

The University of Manitoba

PROTON MAGNETIC RESONANCE STUDIES OF CONFORMATIONAL
PREFERENCES AND ROTATIONAL BARRIERS IN
SOME HALOTOLUENE DERIVATIVES

by

WILLIAM JAMES PEELING

A Thesis

Submitted to

The Faculty of Graduate Studies and Research

The University of Manitoba

In Partial Fulfillment

of the Requirements of the Degree

DOCTOR OF PHILOSOPHY

Winnipeg, Manitoba

September, 1973



PROTON MAGNETIC RESONANCE STUDIES OF CONFORMATIONAL
PREFERENCES AND ROTATIONAL BARRIERS IN
SOME HALOTOLUENE DERIVATIVES

By: William James Peeling

A dissertation submitted to the Faculty of Graduate Studies of
the University of Manitoba in partial fulfillment of the requirements
of the degree of

DOCTOR OF PHILOSOPHY

© 1973

Permission has been granted to the LIBRARY OF THE UNIVER-
SITY OF MANITOBA to lend or sell copies of this dissertation, to
the NATIONAL LIBRARY OF CANADA to microfilm this
dissertation and to lend or sell copies of the film, and UNIVERSITY
MICROFILMS to publish an abstract of this dissertation.

The author reserves other publication rights, and neither the
dissertation nor extensive extracts from it may be printed or other-
wise reproduced without the author's written permission.

ACKNOWLEDGEMENTS

I wish to express my appreciation to Dr. T. Schaefer for his guidance, criticism and encouragement during the course of this study.

I also extend thanks to my colleagues for many interesting discussions, occasionally related to this work, over the past four years. Dr. Bruce Goodwin provided much needed assistance with the computer programming, and Drs. Ludger Ernst and Brian Rowbotham performed many of the syntheses. Their help was greatly appreciated.

Finally I would like to thank the University of Manitoba and the National Research Council of Canada for financial assistance.

ABSTRACT

This thesis describes the proton magnetic resonance (p.m.r.) study of the conformational preferences and barriers to internal rotation in a number of halogenated toluene derivatives.

In chapter II, n.m.r. methods of measuring barriers to internal rotation are discussed, with emphasis on high resolution techniques. Methods of calculating these barriers are reviewed in chapter III.

Chapter IV describes the study by high resolution p.m.r. of the hindered internal rotation in α,α -difluoro-2,6-dichlorotoluene (DFDCT), α,α -dibromo-2,4,6-trichlorotoluene (DBTCT), α,α -diiodo-2,6-dichlorotoluene (DIDCT), α,α -dichloro-2,4,6-tribromotoluene (DCTBT), and $\alpha,\alpha,2,4,6$ -pentabromotoluene (PBT). The stable conformation can be deduced from the p.m.r. spectra for each compound in the temperature region where the resonance lines are not broadened by exchange. The chemical shifts of the protons are explained in terms of solvent effects and intramolecular steric effects. Values of E_a , $\log A$, ΔH^\ddagger , and ΔS^\ddagger for the internal rotations are found for DCTBT and PBT by an analysis of the temperature dependence of the shape of the ring proton signals, and values for ΔG^\ddagger are found in a similar fashion for each compound except DFDCT. It is possible only to set an upper limit on ΔG^\ddagger for this compound. The experimental barrier

heights compare well with barriers calculated by a semi-empirical method employing partial geometrical optimization. A purely empirical relationship is found relating the free energy of activation to the van der Waals volumes and the bond lengths of the halogen substituents. It is concluded that the rotational barriers originate in steric interactions between the ortho halogens and the halogens on the dihalomethyl group.

The study of the conformational preferences and the hindered rotation of the dichloromethyl groups in $\alpha, \alpha', \alpha', 2, 4, 5, 6$ -octachloro-*m*-xylene (MOCX) and $\alpha, \alpha', \alpha', \alpha'', \alpha''-2, 4, 6$ -nonachloromesitylene (NCM) is discussed in chapter V. These compounds exist as mixtures of isomers in solution. The p.m.r. spectrum of MOCX at low temperatures is assigned by comparison to the spectrum of $\alpha, \alpha', \alpha', 2, 4, 6$ -heptachloro-*m*-xylene (MHCX), and the chemical shifts of the protons of MOCX, MHCX, and NCM are rationalized in terms of solvent effects and intramolecular steric effects. The temperature dependent p.m.r. spectra of MOCX in toluene- d_8 solution are fitted to computed spectra based on a set of coupled Bloch equations and the activation parameters for the conformational interconversions are found. Similarly the activation parameters for the rotation of the dichloromethyl groups in the two conformations of NCM are reported for solutions in toluene- d_8 and methylene chloride. In addition, free energies of activation are given for solutions

in bromochloromethane, trichloroethylene, and in carbon disulfide. The free energies of activation are lower in the toluene-d₈ solution than in the other solutions. The symmetrical conformation is more stable than the unsymmetrical one in all the solvents.

TABLE OF CONTENTS

	<u>Page No.</u>
CHAPTER I	INTRODUCTION 1
CHAPTER II	N.M.R. METHODS OF DETERMINING BARRIERS TO INTERNAL ROTATION 5
	1. Introduction 5
	2. High Resolution N.M.R. Methods 5
	(a) Classical lineshape theory 6
	(b) Quantum mechanical lineshape theory 9
	(c) Determination of rate constants from high resolution n.m.r. lineshapes 15
	3. Spin-echo Method 20
	4. Double Resonance Method 23
	5. Other N.M.R. Methods 25
CHAPTER III	THEORETICAL CALCULATIONS OF BARRIERS TO INTERNAL ROTATION 29
	1. Introduction 29
	2. Quantum Mechanical Calculations 31
	(a) <u>Ab initio</u> calculations 31
	(b) Semiempirical methods 35
	(c) Summary of quantum mechanical calculations of barriers 38
	3. Classical Calculations 39
	(a) Basic principles of the classical model 39
	(b) Barber's method 43
	(c) Ernst's method 45

(d) The shape of the rotation barrier	47
---	----

CHAPTER IV	PROTON MAGNETIC RESONANCE STUDIES OF HINDERED ROTATION IN $\alpha,\alpha,2,6$ -TETRAHALOTOLUENE DERIVATIVES	53
------------	---	----

1. Introduction	53
-----------------------	----

2. Experimental	55
-----------------------	----

(a) Preparation of compounds	55
------------------------------------	----

(i) DFDCT	55
-----------------	----

(ii) DBTCT	56
------------------	----

(iii) DIDCT	56
-------------------	----

(iv) DCTBT	57
------------------	----

(v) PBT	58
---------------	----

(b) N.m.r. samples	58
--------------------------	----

(c) N.m.r. spectra	59
--------------------------	----

(d) Temperature measurements	59
------------------------------------	----

(e) Determination of preexchange lifetimes	61
--	----

(f) Determination of activation parameters	63
--	----

3. Results	64
------------------	----

(a) Spectral parameters at low and high exchange rates	64
--	----

(b) Temperature dependence of the spectral parameters	65
---	----

(i) DFDCT	65
-----------------	----

(ii) DBTCT	72
------------------	----

(iii) DIDCT	72
-------------------	----

(iv) DCTBT	72
------------------	----

(v)	PBT	72
(c)	Proton resonance spectra under conditions of exchange	75
(i)	DFDCT	75
(ii)	DBTCT	75
(iii)	DIDCT	76
(iv)	DCTBT	76
(v)	PBT	80
(d)	Experimental activation parameters	80
(e)	Calculated barrier heights	82
4.	Discussion	87
(a)	Spectral parameters at high and low exchange rates	87
(b)	The activation parameters	91
(i)	Errors	91
(ii)	Solvent effects and the effect of para substituents	93
(iii)	The Arrhenius parameters..	94
(iv)	The entropy of activation..	96
(v)	The enthalpy of activation - semiempirical barrier calculations	97
(vi)	The free energy of activation	98
5.	Conclusion	104

CHAPTER V

PROTON MAGNETIC RESONANCE STUDIES OF ROTATIONAL ISOMERISM IN $\alpha, \alpha', \alpha''$ 2,4,5,6-OCTACHLORO-M-XYLENE AND $\alpha, \alpha', \alpha'', \alpha''', \alpha''''$, 2,4,6-NONACHLORO- MESITYLENE	106
--	-----

1.	Introduction	106
2.	Experimental	109
	(a) Preparation of MOCX	109
	(b) Preparation of MHCX	109
	(c) Preparation of NCM	109
	(d) N.m.r. samples	110
	(e) Spectral measurements	110
3.	Results and Discussion	110
	(a) The exchange processes	110
	(i) MOCX	110
	(ii) NCM	111
	(b) N.m.r. spectra in the region of slow exchange	112
	(i) MOCX and MHCX	112
	(ii) NCM	119
	(c) Relative populations of the conformers	123
	(i) MOCX and MHCX	124
	(ii) NCM	126
	(d) Lineshape theory and computer programs	128
	(e) Temperature dependence of the peak positions	129
	(i) MOCX	129
	(ii) NCM	130
	(f) Linewidths in the absence of exchange	131
	(i) MOCX	131
	(ii) NCM	131

(g)	Fitted spectra	133
(h)	The activation parameters	137
	(i) MOCX	137
	(ii) NCM	137
(i)	Error estimates	141
	(i) site frequency errors	141
	(ii) effective T_2 errors	141
	(iii) errors in temperature	142
(j)	Discussion of the activation parameters	143
	(i) free energy profiles for rotation	143
	- MOCX	143
	- NCM	145
	(ii) comparison of the activation parameters	147
	(iii) solvent dependence of the activation paraments for NCM	150
(k)	Solvent effects on ground state stabilities for NCM	150
4.	Conclusion	152
APPENDIX	THE BLOCH EQUATION FORMULATION OF EXCHANGE AMONG FOUR UNCOUPLED SITES	154

LIST OF TABLES

<u>Table No.</u>		<u>Page No.</u>
1	Composition of the n.m.r. samples of the $\alpha, \alpha, 2, 6$ -tetrahalotoluene derivatives.....	60
2	Spectral parameters for the protons of DBTCT, DIDCT, DCTBT and PBT at low temperatures.....	66
3	Spectral parameters for DFDCT at 32°C.....	71
4	Spectral parameters for DCTBT at several low temperatures.....	73
5	Preexchange lifetimes at various temperatures for the $\alpha, \alpha, 2, 6$ -tetrahalotoluene derivatives...	78
6	Activation parameters for the internal rotation in the $\alpha, \alpha, 2, 6$ -tetrahalotoluene derivatives.....	85
7	Results of the semiempirical barrier calculations for PCT, DBTCT, DCTBT, and PBT.....	86
8	"Corrected" chemical shifts of the protons in PCT, DBTCT, DIDCT, DCTBT, and PBT.....	90
9	The free energies of activation and the empirical parameter S^{-1} for the $\alpha, \alpha, 2, 6$ -tetrahalotoluene derivatives.....	100
10	Free energy barrier heights for the symmetrical $\alpha, \alpha, 2, 6$ -tetrahalotoluene derivatives, calculated using the empirical parameter S^{-1}	103
11	Proton chemical shifts of NCM in toluene- d_8 and methylene chloride solution.....	121
12	Conformational enthalpy differences for NCM in several solvents.....	127
13	Activation parameters for the internal rotations in MOCX.....	138
14	Activation parameters for the internal rotations in NCM.....	139
15	Free energies of activation for the internal rotations in NCM in several solvents.....	140

LIST OF FIGURES

<u>Figure No.</u>		<u>Page No.</u>
1	Potential barrier to hindered rotation for the $\alpha, \alpha, 2, 6$ -tetrahalotoluenes as given by Barber.....	48
2	Potential barrier to hindered rotation for the $\alpha, \alpha, 2, 6$ -tetrahalotoluenes as given by Ernst.....	49
3	A spectrum of DBTCT at low temperature.....	67
4	A spectrum of DIDCT at low temperature.....	68
5	A spectrum of DCTBT at low temperature.....	69
6	A spectrum of PBT at low temperature.....	70
7	Internal chemical shift of the ring protons of DCTBT plotted vs. temperature.....	74
8	Calculated and experimental spectra of the ring protons of DBTCT showing exchange broadening.....	77
9	Calculated and experimental spectra of DIDCT showing exchange broadening.....	79
10	Representative experimental and calculated spectra of PBT at various temperatures.....	81
11	Eyring plot for the hindered rotation in DBTCT.....	83
12	Eyring plot for the hindered rotation in PBT.....	84
13	Experimental and calculated p.m.r. spectra of MOCX at -41° C.....	113
14	P.m.r. spectrum of MHCX at -41° C.....	115
15	P.m.r. spectrum of NCM in methylene chloride solution at -36.6° C.....	120
16	Some experimental and calculated spectra of MOCX showing exchange effects.....	132

17	Eyring plot for one of the exchanges in MOCX showing the effect of the different population assumptions.....	134
18	Some calculated and experimental spectra for NCM in methylene chloride solution showing exchange effects.....	135
19	Eyring plots for the internal rotation in NCM in methylene chloride solution.....	136
20	Free energy profile for the internal rotations in MOCX.....	144
21	Free energy profile for the internal rotations in NCM.....	146

A large number of molecules exist as a mixture of conformational isomers or conformers which can be interconverted by rotation about a chemical bond. In general such a rotation is accompanied by a change in the internal energy of the molecule. Two important free energy differences are associated with internal rotation: the difference in free energy between stable isomers, ΔG , and the free energy barrier hindering rotation, ΔG^\ddagger . Knowledge of the temperature dependence of these quantities allows the determination of the respective enthalpies and entropies through the relations

$$\begin{aligned}\Delta G &= \Delta H - T\Delta S \\ \Delta G^\ddagger &= \Delta H^\ddagger - T\Delta S^\ddagger.\end{aligned}\tag{1}$$

These parameters are of interest in view of their importance in relation to physical properties of the molecule and also in determining the structures of macromolecules.

The free energy differences between stable isomers can be determined by a number of physical techniques including infrared, Raman, microwave, and nuclear magnetic resonance (n.m.r.) spectroscopies. A large number of such energy differences are now accurately known, and their origins are well understood.^(1 - 4) Until recently, however, less has been known about the barriers to internal rotation.

These barriers may be determined in several ways. It is sometimes necessary to postulate a barrier of a

certain energy in order to obtain agreement between calculations and experimental observations of, for instance, thermodynamic properties such as entropy and heat capacity, or the n.m.r. spectra of molecules partially oriented in the nematic phase. Techniques such as infrared, Raman, or microwave spectroscopies, electron diffraction, neutron scattering, and dipole moment measurements can be used to determine torsional frequencies. These torsional frequencies can then be used to calculate the potential energy function as a Fourier series in the torsion angle ϕ ,

$$V(\phi) = \frac{1}{2} \sum_{i=1}^n V_i (1 - \cos i\phi). \quad (2)$$

$V(\phi)$ gives the potential energy corresponding to the torsion angle ϕ . The difference between the maximum and minimum values of V is called the potential barrier, and is equivalent to ΔH^\ddagger .

Rates of internal rotation may be determined directly by ultrasonic and dielectric absorption measurements and by n.m.r. and electron spin resonance spectroscopy. The free energy barrier to rotation (also called the free energy of activation) can then be calculated within the theory of absolute reaction rates by

$$k = \frac{\kappa k_B T}{h} \exp(-\Delta G^\ddagger/RT) \quad (3)$$

where k is the rate constant measured at the absolute temperature T , κ is the transmission coefficient, k_B is the

Boltzmann constant, h is Planck's constant, and R is the gas constant. Measurement of k as a function of temperature then allows determination of the enthalpy and entropy of activation through equation (1). Alternatively, equations (1) and (3) may be combined to give

$$k = \frac{\kappa k_B T}{h} \exp(-\Delta H^\ddagger/RT) \exp(\Delta S^\ddagger/R) \quad (4)$$

and a plot of $\ln(k/T)$ vs. $1/T$ yields a straight line with slope proportional to ΔH^\ddagger and intercept proportional to ΔS^\ddagger .

Another common practice has been to construct a linear Arrhenius plot

$$\ln k = -\frac{E_a}{RT} + \ln A \quad (5)$$

and to extract the activation energy E_a from the slope and the frequency factor A from the intercept, and to obtain ΔH^\ddagger and ΔS^\ddagger by

$$\Delta H^\ddagger = E_a - RT \quad (6)$$

$$\Delta S^\ddagger = R \left[\ln \frac{hA}{\kappa k_B T} - 1 \right] \quad (7)$$

However, these equations introduce a temperature dependence into ΔH^\ddagger and ΔS^\ddagger . This temperature dependence is artificial, since it arises from the assumed temperature independence of E_a and A . It is more reasonable to assume temperature-independent ΔH^\ddagger and ΔS^\ddagger values and obtain them as described above. However, the Arrhenius parameters E_a and A may give some insight into the process of the internal rotation through

the simple collision theory of chemical reactions. (5,6)

The various methods of determining conformational energy differences and barriers to internal rotation have been discussed and compared in a number of articles. (3, 4, 7-9) Barriers in a fairly large number of molecules have now been measured by these different techniques. This dissertation describes the application of high resolution continuous wave n.m.r. to studies of rotational isomerism about the $sp^2 - sp^3$ carbon-carbon single bond in a series of halogenated toluene derivatives. In chapter II, a discussion of the various n.m.r. methods used to measure internal rotational barriers is presented, with emphasis on continuous wave techniques. Chapter III briefly describes some methods of calculating these barriers theoretically. In chapters IV and V, the measurements of barriers to internal rotation in a number of halogenated toluene derivatives are described and the results are discussed.

CHAPTER II N.M.R. METHODS OF DETERMINING BARRIERS TO

INTERNAL ROTATION

1. Introduction

Most n.m.r. methods measure directly the rates of internal rotation. When the rotational process causes a nucleus to exchange between magnetically non-equivalent positions or "sites" in the molecule with a rate constant of a similar order of magnitude as the total spread of the n.m.r. spectrum of the nucleus (typically 10^{-1} to 10^5 sec^{-1}), a profound change in the shape of the n.m.r. signals may result. A number of methods and theoretical procedures have been developed whereby one can use all the parameters of n.m.r. spectra which vary with the rate of exchange of the nuclei to determine the rate constants of the exchange. Application of equations (3) to (5) then yields the activation parameters for the internal rotation.

This chapter describes the methods of determining rates of internal rotation from high resolution n.m.r. experiments (section 2), pulse n.m.r. experiments (section 3), and double resonance experiments (section 4). The determination of rotational barriers using other n.m.r. methods is discussed in section 5.

2. High Resolution N.M.R. Methods

High resolution n.m.r. is used to determine barriers

to internal rotation by studying the n.m.r. lineshape. When internal rotation causes magnetically non-equivalent nuclei to exchange sites at a rate of the order of the chemical shift between the nuclei, the shape of the n.m.r. absorption signal is affected. Theoretical expressions for the lineshape as a function of the rate of exchange (and other spectral parameters) can be derived and, by matching the lineshapes calculated theoretically to the experimental spectrum, the rate of internal rotation can be determined.

The methods of calculating the high resolution n.m.r. lineshapes and the determination of the rates of internal rotation from them are described in this section.

(a) Classical lineshape theory

Bloch⁽¹⁰⁾ described the n.m.r. phenomenon by a set of classical equations that provide an adequate formulation in systems which exhibit no nuclear spin-spin coupling. Gutowsky et al⁽¹¹⁾ first modified the Bloch equations to give expressions for the n.m.r. lineshapes in the presence of exchange reactions. For a system of two sites A and B shifted by $\delta\omega/2$ and $-\delta\omega/2$ from their weighted average frequency ω_0 , with relative populations p_A and p_B , the total magnetization in the x - y plane is given by^(12, 13)

$$G = \frac{i\omega_1 M_0 [(\tau_A + \tau_B) + \tau_A \tau_B (\alpha_A p_B + \alpha_B p_A)]}{(1 + \alpha_A \tau_A) (1 + \alpha_B \tau_B) - 1} \quad (8)$$

where the average lifetime at site A is $\tau_A = 1/k_{A \rightarrow B} = \tau/p_B$ and for site B, $\tau_B = 1/k_{B \rightarrow A} = \tau/p_A$ where $\tau = \tau_A \tau_B / (\tau_A + \tau_B)$. M_0 is the static nuclear magnetization at thermal equilibrium, $\omega_1 = \gamma H_1$, H_1 is the strength of the applied rf field of frequency ω , $\alpha_A = (1/T_2) - i(\Delta\omega + \delta\omega/2)$, $\alpha_B = (1/T_2) - i(\Delta\omega - \delta\omega/2)$, and $\Delta\omega = \gamma H_0 - \omega$. T_2 is the inverse linewidth parameter. The n.m.r. absorption signal Y is then given by the imaginary part of the x - y magnetization,

$$Y = \text{Im} (G). \quad (9)$$

It is seen from equation (8) that the shape of the n.m.r. spectrum is determined by $\delta\omega$, T_2 , the lifetimes τ_A and τ_B , and the populations p_A and p_B . At slow exchange rates ($\tau > [\sqrt{2}\pi\delta\omega]^{-1}$), two n.m.r. signals are observed with a separation of $\delta\omega$; decreasing τ causes the signals to broaden and collapse, and for high exchange rates ($\tau\delta\omega < 1$) one signal with a frequency of ω_0 is observed. The point at which the separate signals merge is called the coalescence point.

McConnell⁽¹⁴⁾ included directly in the Bloch equations terms taking into account the exchange. His simple formulation is readily extended to exchange between unequally populated sites, and is particularly amenable to generalization to multi-site exchange processes. For a

general exchange process among n sites of populations p_j it is necessary to solve the n coupled equations for G_j ,

$$- [i(\omega_j - \omega) + \frac{1}{T_{2j}}] G_j + \sum_{k \neq j} \left(p_j \frac{G_k}{\tau_{jk}} - p_k \frac{G_j}{\tau_{kj}} \right) = -i\gamma H_1 M_0 p_j \quad (10)$$

$$j = 1, 2, \dots, n$$

Here ω_j is the frequency of site j in the absence of exchange, and T_{2j} is the effective transverse relaxation time of nuclei in site j . Using the steady state kinetic approximation (since the exchange process is being observed at equilibrium), $p_k \tau_{jk} = p_j \tau_{kj} \equiv \tau'_{jk} = \tau'_{kj}$, where $\tau_{kj} = 1/k_{k \rightarrow j}$. Then the total x-y magnetization is

$$G = \sum_{j=1}^n G_j \quad (11)$$

and equation (9) gives the absorption mode n.m.r. signal. In the appendix, an analytical expression for an exchange among four independent sites is derived using equation (10), and a listing is given of a computer program written to calculate the n.m.r. lineshape for this case.

It is evident that equation (10) can be conveniently expressed in matrix form and solved by matrix techniques. This has been done a number of times, most recently by Reeves and co-workers, ^(15,16) who developed and programmed an efficient matrix formulation of the modified Bloch equations, allowing a concise analysis of multi-site exchange systems. Their method has been applied to the study of both intramolecular ^(15, 17, 18) and intermolecular ⁽¹⁹⁾

exchange reactions among up to fifteen sites.

Extensive reviews of the Bloch equation description of exchange have been published, (20 - 23) and should be consulted for further details.

The Bloch equations are strictly applicable only to an ensemble of independent spins, although they have been applied with some success to descriptions of exchange in systems exhibiting first-order spin-spin coupling. (11, 13, 17, 24 - 27) Since the vast majority of compounds show spin-spin coupling in the n.m.r. spectra, the Bloch formulation has a somewhat limited applicability. In cases in which spin-spin coupling does occur, a quantum mechanical treatment of exchange should be used.

(b) Quantum mechanical lineshape theory

The quantum mechanical treatment of the effect of exchange on high resolution n.m.r. lineshapes is based on the time variation of the components of the density matrix of the system. This treatment has been thoroughly discussed in a number of articles. (21 - 23, 28 - 31) Briefly, the expectation value of any operator A is given by

$$\langle A \rangle = \text{Tr}(\rho A) \quad (12)$$

where ρ is the density matrix of the system. The total magnetization in the x-y plane of a system in an n.m.r. experiment is represented by the expectation value of the operator $I_x + iI_y \equiv I_+^\dagger$. Then from equations (9) and (12),

the absorption mode signal is given by

$$Y = \text{Im}(G) = \text{Im}(\langle I^+ \rangle) = \text{Im}[\text{Tr}(\rho I^+)] \quad (13)$$

The values of the density matrix elements which contribute to the absorption in equations (13) can be found from the equation of motion of the density matrix,

$$\frac{d}{dt} \rho = \frac{i}{\hbar} [\rho, H] \quad (14)$$

where H is the normal high-resolution n.m.r. Hamiltonian:

$$H = \sum_i I_z^i (\omega_i - \omega) + \sum_{i < j} J_{ij} (I^i \cdot I^j) + \sum_i \gamma_i I_x^i H_1 \quad (15)$$

The equation of motion must be modified to account for exchange and relaxation effects:

$$\frac{d}{dt} \rho = \frac{i}{\hbar} [\rho, H] + \left(\frac{\partial \rho}{\partial t} \right)_{\text{exchange}} + \left(\frac{\partial \rho}{\partial t} \right)_{\text{relaxation}} \quad (16)$$

Kaplan⁽³²⁾ and Alexander⁽³³⁾ first used such a

treatment to determine lineshapes of n.m.r. spectra for nuclei undergoing mutual exchange. Representing the exchange by an exchange operator R, the time dependence of the density matrix element for the transition between states k and l is⁽²¹⁾

$$\begin{aligned} \frac{d}{dt} \rho_{kl} = & \frac{1}{\tau} \left[\sum_{n,m} R_{kn} \rho_{nm} R_{ml} - \rho_{kl} \right] - \frac{\rho_{kl}}{T_2} \\ & - i \rho_{kl} \left[\sum_i (\omega_i - \omega) \left\{ (I_z^i)_{kk} - (I_z^i)_{ll} \right\} + \sum_{i < j} J_{ij} \left\{ (I_z^i I_z^j)_{kk} - (I_z^i I_z^j)_{ll} \right\} \right] \\ & + \frac{i}{2} \sum_{i < j} J_{ij} \left[\rho_{, I^+ i I^- j + I^+ j I^- i} \right] + i \omega_1 (\rho_{kk} - \rho_{ll}) \sum_i (I_x^i)_{kl} \quad (17) \end{aligned}$$

where T_2 is the spin-spin relaxation time, providing the proper linewidth in the absence of exchange, and τ is the mean lifetime of the nucleus in each site. R_{kn} permits the inclusion of the density matrix elements in a way appropriate to the exchanging system. Under unsaturated steady-state conditions, the time derivatives in equation (17) are set equal to zero, yielding a set of simultaneous equations with complex coefficients. Solution of these equations gives the values of the elements of the density matrix necessary to calculate the n.m.r. absorption line-shape from equation (13).

Computer programs based on these equations were written to examine the mutual exchange between two coupled nuclei^(34,35) very soon after the equations were first expounded. Since then a large number of groups have written programs to calculate lineshapes for a variety of systems undergoing mutual exchange; for instance, Forsén and co-workers⁽³⁶⁾ have described a program which solves the lineshape equations for some systems of up to four spins and have illustrated its use in analyzing some complex exchange processes.^(37 - 39) Different exchange processes for systems of up to four spins have been studied by Derendyaev.⁽⁴⁰⁾

Since equation (13) involves the trace of the matrix ρI^+ , Y is independent of the representation defined by the basis functions. Yamamoto and Nakanishi⁽⁴¹⁾ have recently