequency quadrupler which produced the phase reference signal. The incoming N.M.R. signal from the probe was then mixed with the phase reference signal in the input transformer of the receiver to produce a phase detected signal. However it was found that the power available from the transmitter did not drive the quadrupler to 40 Mc./s. and as a result the zero-beat of the free induction decay against the phase reference signal, a condition necessary to define resonance, was being accomplished against the 10 Mc./s. leakage only. The action of frequency quadrupling in one stage produced a signal with changing amplitude between cycles—a condition not suitable for the intended operation. As a result an amplifying stage was used in order to raise the power available from the transmitter to that required for frequency modulation. (Figure VIII). Further, in order to achieve more efficient frequency multiplication with a reasonably uniform output amplitude, two stages of frequency doubling were used. (Figure IX).

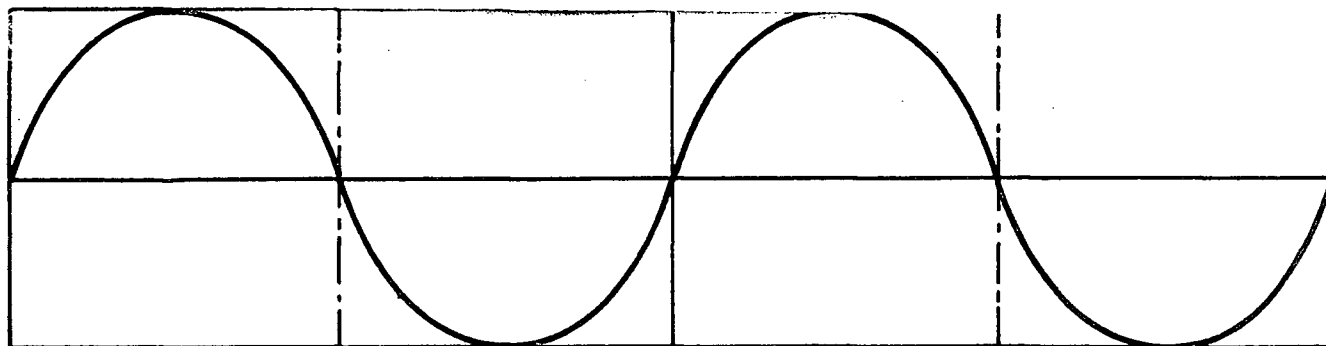
C) Magnet Systems:

The results reported in this thesis were obtained on a Varian 12" magnet shimmed for high resolution. The magnet was the first to be marketed by Varian Associates and was obtained in 1963 from the

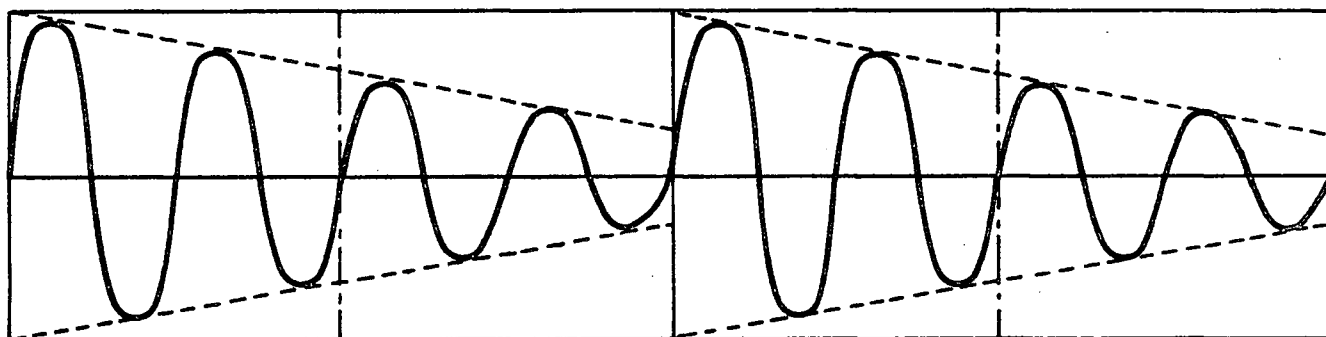


REFERENCE SIGNAL AMPLIFIER, MULTIPLIER, PHASER AND ATTENUATOR

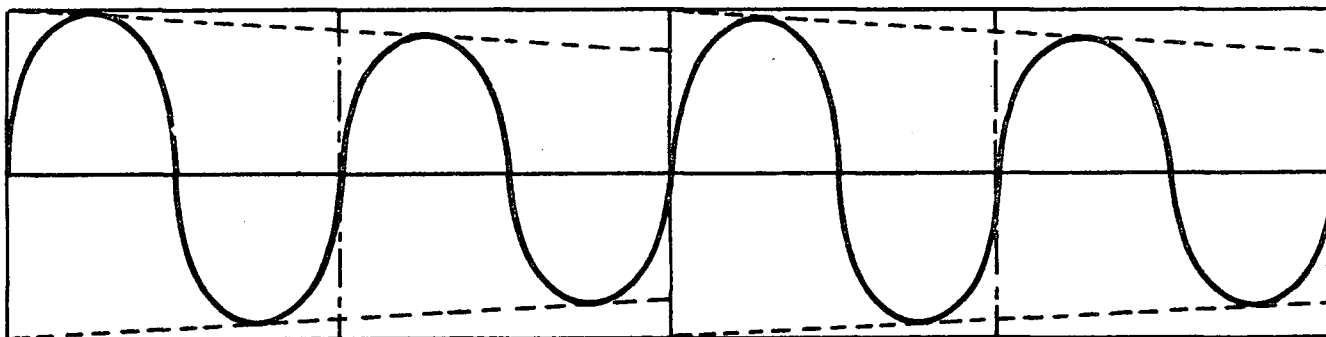
(a)
Fundamental
Frequency



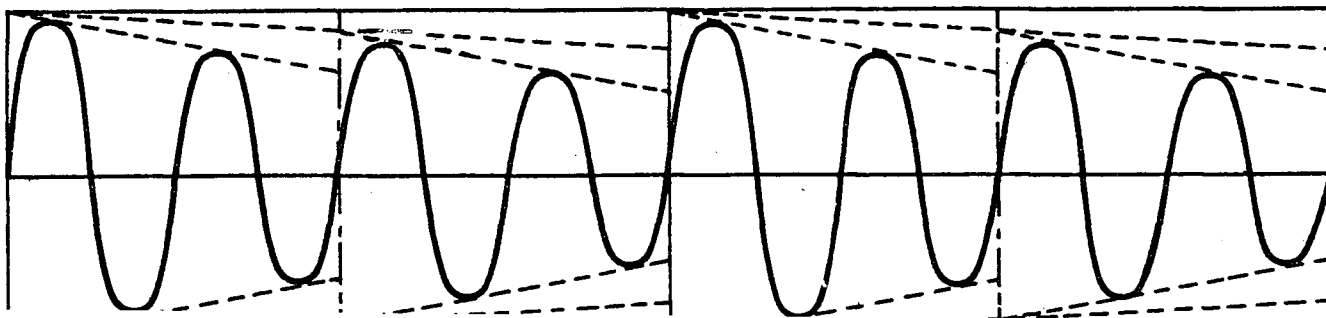
(b)
Frequency
Quadrupling
In One Stage



(c)
Frequency
Doubling



(d)
Frequency
Quadrupling
By Two Successive
Doubling Stages



Shell Development Oil Company.

The magnetic field was stabilized by means of a Varian V-K3506 Super-Stabilizer.

In order to obtain maximum field homogeneity, the Varian field homogeneity attachment coils were modified to allow sufficient room for the probe assembly to fit in the center of the magnet gap. The outer shape of the coil system was cut leaving a coil area comparable to the area of the magnetic pole faces. Contact cement was placed around the rim of the pole faces and the homogeneity coil plates were glued to the polefaces and aligned during the short period necessary for the glue to set.

The temperature of the magnet cooling water was held at a constant 19°C by means of a contact Jumo thermometer. Whenever the temperature rose above 19°C a relay switch initiated the flow of raw water through the circulating coils in the fiber-glass-lined drum. As an added preventive measure the high voltage power supply was automatically cut off if the magnet temperature ever exceeded 35°C .

Careful control of the surrounding temperature of the magnet system was achieved by insulating the magnet housing with styrofoam. Furthermore, a box, inner-lined with styrofoam, was constructed around the magnet. Plug-in panels and a sliding door assembly enabled complete accessibility to the probe as well as complete insulation from outside temperature fluctuations during an experiment.

Variable high temperature experiments--30-200°C-- were carried out by directing an air flow through a 650 watt heater. The heated air then passed through a stainless steel and teflon tube, both connected in series, and in this manner was directed into the probe assembly and passed around the sample tube. Stabilization of the air flow was accomplished by connecting a large ballast tank into the circuit before the heater. The flow rate was controlled by a needle valve and the air pressure was monitored before and after the needle valve.

Low temperature --20--100°C-- experiments were carried out by directing a flow of dry nitrogen gas through a set of circulating coils immersed in a dewar of liquid nitrogen and then directed into the probe.

Temperatures were measured with a copper-constantin thermocouple the sensing end of which was placed in an N.M.R. sample tube in order to simulate accurately the sample temperature. Temperature control during an experiment was monitored on a Speedomax recorder by the use of a second thermocouple located just above the sample in the variable temperature insert. In this manner temperatures are reliably quoted to an accuracy of $\pm 0.5^{\circ}\text{C}$.

Nuclear magnetic resonance signals were observed on a Tektronix model number 545A oscilloscope. This unit was used in conjunction with both the high resolution and spin echo spectrometers.

D) Measurement and Reliability:

The Carr-Purcell traces were photographed with a Polaroid oscilloscope camera using type #47, 3000 A.S.A. film and photographs were subsequently measured for echo amplitudes.

Carr-Purcell (9) measurements of T_2 are reliable only to within the stability limitations of the spectrometer. Earlier publications concerned with the measurement of relaxation times using the Carr-Purcell method quoted values of T_2 to within 15-25%. The present work was directed toward the attainment of more accurate and reproducible values of T_2 . Effects of diffusion were further minimized by working in a very homogenous H_0 field. The non-spinning samples had a T_2^* , measured from the free induction tail, of 50 milliseconds and in a $\pi/2, \pi, \pi, \dots$ pulse sequence, overlap of the detected pulses and echoes occurred. In many cases, at each pulse repetition frequency an average of at least two traces was used in quoting the value of $T_{2(C.P.)}$.

E) Computer Programs:

A computer program,* "BESFIT", was written in order to provide statistically the best fit of the experimental data in the determination of the rate constant k and the chemical shift ω . This iterative FORTRAN program was designed for use on the I.B.M. 7040 computer.

The values of $T_{2(C.P.)}$, the observed time constant of the

exponential decay in the Carr-Purcell experiment, T_2^0 , the natural relaxation time and τ , the π pulse repetition frequency, are read in as data for a given set of temperatures. In order to initiate execution of the program, reasonable guesses of k and ω are also read in as data. The best fit of the data to the equation

$$r_1 = \frac{1}{T_2(\text{C.P.})} - \frac{1}{T_2^0} = k - \frac{1}{2\tau} \sinh^{-1} F \quad (23)$$

is computed and the sum of the squares of the errors is printed out. The trial values of the rate constant and the chemical shift are now changed by computed increments obtained by differentiating equation (23) with respect to k and ω . The entire process is repeated with new trial values of k and ω . The best fit determination of the data is printed out on the basis of the minimum of the sum of the squares of the errors. Generally twenty iterations are allowed in order to converge on a value within $\pm 0.5 \text{ sec}^{-1}$ of the rate constant and chemical shift. Three subroutines to the program have been added in order to compute k and ω according as k is less than, equal to or greater than ω . The program is designed to change automatically from one subroutine to another in order to establish the best fit of the data on the basis of the trial values of k and of ω .

* Thanks are accorded to Mr. R. Wolfe and to Dr. J. F. Herring for teaching me some of the complexities of computer programing.

The program retains the computed values of k for a given temperature and enters this data into a fourth subroutine designed to compute the energy of activation, E_a , and the frequency factor, A , according to the Arrhenius equation,

$$k = Ae^{-E_a/RT} \quad (29)$$

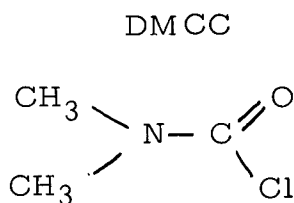
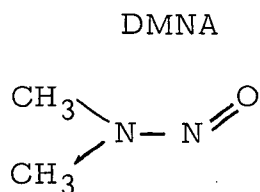
Once again reasonable guesses of E_a and A are read into the program.

A least squares program is used for the calculation of k from the "short τ limit" plot of $1/T_{2(C.P.)}$ vs $(\omega\tau)^2$, and the subsequent evaluation of the energy of activation and the frequency factor in the Arrhenius plot of $\log k$ vs $1/T$.

EXPERIMENTAL RESULTS

CHAPTER III

Carr-Purcell spin echo experiments have been carried out on the protons in N,N-dimethylnitrosamine (DMNA) and N,N-dimethylcarbamyyl chloride (DMCC).



Using the steady-state method it is possible to study hindered internal rotation in a molecule without any contributions to the spectrum from non-exchanging nuclei providing signals do not overlap. The relatively small proton chemical shifts and large H_1 fields used in the pulse method impose a non-selective condition upon the experiment. In this regard the molecules under investigation were chosen because all of their protons participate in the exchange.

A) N,N-Dimethylnitrosamine:

DMNA was selected as a suitable molecule for testing the BRW (28) theory since the chemical shift between the two methyl groups is large and there are no interfering protons in the system. The compound is a liquid over a large temperature range. It is very stable and relatively nonhygroscopic. Unfortunately the full temperature range covering the

three exchange regions could not be studied as the coalescence temperature of 190°C is well above the boiling point of the sample. In this regard more homogeneous magnetic fields were required for DMNA in order to investigate the exchange rates at higher temperatures where diffusion processes are rapid.

(i) Free Induction Tail Experiments:

In figure X the diode-detected free induction decay for N,N-dimethylnitrosamine is illustrated for a series of temperatures up to 195°C . At room temperature the steady state spectrum of DMNA shows two signals of equal intensity chemically shifted by 30.3 c.s. at 40 Mc./s.

When nuclei are restricted to a certain site, the free induction decay signal is the sum of the free precessions from all signals (26). A resolved chemical shift appears in the free induction decay as an amplitude modulation. This modulation appears because the transverse components of magnetization rotate at different angular velocities with respect to the rotating frame in A and B and in the stationary co-ordinate system the magnetization M_x is given by:

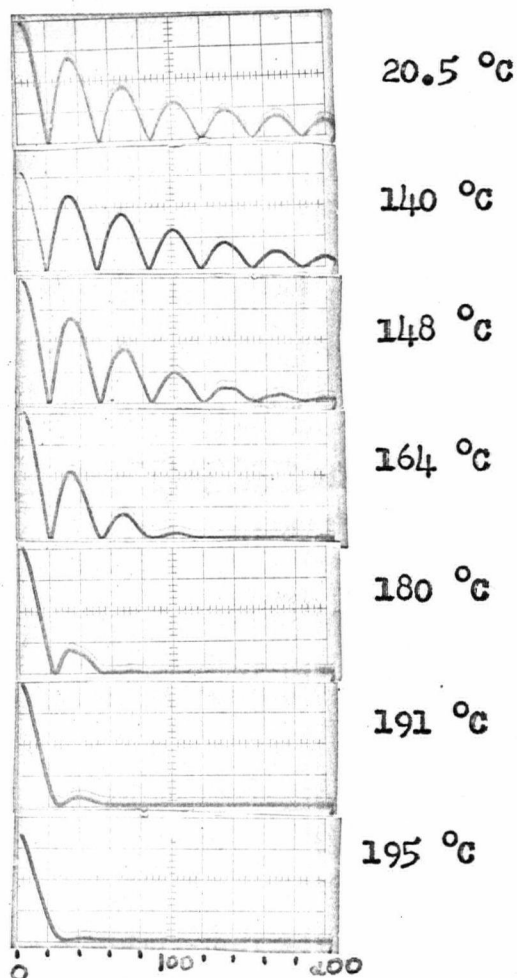
$$M_x = M_o \sin \Theta_1 \left[P_a \sin \omega_a t e^{-t/T_{2a}^*} + P_b \sin \omega_b t e^{-t/T_{2b}^*} \right] \quad (30)$$

where: $\Theta_1 = \omega_1 t_w$

P_a, P_b are the populations in sites A and B.

FREE INDUCTION TAIL EXPERIMENTS

N,N-DIMETHYLNITROSAMINE



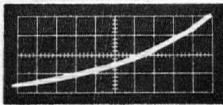
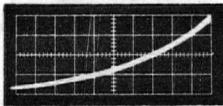
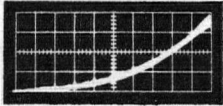
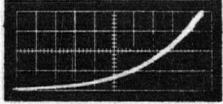
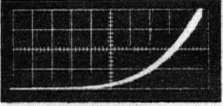


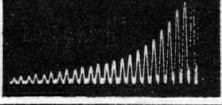
Free induction tail signals for pure N,N-Dimethylnitrosamine at various temperatures. At 20.5°C the measured modulation period is 33.2 msec., corresponding to a chemical shift difference of 30.2 c.s. Room temperature steady-state measurements at 40 Mc.s. produce a chemical shift of 30.3 c.s. Time scale in all of the above is 20 msec/cm.

At room temperature, using diode detection, the free induction signal shows the modulations expected for small exchange rates. The measured modulation period is 33.2 milliseconds corresponding to a chemical shift of 30.2 c.s. This is in excellent agreement with the steady state value. The sample was not spinning as this is likely to cause additional modulations to the free induction tail. As the temperature is increased, the signal is altered corresponding to the larger exchange rates. At 195°C the modulations have virtually been removed from the free induction decay. It is interesting to compare the changes with temperature in the free induction decay of DMNA with those obtained by Reeves and Wells (50) for the unequally populated case of methyl nitrite. The behaviour of the free induction decay signals of DMNA corresponds qualitatively to the predictions made by Woessner (26).

(ii) Carr-Purcell Trains:

Spin echo Carr-Purcell trains of the protons in DMNA are illustrated in figure XI. The traces were recorded at a sample temperature of 135°C and the Meiboom-Gill phase shift (49) was used in all cases. The spin echo trains in figure XI correspond to the π pulse spacing indicated in the left column. The calculated T_2 values shown in column 3 vary from 10.1 seconds in the limit of rapid pulsing to 0.2 seconds when the pulse interval, 2τ , is 40.75 milliseconds. In order to obtain a full scale display of the decay, the corresponding settings of the time base are changed and recorded in column 4.

CARR-PURCELL TRAINS; N,N-DIMETHYLNITROSAMINE

Pulse Interval (2τ), (msec)		T_2 (C.P.) (sec)	Time Base (sec/div)
1.30		10.1	2.0
2.05		9.21	2.0
2.58		6.30	2.0
8.11		2.68	1.0
10.24		2.03	1.0
13.02		1.44	0.5
20.48		0.72	0.2
40.72		0.20	0.1

When pulsing rapidly, and with the sample placed in a homogeneous H_0 field, no individual echoes are resolved. At 40.75 milliseconds, the decay is still exponential but with such a large π pulse spacing individual echoes are now resolved. The amplitudes of the echoes are not modulated in the Carr-Purcell train as the transverse components of magnetization are all rephased when the echo maxima occurs.

The measurement of T_2 from Carr-Purcell trains is very sensitive to the proper adjustment of the baseline. Any deviations in the baseline after a trace has been photographed is indicative of magnetic field drift from the resonance condition. In this connection, prior to observing a decay, the zero beat of the free induction tail, using phase sensitive detection, was checked for the resonance condition. A series of π - pulses was inserted and reverting to diode detection, the baseline was adjusted on the longest time scale. In the actual decay the π pulses were removed shortly before the trace had swept full scale and the drop to the original baseline indicated no field drift.

Careful attention to spectrometer conditions during an experiment, the inclusion of the 90° phase shift (49) and working in a homogeneous H_0 field has increased the reproducibility of the spin echo trains. In this regard the T_2 values are estimated to have a random error $\pm 5\%$. Previous claims (46) estimate T_2 to within 10-20% and at higher temperatures their error in some cases was 40%.

(iii) Limiting Cases--Off and On Resonance:

For the case of N,N-dimethylnitrosamine, another feature of the

spin echo experiment was introduced to provide an independent check of the rate constant data. Wayne, Zamir and Strange (51) have suggested that accumulated error in the 180° pulses can be corrected by working at certain off resonance conditions without using the Meiboom-Gill 90° phase shift. The condition that must be observed in the $\pi - \pi$ pulse separation is:

$$2\tau = (2n + 1 \pm \frac{1}{2}) T \quad (31)$$

where: $T = \frac{2\pi}{(\Delta\omega)_0}$

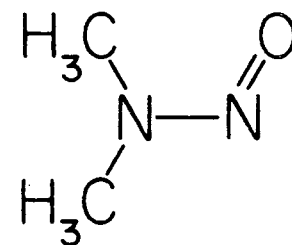
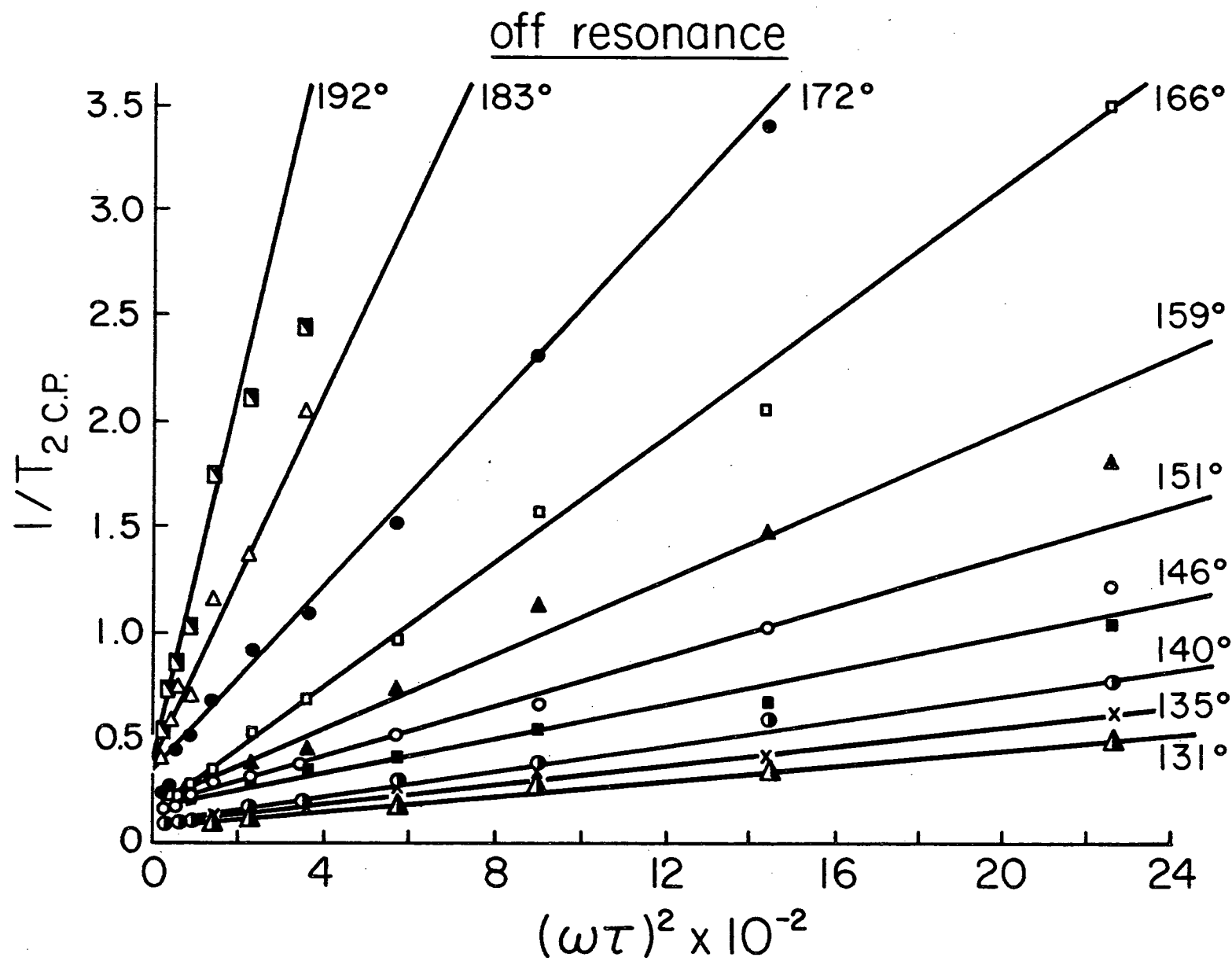
n is an integer

$(\Delta\omega)_0$ is the frequency difference from the resonance condition.

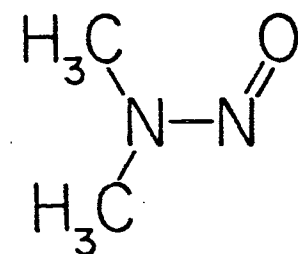
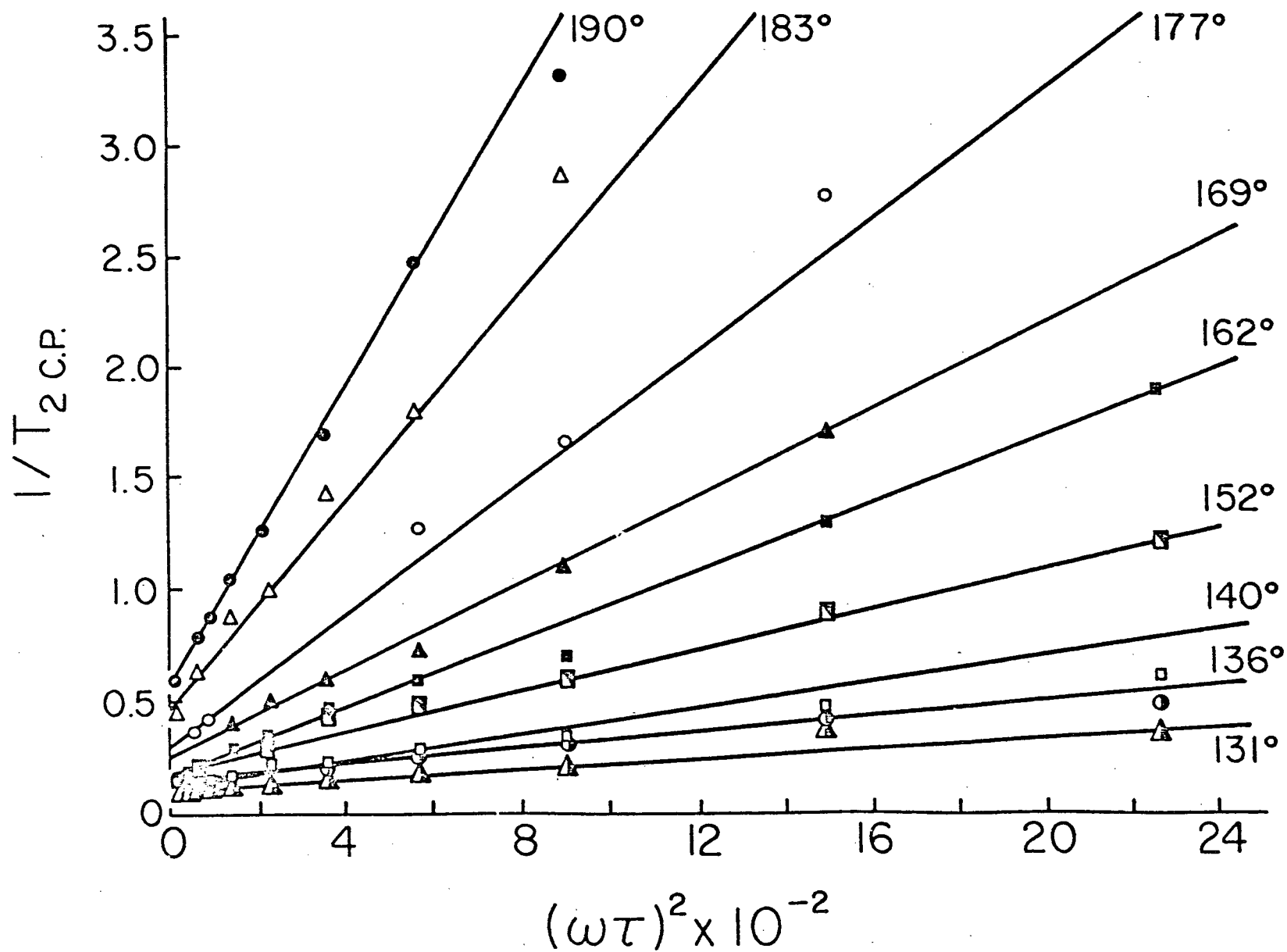
Rate constant determinations for DMNA are measured at approximately 4.5 Kc.s. off resonance. At this point variations in T_2 were recorded for π -pulse intervals ranging from 1.0 to 10.0 milliseconds. The off resonance experiments were limited by the narrow pulse interval range over which T_2 could be measured reliably. The resonance position was periodically checked by the number of modulations of the phase sensitive detected free induction decay signal.

The proton T_2 values measured for DMNA are given in figures XII and XIII for the off and on resonance conditions. The data are presented as plots of $1/T_2(\text{C.P.})$ as a function of $(\omega\tau)^2$. This follows from the short τ limit expression

$$r_1 = \frac{2}{3} k (\omega\tau)^2 \quad (27)$$



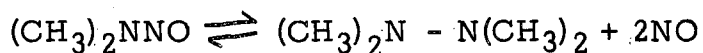
on resonance



presented in the Bloom, Reeves and Wells theory (28). Within the validity of equation (27) the slopes ($\times 3/2$) of the lines in figures XII and XIII give an estimation of the rate constants for the exchange at each temperature. The values of ω were obtained from steady state measurements. Extrapolation of the lines to $(\omega\tau)^2 = 0$ provides a value of T_2^0 , the natural relaxation time.

A least squares computer program was designed to evaluate the rate constants and values of T_2^0 . Generally the correlation between $1/T_2$ and $(\omega\tau)^2$ was better than 0.95.

A comparison of figures XII and XIII shows good agreement between the off and on resonance data. A large temperature dependence of T_2^0 is observed in DMNA. However it is rather unusual that the natural relaxation time decreases with increasing temperature. Since the exchange region for this compound requires a high sample temperature the production of small but increasing amounts of paramagnetic nitric oxide as the temperature is raised, leads to this T_2^0 temperature dependence. This behaviour is associated with the equilibrium:



Values of the rate constants computed from the short τ limit plot for the on and off resonance condition are listed in table I.

TABLE I

N, N-DIMETHYLNITROSAMINE

RATE CONSTANTS FROM $r_1 \approx k + k \pm \frac{2}{3} k (\omega\tau)^2$

Off ω_0		On ω_0	
T(°C)	k(sec ⁻¹)	T(°C)	k(sec ⁻¹)
131	2.52	131	2.20
135	3.27	136	1.92
140	4.57	140	1.97
146	5.75	152	6.44
151	7.56	162	8.73
159	11.8	169	14.6
166	21.8	177	25.5
172	33.0	183	27.4
183	48.7	190	61.5
192	129		

The most important parameter derived from these experiments is the rate constant k . It is seen from table I that agreement between the rate constants from the on resonance measurements using the 90° phase shift with the off resonance values is satisfactory. Further it is reasonable to expect, in this case, that there is a better agreement in the lower temperatures where diffusion effects are not as rapid.

(iv) Calculation of ' r_1 ':

The time constant T_2 for the decay of the echo amplitudes in the Carr-Purcell experiment is a function of T_2^0 , the natural relaxation time, of the populations in the sites A and B, (for DMNA, $p_a = p_b = 0.5$) of the chemical shift, $\omega_a - \omega_b$ and of the pulse repetition frequency $2\mathcal{V}$. It is interesting then to plot $\ln 1/T_2$ as a function of $\ln 1/2\mathcal{V}$ and derive the rate constants from the best fit determination to equation (23):

$$r_1 = k - \left(\frac{1}{2\mathcal{V}}\right) \sinh^{-1} F \quad (23)$$

A comparison of the data off and on resonance is illustrated for DMNA in figure XIV. The general shapes of the curves for the complete dependence of $T_2(\text{C.P.})$ upon the pulse repetition frequency is not seen in figure XIV. This is especially the case for the off resonance results because of the limited pulse interval range over which T_2 could be measured.

Only the region below the coalescence temperature could be studied for DMNA. The on resonance measurements extend over a greater range of pulse intervals.

The data was computerized to obtain the value of k using equation (23). Trial values of k and T_2^0 for the program were obtained from the slope and intercept in the short \mathcal{V} limit approximation. The value of ω was obtained from high resolution studies. Values of the rate constant k obtained from the best fit to the data are listed in table II.

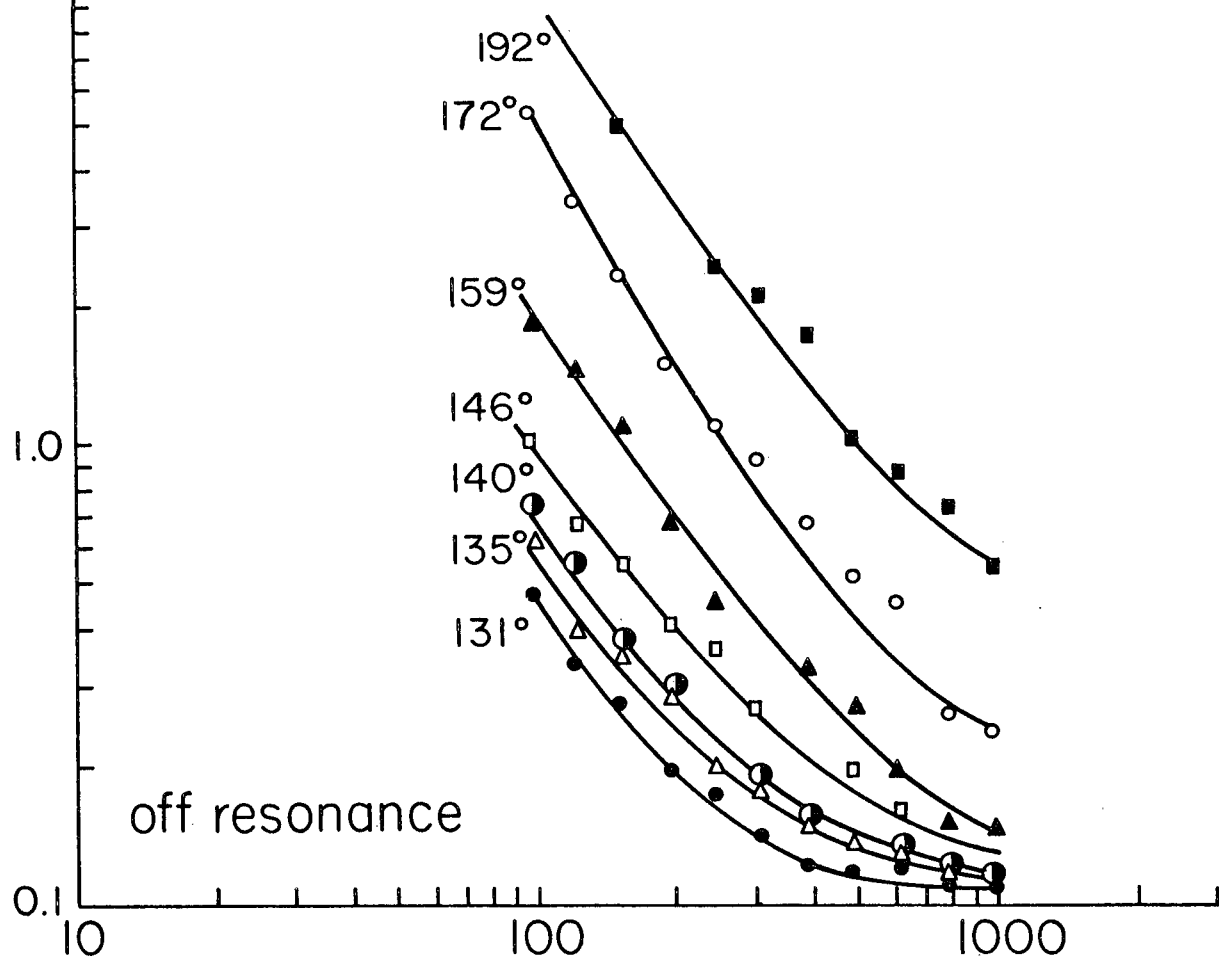
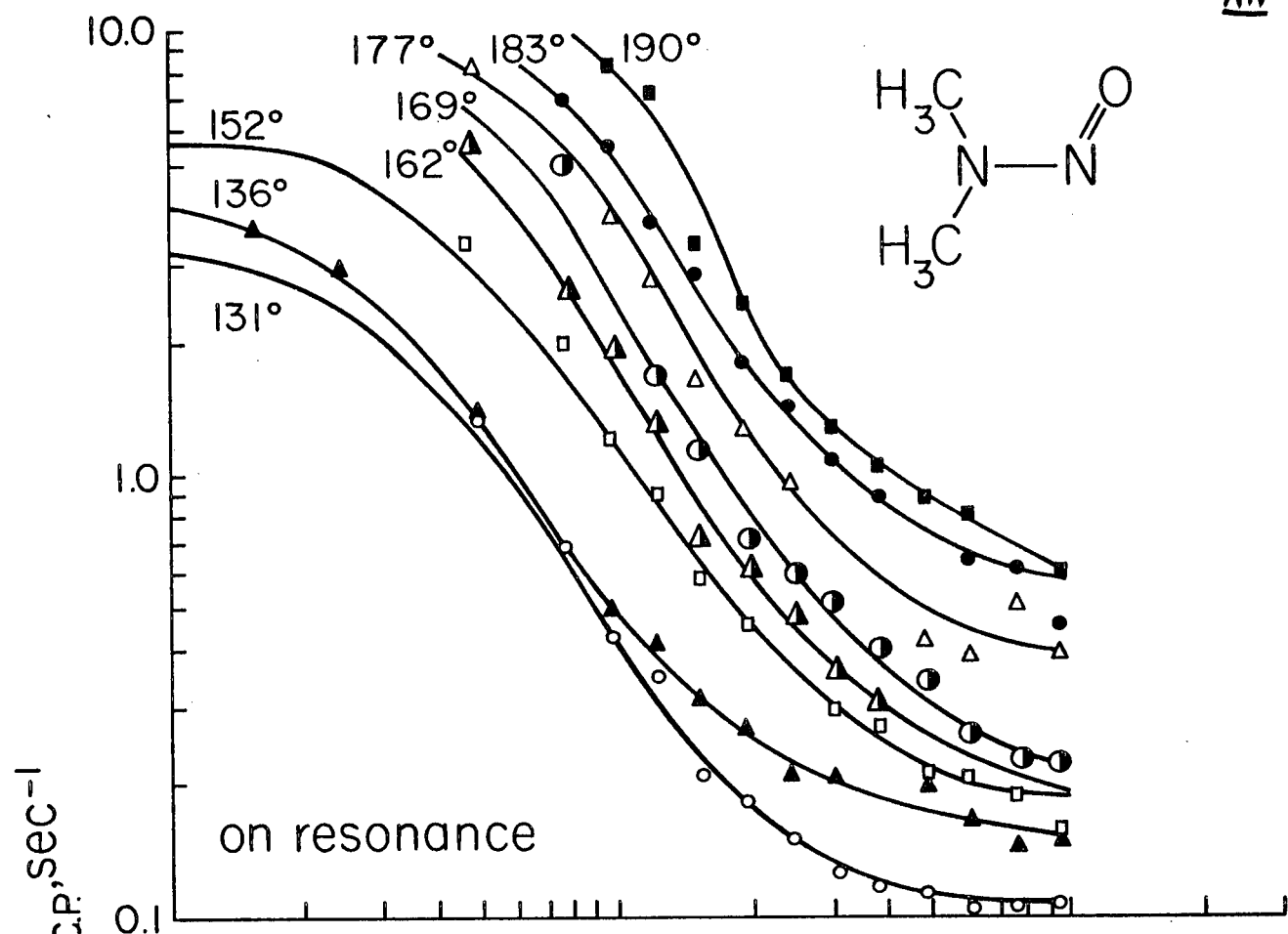


TABLE II

N,N-DIMETHYLNITROSAMINERATE CONSTANTS FROM $r_1 = k - (\frac{1}{2\tau}) \sinh^{-1} F$

Off ω_o		On ω_o	
T($^{\circ}$ C)	k(sec $^{-1}$)	T($^{\circ}$ C)	k(sec $^{-1}$)
131	2.20	131	3.20
135	2.80	136	3.20
140	3.70	140	3.40
146	5.10	152	6.30
151	5.80	162	8.00
159	10.1	169	31.9
166	25.4	177	41.9
172	55.4	183	47.5
183	74.9	190	61.8
192	102		

Agreement of the rate constants between the two methods is satisfactory. Further discussions of the $\ln 1/T_2(\text{C.P.})$ versus $\ln 1/2\tau$ graphs are postponed since the general shape of the lines for the complete dependence of T_2 upon τ -pulse spacing is best seen in N,N-dimethylcarbonyl chloride.

A comparison of the rate constant data for selected temperatures of dimethylnitrosamine are presented in table III. Included are unpublished A-60 steady state measurements made in this laboratory by

Drs. L. W. Reeves and E. J. Wells.

TABLE III
COMPARISON OF RATE CONSTANTS

T	k ^(A)	k ^(A)	k ^(B)	k ^(C)	k ^(C)
°C	off ω_0	on ω_0	A-60	off ω_0	on ω_0
140	4.57	1.97	2.55	3.70	3.40
151	7.56	6.44	4.90	5.80	6.30
160	11.8	8.73	10.3	10.1	8.00
183	48.7	27.4	44.0	74.9	47.5
192	129	61.5	-	102	61.8

(A) --Least Square Analysis of $r_1 \approx k + k \pm \frac{2}{3} k(\omega\tau)^2$

(B) --Steady State A-60

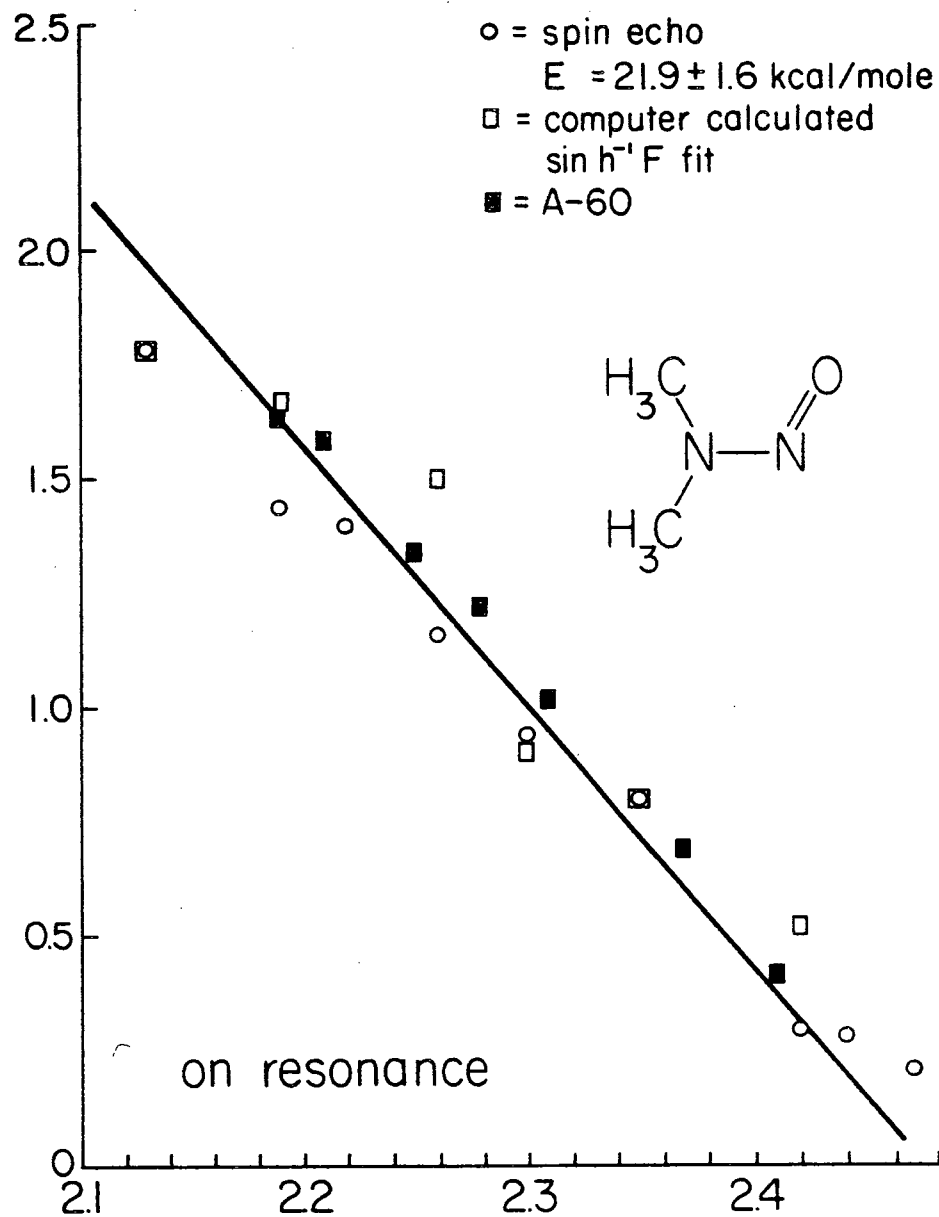
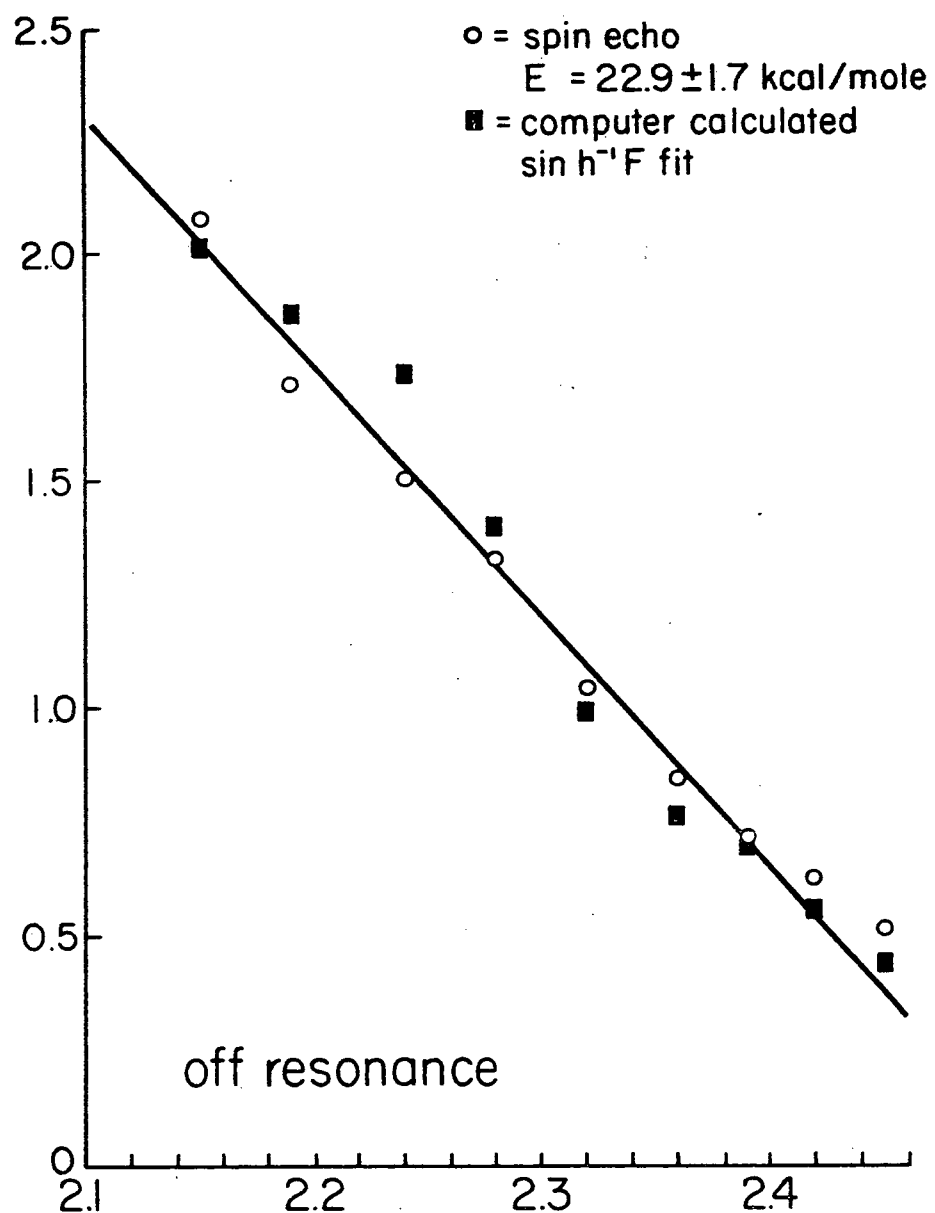
(C)--Computer Calculated --time constant ' r_1 '.

(v) Activation Parameters:

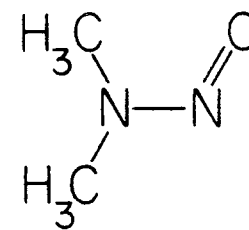
The temperature dependence of the rate constant for dimethylnitrosamine is illustrated in figure XV for the off and on resonance experiments. The activation energy E_a and frequency factor A are determined from the Arrhenius equation

$$k = A \exp(-E_a/RT) \quad (29)$$

by the slope and intercept of the lines. Activation energies are determined as least square lines to all rate constant determinations. The off



$1/T \times 10^{-3} (^{\circ}K^{-1})$



resonance graph includes the rate constant data determined from the short γ limit approximation and the $\sinh^{-1}F$ fit. In addition the on resonance line includes the steady state rate constant data of Reeves and Wells. The reported errors in the activation energy are quoted for a 90% confidence limit. Agreement between the two methods is very satisfactory. In table IV, the activation parameters are listed for the off and on resonance experiments. Values of the activation parameters obtained by other workers are also tabulated. ΔH^* is determined from

$$\Delta H^* = E_a - RT_c \quad (32)$$

where T_c is the coalescence temperature which for DMNA is 190°C . The probable statistical errors in ΔH^* are similar to those quoted for the activation energy. The frequency factor, A , is used in the determination of the entropy, ΔS^* , according to the equation

$$A = \gamma e^{\left(\frac{KT}{h}\right)} e^{\frac{\Delta S^*}{R}} \quad (33)$$

where K is the Boltzmann constant $= 1.381 \times 10^{-16}$ erg/ $^\circ\text{C}$

T_c is the coalescence temperature $= 463^\circ\text{K}$

h is the Planck's constant $= 6.624 \times 10^{-27}$ erg.sec.

R is the gas constant $= 1.98$ cal/ $^\circ\text{C}$ /mole.

and γ , the transmission coefficient $= 1$.

TABLE IV

N,N-DIMETHYLNITROSAMINECOMPARISON OF ACTIVATION PARAMETERS

METHOD	ω_0	A	E_a	ΔH^\ddagger	ΔS^\ddagger	REF
Short γ	off	6.04×10^{12}	22.9 ± 1.7	21.9	-3.92	
Short γ	on	1.00×10^{12}	21.9 ± 1.6	21.0	-2.93	
Sinh ⁻¹	off	1.13×10^{11}	19.7 ± 3.4	18.8	-10.9	
Sinh ⁻¹	on	1.20×10^{14}	25.5 ± 2.5	24.6	1.04	
S.S.	40Mc	0.7×10^{13}	23.0			(37)
S.S.	60Mc	1.6×10^{11}	25 ± 5			(39)

The calculation of r_1 off resonance was limited by the narrow pulse interval range over which T_2 could be measured.

B) N,N-Dimethylcarbonyl Chloride:

The equations derived in the Bloom, Reeves and Wells theory (28) are tested experimentally by conducting Carr-Purcell spin echo measurements on the protons in dimethylcarbonyl chloride. In this study an attempt has been made to minimize the effects of errors by carrying out the measurements over as large a temperature range as possible. DMCC has a boiling point of 165°C. The results reported here were obtained over a range of 129°C (-27°C to 102°C) for temperatures above and below coalescence.

All measurements for this compound were carried out at 40 Mc./s. At each of the temperatures, $1/T_2$ was measured as a function of π -pulse spacing. At least 16 pulse separations were used ranging from 1.0 milliseconds in the limit of rapid pulsing to 0.4 seconds.

The chemical shift between the two methyl groups has been measured in our laboratory as 11.0 c.s. at 100 Mc./s. at -20°C where the effect of exchange on the chemical shift is negligible. This chemical shift corresponds to a modulation period of 227 milliseconds. Since T_2^* is approximately 50 milliseconds no modulations appear on the free induction tail for DMCC.

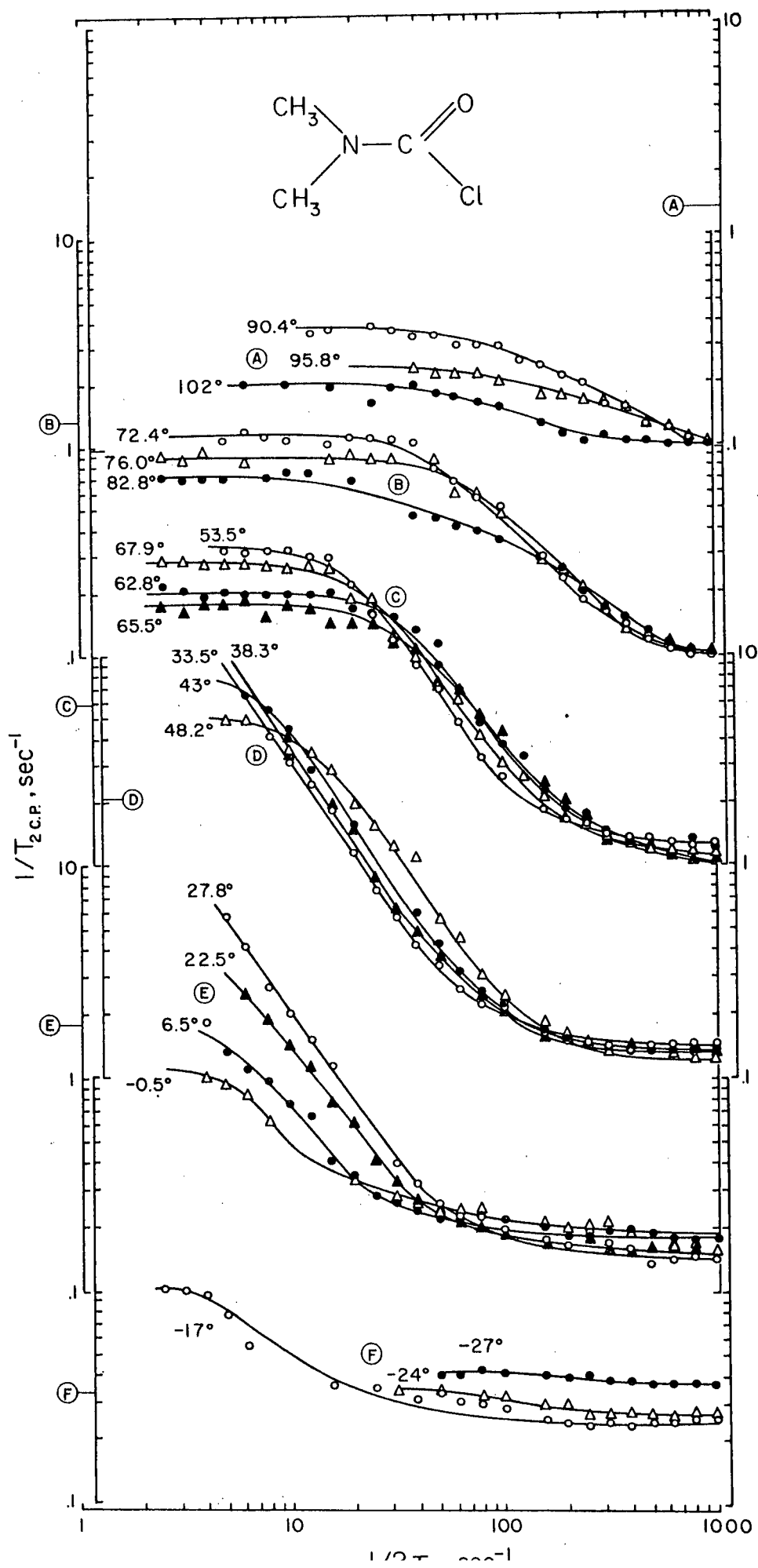
Carr-Purcell trains were recorded using the same method as reported for DMNA.

(i) The Calculation of ' r_1 ':

The rate constant k and chemical shift ω between the methyl groups may be obtained from the observed dependence of T_2 upon the π -pulse spacing according to equation (23).

In figure XVI, $\ln 1/T_2(\text{C.P.})$ is plotted as a function of $\ln 1/2\tau$ from -27°C to $+102^{\circ}\text{C}$. The coalescence temperature for DMCC is approximately 50°C at 40 Mc./s. The curves follow the general shape predicted by Gutowsky (30).

At -27°C chemical exchange effects are virtually absent and the value of T_2 is independent of the pulse repetition frequency. As the temperature increases, chemical exchange effects occur. If a nucleus



jumps from site A to site B, its precessional frequency changes from ω_a to ω_b and the dephasing rate of the nuclear moments changes. In the limit of rapid pulsing, the value of $1/T_2$ approaches $1/T_2^0$ in the absence of exchange since the dephasing as a result of the exchange is negligible. When the π -pulse spacing is large, all of the nuclei involved in the exchange will have transferred between A and B many times between pulses. As a result in this limit, the curve approaches the linewidth in the exchange broadened steady state spectrum for the fast exchange limit.

The computer program, BESFIT, was used to derive the values of k and ω on the basis of trial values of the rate constant and chemical shift. Trial values were normally selected from measurements in the limit of slow and rapid pulsing. The proton spin echo determinations for these parameters are listed in table V.

In the slow exchange region the values of k and ω were easily determined. At higher temperatures however the convergence limit was altered in order to fit the experimental data.

TABLE V

N,N-DIMETHYLCARBAMYL CHLORIDE

"BESFIT" TO $r_1 = k - \left(\frac{1}{2\zeta}\right) \sinh^{-1} F$

TEMPERATURE °C	k sec ⁻¹	ω rad./sec.
-27.0	0.99	13.7
-24.0	1.08	17.6
-17.0	0.65	13.8
-0.50	0.86	13.8
6.50	1.42	13.8
22.5	3.54	13.7
27.8	6.41	13.7
38.3	9.59	13.7
43.0	17.4	16.6
48.2	27.2	16.3
53.5	40.0	16.2
57.9	58.5	17.5
62.8	73.3	16.3
65.5	83.2	16.4
76.0	113	14.1
95.8	349	10.3

(ii) Limiting Cases:

There are certain aspects of equation (23) in the limits of slow and rapid exchange which are of interest in this investigation. It follows from equation (27) that a plot of $1/T_{2(C.P.)}$ as a function of $(\omega\tau)^2$ gives a straight line whose slope is an approximate measure of the rate constant for the transfer process. The results for DMCC are illustrated in figure XVII. In order to avoid crowding of the points in the limit of rapid pulsing, the values of $1/T_{2(C.P.)}$ are plotted without scale and the temperatures are vertically displaced on the diagram. For each of the lines, the correlation in the least squares analysis between $1/T_{2(C.P.)}$ and $(\omega\tau)^2$ up to 72.4°C is better than 0.96.

These results used in figure XVII fall within the limits of $k\tau \ll 1$, $\omega\tau \ll 1$. Equation (27) is applicable in the slow and fast exchange region.

The rate constants derived from the least squares fit to the straight lines are presented in table VI.

For very rapid exchange ($k \gg \omega$) and a large τ -pulse spacing, equation (28) may be used as the limiting expression to derive the rate constant. The chemical shift was obtained from steady state measurements. The calculated rate constants are presented in table VI. For comparison purposes results obtained for this molecule by Allerhand and Gutowsky (29) are also presented. His results have been calculated from Carr-Purcell proton spin echo measurements made at 26.9 Mc./s. for the pure liquid.

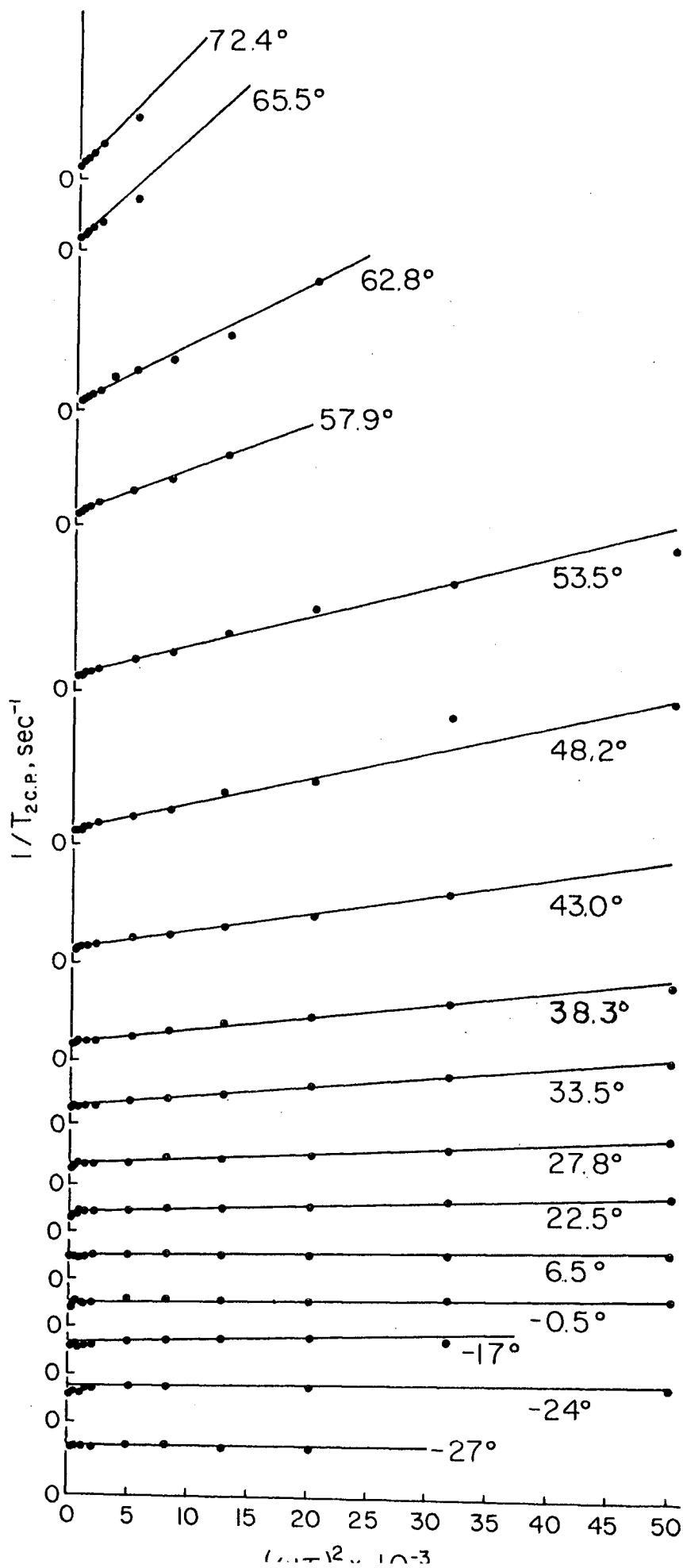


TABLE VI
N,N-DIMETHYLCARBAMYL CHLORIDE
RATE CONSTANTS

TEMPERATURE °C	SHORT τ $r_1 = \frac{2}{3}k(\omega\tau)^2$	REF. (29)	LONG $r_1 = \omega^2/2k$
-27.0	2.25		
-24.0	1.35		
-17.0	5.64		
-0.50	1.80		
6.50	2.40		
22.5	5.28		
26.5		5.3	
33.0	10.3	5.1	
38.3	15.3	10.0	
43.0	21.8	11.8	
47.0		13.0	
48.2	32.9		19.1
53.5	39.0	27.5	28.7
57.9	57.5		34.7
60.0		40.0	
62.8	76.1		47.3
65.5	112		53.4
72.4	152	92.0	83.7
76.0	200		108
79.0		138	
82.8	152		131
90.4			258
95.8			348
102			476

In table VI values of the rate constants in the long τ limit could only be obtained above 48°C since r_1 is derived from the linear part of the curves in figure XVI. Gutowsky (29) has investigated chemical exchange in DMCC over a 52° temperature range. His rate constant

values are in good agreement with the results presented here in the limit of slow pulsing.

(iii) T_2^O and T_1 Data:

The contributions to the steady state apparent linewidth for a molecular system in which nuclear transfer occurs are given by the following parameters:

$$\frac{1}{T_2^*} = \frac{1}{T_2^O} + \frac{1}{T_2'} + \frac{1}{T_{2EX}} \quad (34)$$

T_2^O is the nuclear transverse relaxation time in the absence of exchange. Instrumental contributions to the linewidth are given by $1/T_2'$, and $1/T_{2EX}$ includes the exchange effects. $1/T_2^O$ is relatively small for protons in liquids compared to $1/T_2'$ so that the measurement of the natural relaxation time using steady state methods is quite restrictive. Removal of $1/T_2'$ is made possible by observing the dependence of the measured T_2 as a function of pulse separation. In this regard an accurate measurement of T_2^O should be possible using the spin echo method.

In liquids molecular rotation and diffusion take place rapidly. Following the assumptions of Brownian motion, Bloembergen, Purcell and Pound (4) have calculated that T_1 and T_2^O are approximately equal when $2\pi\nu_0\tau_c \ll 1$ where τ_c is the correlation time and is a measure of the time of local field fluctuations.

The temperature dependence of $1/T_2^0$ for the protons in DMCC is illustrated in figure XVIII. Values of T_2^0 were obtained from the short τ limit approximation at $(\omega\tau)^2 = 0$ and from the extrapolation of the curves in figure XVI to the limit of fast pulsing. At several temperatures T_1 was measured from the amplitude decay of the free induction tail in a $180-90^\circ$ two pulse experiment.

From the slope of the line in figure XVIII, the activation energy, ΔE_{vis} , for motion in the pure liquid may be obtained from the equation

$$\eta = A \exp(\Delta E_{\text{vis}}/RT) \quad (35)$$

where η is the viscosity coefficient and $\eta \propto \tau_c \propto \frac{1}{T_1}$.

From a least squares fit to the line in figure XVIII, the energy of activation is 1.70 Kcal./mole. For comparison purposes ΔE_{vis} for CHCl_3 is 1.76 Kcal./mole.

In table VII a comparison of T_2^0 with the values reported by Allerhand and Gutowsky (29) is presented.

Unlike dimethylnitrosamine which exhibited an unusual T_2^0 temperature dependence, T_2^0 for DMCC increases from 2.7 seconds at -27.0°C to 10.3 seconds at 102°C .

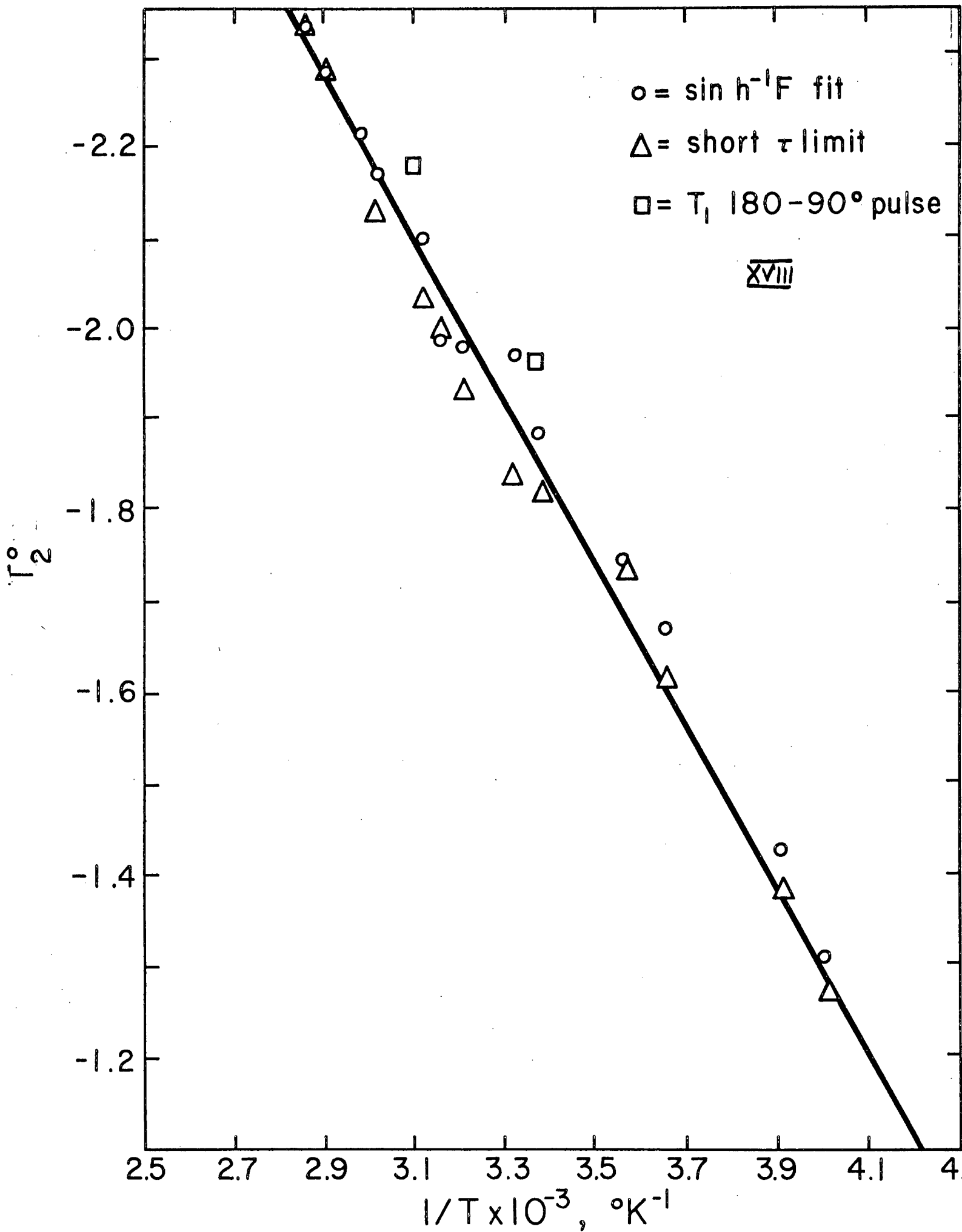
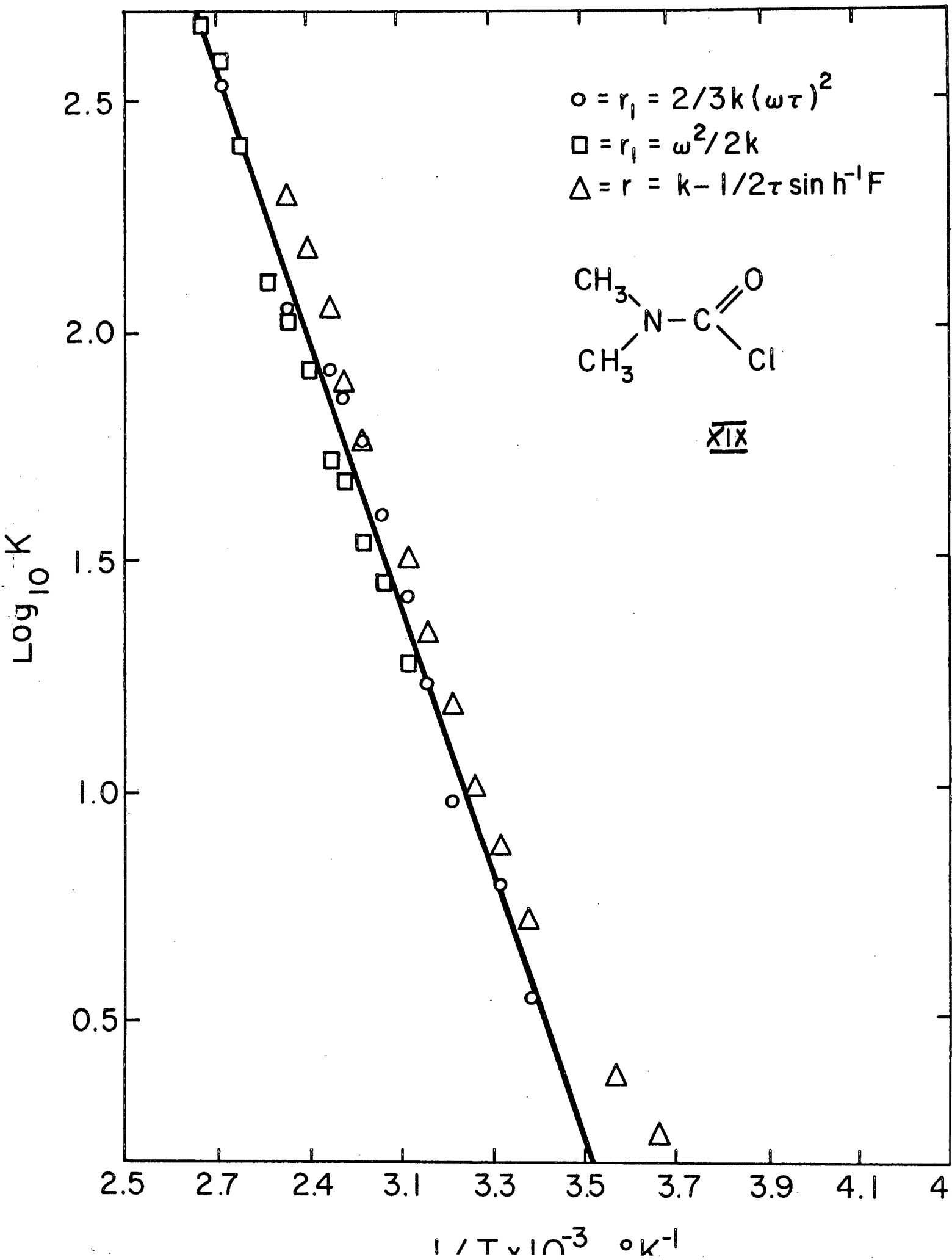


TABLE VII
TEMPERATURE DEPENDENCE OF T_2^O

TEMPERATURE	T_2^O	T_2^O (Ref 29)
$^{\circ}\text{C}$	SEC.	SEC.
26.5	6.2	4.5
33.0	6.8	5.7
38.0	6.8	6.2
42.5	7.4	5.6
47.0	7.6	8.0
54.0	7.6	8.6
60.0	8.9	9.0
71.0	9.8	9.3
79.0	10.3	8.8

(iv) Activation Parameters:

The temperature dependence of the rate constant for dimethylcarbamyl chloride is illustrated in figure XIX. For comparison purposes the rate constants are plotted as a function of temperature for the two limiting cases in the regions of slow and rapid pulsing. Rate constants obtained from the best fit to equation (23) are also included in the diagram.



In table VIII the activation parameters are listed. All values of E_a and A were calculated from the least squares line. The enthalpy, ΔH^\ddagger , and entropy, ΔS^\ddagger , were calculated in the same manner as described for dimethylnitrosamine. Table VIII contains values of the activation parameters reported for DMCC by Rogers and Woodbrey (34) using high resolution methods. Included as well are the spin echo results of Allerhand and Gutowsky (29).

TABLE VIII
N,N-DIMETHYLCARBAMYL CHLORIDE
ACTIVATION PARAMETERS

METHOD	A	E_a	ΔH^\ddagger	ΔS^\ddagger	REF.
SPIN ECHO	1.03×10^{11}	14.0 ± 0.7	13.3	-10.3	-
SPIN ECHO	1.16×10^{11}	14.4 ± 0.9	13.7	-10.0	-
SPIN ECHO	4.28×10^{10}	13.6 ± 1.1	12.9	-11.9	-
SPIN ECHO	7.90×10^{10}	14.0 ± 0.9	13.3	-10.5	(29)
S.S	2.50×10^7	9.7 ± 0.5	-	-	(29)
S.S	1.30×10^6	7.3 ± 0.5	-	-	(34)

In table VIII ΔH^\ddagger and ΔS^\ddagger are evaluated at 326°K. Steady state comparison measurements were obtained from the intensity ratios of the signals. An HA-100 temperature study using the complete theoretical line-shape fit for DMCC is presently in progress in our laboratory.

In the spin echo study of DMNA and DMCC the rate constant is the important parameter. Errors in the exchange rate, k , are considered to be $\pm 15\%$. Chemical shift values are reported to within $\pm 5\%$. An attempt was made to accurately measure T_2 in the Carr-Purcell experiment. The accuracy of T_2 measurements was poorer for DMNA at higher temperatures. Since the determination of T_2^O involves an extrapolation in the limit of fast pulsing an error of $\pm 10\%$ is claimed. The π -pulse repetition period was measured throughout the experiment with a Hewlett-Packard counter. Values of 2τ are accurate to better than 1%.

DISCUSSION

CHAPTER IV

The hindered internal rotation about the N-C and N-N bonds in DMCC and DMNA is an exchange process which has previously been studied by high resolution N.M.R. (34,37,39). For DMCC, determinations have been made by independent workers for the activation energy, E_a , which range from 7 to 14 Kcal/mole. In each case the error is approximately ± 1 Kcal/mole and the analyses only account for random errors. Previous studies measured the exchange rate over a narrow temperature range in which case systematic errors could not be detected or were not considered. The effect of systematic errors may be very serious and could result from false assumptions in the treatment of the experimental data.

In this investigation the spin echo method has been used to study exchange processes in two molecules. It is felt that this method could serve as an independent check on steady state measurements of rate constants. Only when both methods agree could a satisfactory set of data be established for the rate process.

A) Experimental Consideration:

The proton T_2 values for DMNA were obtained from two experiments differing only in their method of eliminating accumulated

error in the width of the 180° pulses. Both methods have the advantage of simplicity in operation and a slight improvement in the apparent signal to noise ratio was noted using the off resonance method of Wayne, Zamir and Strange (51). However, by working on resonance and using the 90° phase shift (49) the range of pulse intervals over which T_2 could be measured was extended. The Meiboom-Gill modification has generally been accepted as adequate in preventing errors and instabilities in the r.f. pulse widths from not becoming cumulative in their effects upon the echo amplitudes, but does introduce problems of radiation damping (53) in common with adiabatic fast passage (3).

All spin echo measurements were made at 40 Mc./s. In the investigation of the two molecules it is possible that systematic errors resulted from inhomogeneities in the H_1 field. The H_1 field homogeneity could be improved by placing the sample in a tube specially designed so that all of the sample rests in a spherical bulb at the end of the tube. The sample tube is then lowered slowly into the probe while observing the signal following the 180° pulse. The elimination of the decay signal insures that the sample is located in a homogeneous H_1 field.

Random errors result from the measurement of T_2 in the Carr-Purcell experiment. The exponential decays are measured directly from the photographs by plotting the logarithm of the echo amplitude as a function of time. In attempting to investigate the accuracy of T_2

measurements, baseline adjustments are important. A deviation of 1% in the baseline could introduce an error of 5% in the value of T_2 . The use of a high speed recorder and a logarithmic amplifier would be advantageous to the measurement of T_2 . Digital averaging techniques could be used to eliminate random but not systematic errors.

In these experiments the resonance condition was fairly difficult to maintain in the homogeneous H_0 field. Small magnetic field drifts even over five minutes necessitated readjustments. The choice of diode or phase sensitive detection does not affect the magnitudes of the echoes in the Carr-Purcell train. Using diode detection, the echo envelope is predicted to be slightly more complicated (28). Ideally then reproducible Carr-Purcell trains could be obtained by stabilizing the magnetic field with a field frequency lock system. As such there would be strict adherence to the resonance condition and the echo decay could be phase sensitive detected. Experimentally at the present time this is a difficult procedure.

When the barrier hindering a simple internal rotation in a molecule is ~ 15 Kcals, then assuming $\Delta S^* = 0$, the rotational isomers usually have distinguishable high resolution N.M.R. spectra at room temperature. In the spin echo method however, nuclei within γH_1 of the exchanging nuclei will interfere with the observation of the exchange effects. In this regard selective site pulsing would be possible by decreasing the power of the H_1 field. However the necessary

compensating feature is the resultant increase in the pulse width required to maintain the $90-180^\circ$ Carr-Purcell condition (58). In this case calculations have been made which show that calculated curves for a rate of 10^5 sec^{-1} indicate that errors of as much as 10% would result from the assumption that $t_w = 0$, where t_w is the pulse width.

B) Sensitivity of the Rate Constant and Activation Parameters to Systematic

Errors:

The importance of systematic errors in the spin echo method is indicated by the comparison of the rate constant data and the activation parameters presented for DMNA and DMCC.

In table IV the activation energies for the barrier to internal rotation in DMNA are in good agreement within the quoted errors. The values of the entropy of activation range from -3.92 e.u. to $+1.04 \text{ e.u.}$. The reported value of $\Delta S^* = -10.9 \text{ e.u.}$ for the off resonance dependence of T_2 upon pulse spacing is not considered to be significant in light of the limited range of pulse intervals available. For the hindered internal rotation in these systems the entropy of activation is expected to be approximately zero, since there is little change in the degree of randomness of the activated complex. Assuming that ΔS is zero and hence calculating the frequency factor from KT/h to be approximately 10^{13} sec^{-1} , the activation energy E_a can be calculated from the Arrhenius equation. At the coalescence temperature which for DMNA is 463°K

the rate constant k is calculated from

$$k = \frac{\pi \Delta \nu}{\sqrt{2}} \quad (36)$$

where $\Delta \nu$ is the chemical shift between the methyl groups in c./s.

For DMNA $k_{T_C} = 67.1 \text{ sec.}^{-1}$ and substituting into the Arrhenius equation the activation energy is 23.6 Kcal./mole. For DMCC at its coalescence temperature of 326°K $k_{T_C} = 9.79 \text{ sec.}^{-1}$ and $E_a = 18.1 \text{ Kcal./mole.}$ However consistently low values of the entropy averaging -10 e.u. are reported for DMCC. It is apparent that these low entropies result from systematic errors. The steady state measurements of Gutowsky (29) and Rogers (34) report frequency factors in the region of 10^6 to 10^7 sec.^{-1} . It is clear that these abnormal frequency factors must be regarded with suspicion.

In the spin echo method the value of k is determined from the complete dependence of T_2 upon pulse repetition period. Normally the steady state measurement of the chemical shift in the absence of exchange effects is used. As such k can be determined over the entire exchange region. The intercept of the line at infinite temperature $\frac{1}{T} = 0$ in the Arrhenius plot can be used directly to calculate the entropy of activation at T_C from the equation

$$\Delta S^* = 4.57 \left[\log_{10} A - 0.4335 - \log \left(\frac{KT}{h} \right) \right]. \quad (37)$$

For high resolution studies the calculation of ΔS^* is slightly more complicated and caution is required in the evaluation of the frequency

factor A. In the slow exchange region, the intercept to log k of the Arrhenius line is the frequency factor. In the fast exchange region the frequency factor no longer corresponds to the intercept but is modified by the chemical shift term. The transverse relaxation time is given by:

$$\frac{1}{T_2} - \frac{1}{T_2^O} = p_a^2 p_b^2 (\omega_A - \omega_B)^2 \cdot \frac{2}{k} \quad (38)$$

where: $\frac{1}{T_2} = \pi \Delta \nu_{1/2}$

p_a, p_b are the fractional populations in the exchange sites.

For equal populations,

$$\frac{1}{T_2} - \frac{1}{T_2^O} = \frac{(\omega_A - \omega_B)^2}{8k} = \frac{\pi^2 (\nu_A - \nu_B)^2}{2k} \quad (39)$$

so that the frequency factor in the fast exchange region is given by:

$$A = \frac{\pi^2 (\nu_A - \nu_B)^2}{2 \times (\text{intercept})} \quad (40)$$

from which the calculation of ΔS is straightforward.

The plot of log k as a function of $1/T$ is usually linear. From the slope of the line the activation energy is calculated. However, Gutowsky has stated (46) that this value of E_a represents the apparent activation energy which is a composite quantity including not only the true activation energy but an additional term α which might impart a slight temperature dependence of the activation energy itself. This then is a systematic error which will also change the frequency factor from A to A'. The Arrhenius equation takes the form:

$$k' = A' \exp \left[-(E_a + \alpha) / RT \right] \quad (41)$$

and k' is the apparent rate constant.

From the T_2 spin echo measurements, the most difficult regions to accurately fit the experimental data are in the very slow and very fast exchange regions. Assume then at the coalescence temperature T_c , the apparent and true rate constants are approximately equal. On this basis it is seen that a systematic error will add the term (α/T_c) to ΔS^* . In the two compounds studied the coalescence temperature of DMNA is 190°C compared with 50°C for DMCC. It is conceivable that such a systematic error as described could account for the consistently low values of ΔS^* reported for DMCC.

For both compounds the spin echo results appear to be converging on the "correct" value of KT/h for the frequency factor. However, the consistently low frequency factors obtained from the steady state method is indicative of systematic instrumental errors in addition to random errors in the measurement. By observing the dependence of the measured T_2 as a function of pulse repetition frequency it is possible to eliminate the instrumental contributions to the linewidth given by $1/T_2$. The possibility of saturation broadening (3) of the resonance line introduces a systematic error in the steady state method, but this can and usually is avoided. For high resolution studies H_1 , T_1 and T_2^0 are small enough so that saturation effects to the lineshape will be negligible. For a fixed H_1 field saturation broadening depends upon T_1 and T_2^0 which are

of course temperature dependent. As a result saturation will vary throughout the temperature range of the investigation.

In the spin echo method molecular diffusion processes will reduce the apparent value of T_2 . The extent to which the decays are attenuated depends upon the temperature and the pulse repetition frequency. In the Carr-Purcell experiment diffusion effects are minimized when the pulse spacing is small. In table III the rate constants for DMNA are listed for the on and off resonance experiments and compared to the steady state values of Reeves and Wells. At lower temperatures, where exchange effects are virtually absent, agreement in the values of k for all methods is satisfactory. At approximately 160°C , the values of k measured off resonance are slightly greater, until at 192°C $k_{\text{off}}\omega_0 = 2k_{\text{on}}\omega_0$. The off resonance dependence of T_2 was measured only over a narrow range of pulse intervals extending from 1.0 to 10.0 milliseconds.

DMNA was studied only in the slow exchange region up to approximately 190°C . In this region the fact that the values of k are rather high compared to the on resonance and steady state values indicates that the observed T_2 is too short. Since the rate constants are consistently high both in the limit of rapid pulsing and for the complete fit to the experimental data, the off resonance method of measuring T_2 suggested by Wayne, Zamir and Strange (51) appears to be affected by a systematic error which attenuates the Carr-Purcell decay. Molecular diffusion processes will introduce a systematic error in the

measurement of T_2 . However, diffusion effects will be more pronounced at higher temperatures in the fast exchange region. In table III there is good agreement in the rate constant data between the A-60 results obtained by Reeves and Wells and the complete fit to the on-resonance spin echo measurements. Further, the activation energy and the entropy value of +1.04 e.u. obtained by the spin echo method is in good agreement with the energy of activation for DMNA corresponding to $\Delta S = 0$.

DMCC was investigated by the spin echo method from the slow exchange region where at -27°C exchange effects are virtually absent up to 102°C where $k \gg \omega$. The rate constant data is presented in tables V and VI. In the limit of slow pulsing ($r_1 = \omega^2/2k$), the values of k were calculated from r_1 which was measured directly from the linear portion of the $\ln 1/T_2$ versus $\ln 1/2\tau$ curves in figure XVI. In table VI it is noticed immediately that the values of the rate constant for large pulse spacing are approximately one half of k derived from the short τ limit expression. If τ is large compared with k all of the nuclei will have exchanged many times between pulses and steady state conditions are approximated. In this region it is apparent that there is the possibility of a systematic error introduced because of diffusion effects. As a result, T_2 is decreased and since $\frac{1}{T_2} \propto \frac{1}{k}$ the value of k is less than the "true" rate constant for the exchange. Rate constants measured in the short τ limit agree favourably with the values of k obtained from the complete dependence of $1/T_2$ upon the pulse interval. It is interesting

to note that the rate constant data of Allerhand and Gutowsky (29) agree only with our spin echo results reported for the long τ limit. In their paper (29), results are reported in detail for N,N-dimethyltrichloroacetamide and in each section only the final results and no T_2 dependence diagrams are illustrated for DMCC. In light of the agreement with our spin echo results added to the fact that Allerhand and Gutowsky have worked in relatively inhomogeneous H_0 ($T_2^* \approx 5$ msec.) fields, it is suggested that diffusion effects have contributed to reducing their values of k for the exchange process.

For $\Delta S^* = 0$, the activation energy for DMCC is 18.1 Kcal/mole from equation (36) and the Arrhenius equation. The reported values of E_a all agree within experimental error. However the low frequency factors of $\sim 10^{11}$ lead to values of ΔS which average at ~ -10 e.u. Previous high resolution studies of the hindered rotation in DMCC (29,34) reported frequency factors of 10^7 and 10^6 . The spin echo results reported by Allerhand and Gutowsky (29) extended over a temperature range of 52° which makes it slightly more difficult to detect systematic errors. An HA-100 temperature study of DMCC is in progress in our laboratory. It is hoped that a full theoretical line shape fit to the experimental data will converge on the true rate constants for the exchange process. The spin echo method represents an interesting technique for the study of hindered rotation in DMCC. There has been considerable discussion of the experimentally determined entropies of activation and at this time

this should still be considered as an unsolved experimental problem.

DMCC and DMNA were suitably chosen for this spin echo study as they differ in chemical shift between the methyl groups and they can be studied over non-overlapping temperature regions. The results derived from the two compounds have indicated the importance of considering systematic errors in the evaluation of the activation parameters. The limiting expressions in the BRW (28) theory provide a simple experimental verification of the theory and provide an estimation of the rate constants and activation parameters. However, the information content of the $1/T_2(\text{C.P.})$ versus $1/2\mathcal{V}$ curves is more exact providing a large range of pulse intervals are used. In attempting to obtain the best fit of the experimental data to the equation

$$r_1 = k - \frac{1}{2\mathcal{V}} \sinh^{-1} F \quad (23)$$

no problems were encountered in fitting the data in the region where $\omega > k$. This was the case for both DMNA and DMCC. DMNA could not be studied above coalescence. For DMCC it was difficult to fit the data properly in the fast exchange region. This was due in part to the choice of initial trial values of k and ω . For $k > \omega$, the convergence limit to the best fit of the experimental data had to be changed in order to compute a value of k and ω . In general for DMCC, the computed rate constants have converged on values which are lower in the fast exchange region, than the experimentally determined values of k from

equation (28).

The chemical shift for a two site system undergoing exchange can be determined from the $1/T_2$ versus $1/2\tau$ curves as the chemical shift term ω appears in equation (23). From table V it is seen that the values of ω correspond to the chemical shift value reported for DMCC by the steady state method. Above the coalescence temperature the values of ω become appreciably larger. If systematic errors in the spin echo method tend to make $1/T_2$ too long, then in the fast exchange limit, substituting trial values into equation (23), the chemical shift is too large. Since the computer program varies k as well as ω in order to obtain the best fit to the experimental data, the high values of ω may result from a systematic error in the temperature dependence of the rate constant. The chemical shift itself is probably temperature insensitive, and in any case it would seem fortuitous if any temperature dependence of ω occurred only above T_c which has no special significance from the point of view of chemical structure. As a result the value of ω from the low temperature high resolution spectrum is considered as acceptable.

Allerhand and Gutowsky (46) have encountered similar problems in attempting to fit experimental spin echo data in the fast exchange region. In their study of cyclohexane and cyclohexane- d_{11} , at lower temperatures k , ω and $1/T_2^0$ could be determined. As the temperature was increased the natural relaxation time could no longer be determined and in the region where $k \gg \omega$, an assumed value of ω was used. As

yet unpublished results by Reeves has investigated the chair-chair isomerization of cyclohexane. A careful HA-100 high resolution study investigated the exchange over approximately 100° in small temperature increments. The reported activation energy is 12.1 Kcal/mole from line-width studies. This is higher than the previous values reported by Gutowsky (46) and Anet (44,45). Most important, the frequency factor is $1.15 \times 10^{14} \text{ sec.}^{-1}$ corresponding to an entropy of activation of +4.4 e.u. Once again attempts to fit the spin echo data in the fast exchange were not conclusive. However, these results are indicative of the fact that systematic errors limiting previous high resolution studies are further minimized at higher frequencies.

The temperature dependence of T_2^0 , the natural relaxation time is illustrated in figure XVIII for DMCC. The extrapolation of the line to $(\omega\gamma)^2 = 0$ in the short γ limit plot (figure XVII) gives values of T_2^0 which are in good agreement with the results obtained from the complete T_2 dependence upon pulse repetition frequency. Incorrect values of T_2^0 will introduce an error factor in the determination of the rate constant. It is conceivable that such an error will affect the values of k and ω in the fastest exchange region. In regions below this, the exchange contribution to $1/T_2$ is much larger than $1/T_2^0$. The range of rate constant measurements using the spin echo method is limited by the upper temperature limit of $1/T_2^0$ according to the equation

$$\frac{1}{T_2} = \frac{1}{T_2^0} + \frac{\omega^2}{2k}. \quad (28)$$

It is noteworthy to mention at this point that one of the most careful studies involving the measurement of the spin lattice relaxation time has been done by N. J. Trappeniers (54,55,56). His experiments involved the use of the pulse method to measure T_1 in polymers and to establish a "spin relaxation phase diagram" in methane and deuterated methanes. Mehlkopf and Smidt (57) have described their spin echo attachment to a steady state 60 Mc./s. spectrometer. They indicate the possible errors which are introduced for incorrect adjustment of the 180° pulse and they describe a method for eliminating field drift effects.

C) Comments on the Spin Echo Method:

The spin echo method represents a fairly well-established technique for measuring rate constants. Most important it introduces an independent means of verifying high resolution experiments. The spin echo rate determinations not only include the regions available to the high resolution method but extend the measurement to faster rates. All measurements in this investigation were carried out using an r.f. frequency of 40 Mc./s. In the fast exchange region the rate is directly proportional to the square of the chemical shift so that with an increase in the r.f. frequency above 40 Mc./s. the spin echo measurements will extend the rates to several fold faster compared to the present maximum.

The main disadvantage of the spin echo method to date is its lack of selectivity. In particular for exchange studies non-exchanging

nuclei within a range of γH_1 have to be selectively deuterated. The rate constant data is obtained from the complete dependence of T_2 upon pulse interval. Approximate expressions in the limit of slow and fast pulsing represent an internal check on the rate constant data.

High resolution rate constant measurements are limited by the effects of inhomogeneous fields which broaden the signal. The spin echo method has the advantage of extending beyond this region by rapid pulsing in the Carr-Purcell experiment. Further, effective heteronuclear decoupling occurs in the spin echo method where the exchange signals are modulated equally in the transfer sites.

Nevertheless it is important to recognize that systematic limitations do exist in the spin echo method. This study is an attempt to minimize systematic errors. Many papers in the literature discussing N.M.R. rate measurements must be read with caution if abnormal frequency factors are reported. The "true" values of rate constants in magnetic resonance should be the result of a spin echo investigation extending over as wide a temperature range as possible in addition to a high resolution study which includes a complete theoretical line shape fit to the experimental data. We should look forward to the time when a single hindered barrier has been studied by: (a) Carr-Purcell measurements of T_2 in comparison to full line shape calculations of high resolution spectra preferably in a field frequency locked mode, and (b) the double resonance method (59) compared to studies by the rotary echo method in the very

slow exchange region (60).

BIBLIOGRAPHY

1. F. Bloch. Phys. Rev., 70, 460 (1946)
2. I. I. Rabi, N. F. Ramsey and J. Schwinger.
Rev. of Mod. Phys. 26, 167 (1954)
3. "High Resolution Nuclear Magnetic Resonance Spectroscopy".
J. A. Pople, W. G. Schneider, H. J. Bernstein. McGraw-Hill,
(1959).
4. N. Bloembergen, E. M. Purcell and R. V. Pound.
Phys. Rev. 73, 679 (1948)
5. H. C. Torrey, Phys. Rev. 76, 1059 (1949)
6. E. L. Hahn. Phys. Rev. 77, 297 (1950)
7. E. L. Hahn. Phys. Rev. 80, 580 (1950)
8. B. Muller and M. Bloom. Can. J. Phys. 38, 1318 (1960)
9. H. Y. Carr and E. M. Purcell. Phys. Rev. 94, 630 (1954)
10. D. C. Douglas and D. W. McCall. J. Phys. Chem. 62, 1102 (1958)
11. J. H. Rugheimer and P. S. Hubbard. J. Chem. Phys. 39, 552 (1963)
12. D. E. Woessner. J. Chem. Phys. 34, 2057 (1961)
13. D. E. Woessner. J. Chem. Phys. 41, 84 (1964)
14. D. E. Woessner. J. Phys. Chem. 67, 1365 (1963)
15. E. O. Stejskal and J. E. Tanner. J. Chem. Phys. 42, 288 (1965)
16. H. S. Gutowsky, D. W. McCall and C. P. Slichter.
J. Chem. Phys. 21, 279 (1953)

17. H. S. Gutowsky and A. Saika. J. Chem. Phys. 21, 1688 (1953)
18. A. Loewenstein and S. Meiboom. J. Chem. Phys. 27, 1067 (1957)
19. E. L. Hahn and D. E. Maxwell. Phys. Rev. 88, 1070 (1952)
20. H. M. McConnell, J. Chem. Phys. 28, 430 (1958)
21. S. Alexander. J. Chem. Phys. 37, 967 (1962)
22. S. Alexander. J. Chem. Phys. 37, 974 (1962)
23. S. Alexander. J. Chem. Phys. 38, 1787 (1963)
24. L. Piette and W. A. Anderson. J. Chem. Phys. 30, 899 (1959)
25. A. Lowenstein and T. Connor. Ber. Bunsenges Physik Chem.
67, 280 (1963)
26. D. E. Woessner. J. Chem. Phys. 35, 41 (1961)
27. Z. Luz and S. Meiboom. J. Chem. Phys. 39, 366 (1963)
28. M. Bloom, L. W. Reeves and E. J. Wells.
J. Chem. Phys. 42, 1615 (1965)
29. A. Allerhand and H. S. Gutowsky. J. Chem. Phys. 41, 2115 (1964)
30. A. Allerhand and H. S. Gutowsky. J. Chem. Phys. 42, 1587 (1965)
31. J. G. Powles and J. H. Strange. Mol. Phys. 8, 169 (1964)
32. H. S. Gutowsky, R. L. Vold and E. J. Wells.
J. Chem. Phys. 43, 4107 (1965)
33. A. Allerhand. J. Chem. Phys. 44, 1 (1966)
34. M. T. Rogers and J. C. Woodbrey. J. Phys. Chem. 66, 540 (1962)
35. A. Loewenstein and S. Meiboom. J. Chem. Phys. 27, 1067 (1957)
36. K. H. Abramson, E. Krakower, P. T. Inglefield and L. W. Reeves.
Can. J. Chem. In Press.

37. W. D. Phillips. Ann. N.Y. Acad. Sci. 70, 817 (1958)
38. H. W. Brown and D. P. Hollis. J. Mol. Spec. 13, 305 (1964)
39. D. J. Blears. J.A.C.S. Sup. 2, 6256 (1964)
40. J. C. Woodbrey and M. T. Rogers. J.A.C.S. 84, 13 (1962)
41. A. G. Whittaker and S. Siegel. J. Chem. Phys. 42, 3320 (1965)
42. E. S. Gore, D. J. Blears and S. S. Danyluk. Can. J. Chem. 43, 2135 (1965)
43. F. A. Bovey, F. P. Hood, E. W. Anderson and R. L. Kornegay. J. Chem. Phys. 41, 2041 (1964)
44. F. A. L. Anet, M. Ahmad and L. D. Hall. Proc. Chem. Soc. 145 (1964)
45. F. A. L. Anet and M. Z. Haq. J. A. C. S. 87, 3147 (1965)
46. A. Allerhand, Fu-Ming Chen and H. S. Gutowsky. J. Chem. Phys. 42, 3040 (1963)
47. A. Allerhand and H. S. Gutowsky. 42, 4203 (1965)
48. H. S. Gutowsky and Fu-Ming Chen. J. Phys. Chem. 69, 3216 (1965)
49. S. Meiboom and D. Gill. Rev. Sci. Instr. 29, 688 (1958)
50. L. W. Reeves and E. J. Wells. Disc. Far. Soc. 34, 177 (1962)
51. R. C. Wayne, D. Zamir and J. H. Strange. Rev. Sci. Instr. 35 1051 (1964)
52. S. L. Gordon and J. D. Baldeschwieler. J. Chem. Phys. 41, 571 (1964)

53. A. Szöke and S. Meiboom. Phys. Rev. 113, 585 (1959)
54. N. J. Trappeniers, C. J. Gerritsma and P. H. Oosting.
Physica, 30, 997 (1964)
55. N. J. Trappeniers, C. J. Gerritsma and P. H. Oosting.
Physica, 31, 202 (1965)
56. N. J. Trappeniers, C. J. Gerritsma and P. H. Oosting.
Physics Letters, 16, 44 (1965)
57. A. F. Mehlkopf and J. Smidt. J. Sci. Instr. 43, 253 (1966)
58. C. S. Johnson Jr. and M. Saunders. J. Chem. Phys. 43, 4170
(1965)
59. S. Forsen and R. A. Hoffman. J. Chem. Phys. 39, 2892 (1963)
60. E. J. Wells. Private Communication.