nuclear
magnetic
resonance

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Nuclear Magnetic Resonance

APPLICATIONS TO ORGANIC CHEMISTRY

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Preface

This brief book is the outgrowth of some forty lectures in which it was attempted to explain the phenomenon of nuclear magnetic resonance absorption and the uses of high-resolution nuclear magnetic resonance spectroscopy to organic chemists whose background, like that of the author, has often been deficient in nuclear and electromagnetic theory. Quite a number of suggestions were received for presentation of the material in printed form with illustrations based on the lecture slides. This has now been done, and it is hoped that the result will be of service to practicing chemists and students as a guide to various applications of NMR spectroscopy and an introduction to more authoritative works. Throughout, the coverage is illustrative rather than comprehensive.

The author apologizes for choosing rather too many examples of applications from his own research, but it is always easiest to write about what one knows best. He is greatly indebted to Dr. W. D. Phillips of the E. I. du Pont Company for helping to kindle his interest in NMR research and to Dr. James N. Shoolery of Varian Associates and Professors V. Schomaker and H. M. McConnel for many patient hours of explanation with respect to both simple and difficult points of theory. The Office of Naval Research supported much of the research described herein which was carried out at the California Institute of Technology.

Dr. Shoolery kindly supplied material for several of the figures, and Dr. Marjorie C. Caserio helped greatly with many of the details in getting the book together. Helpful suggestions were received from Professors D. Y. Curtin, R. Breslow, and D. E. Applequist. Professors William S. Johnson and E. E. van Tamelen supplied several unpublished spectra for Chapters 2 and 3.

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CHAPTER 1

Introduction. The Nuclear Resonance Phenomenon

1-1. Introduction

The development of nuclear magnetic resonance spectroscopy subsequent to the initial discoveries by Purcell [1] and Bloch [2] in 1946 is now recognized as one of the most important events in the last fifty years for the advancement of organic chemistry. Nuclear magnetic resonance (NMR) techniques are throwing new light on many difficult organic problems. With the possible exception of gas-liquid chromatography, no new experimental method has been so rapidly accepted or proved so widely applicable. It is the purpose of this book to present the elements of NMR spectroscopy in a form suitable for practical use by organic chemists. Examples of applications will be mainly drawn from high-resolution proton resonance spectroscopy, but the principles so illustrated will often be useful in dealing with other types of NMR spectroscopy.

An NMR spectrometer consists basically of a magnet, radio-frequency (rf) transmitter or oscillator, and a suitable rf detector. When a sample of a material comprised of atoms having nuclei with certain magnetic properties (to be described later) is placed in the magnet pole gap and subjected to the rf field of the oscillator, absorption of rf energy (resonance) occurs at particular combinations of the oscillator frequency and the magnetic field strength and an rf signal is picked up by the detector. Customarily, the detector output is measured at constant oscillator frequency as a function of the magnetic field strength, although there

[1] E. M. Purcell, H. C. Torrey, and R. V. Pound, *Phys. Rev.*, **69**, 37 (1946).
[2] F. Bloch, W. W. Hansen, and M. E. Packard, *Phys. Rev.*, **69**, 127 (1946).

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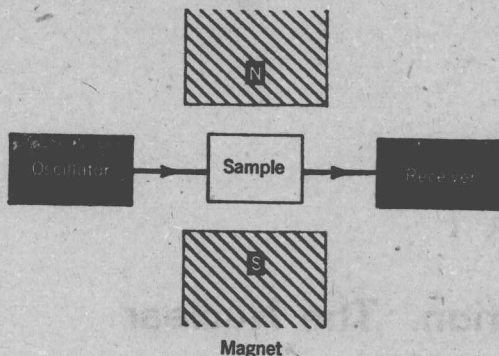
Magnet

are advantages to the alternative procedure of maintaining the magnetic field constant and varying the oscillator frequency.[3]

Information of chemical interest arises from the fact that nuclei of atoms in different chemical environments are also generally in quite different magnetic environments and come into resonance with a fixed-frequency oscillator at different values of the applied magnetic field. Figure 1-1 shows a nuclear magnetic resonance spectrogram of a typical organic molecule, N-ethylethylenimine.
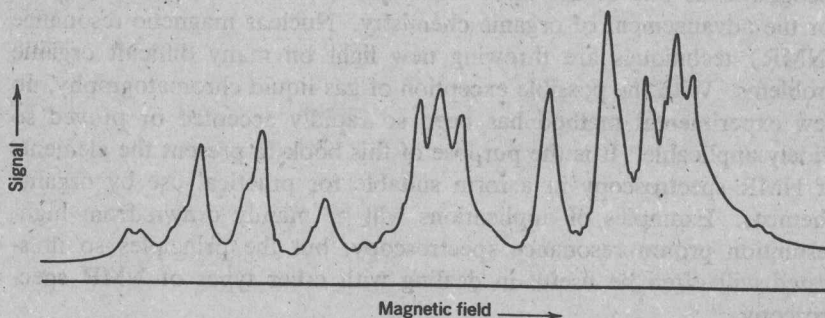
Fig. 1-1. Proton NMR spectrum of N-ethylethylenimine at an oscillator frequency of 40 Mc and a magnetic field of 9,400 gauss.

Besides the obvious utility of such a spectrogram to serve as a finger-print of the compound in question, much more information can be gleaned from the spectrum than is provided by a qualitative examination of its major features. For example, it can be stated with a high degree of certainty that an ethyl group is present and also that the methyl of the ethyl group is rotating about the bond connecting it to the methylene considerably more than 15 times per second. In addition, the spectrum

[3] E. B. Baker and L. W. Burd, *Rev. Sci. Instr.,* **28,** 313 (1957).

shows the imine nitrogen to have a configuration such that the nitrogen atom and the three carbon atoms to which it is directly attached do not lie in a plane. Furthermore, we can say that the nitrogen atom is not undergoing configurational inversion of the kind shown in the following equation at a rate approaching or greater than 80 times per second.
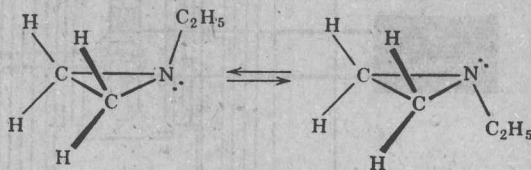
Clearly, the NMR spectrum of the compound is a veritable treasure trove of useful information not easily obtainable in any other way.

We shall now consider the connection between the structure of an organic molecule and its NMR spectrum with the intention of ultimately getting at the principles which enable one to derive the kind of inferences made above. At the outset, we shall show how magnetic nuclei can absorb rf energy and produce an rf signal in the detector. Only the "crossed-coil" nuclear induction apparatus developed by Bloch, Hansen, and Packard [2] will be considered, since it provides the basis for the commercially available high-resolution spectrometers.

1-2. Nuclear Magnetic Resonance Spectrometers

A block diagram of an NMR spectrometer utilizing an electromagnet is shown in Fig. 1-2. For high-resolution spectra, the magnet will have pole faces up to 12 in. in diameter, a pole gap of about 1.75 in., and a field of up to 14,000 gauss. The magnet is energized by a highly stable d-c power supply. If a fixed-frequency rf oscillator is employed, one "sweeps" through the resonance by varying the total magnetic field through injection of the linearly varying output from a "sweep generator" into coils either wound around the magnet pole faces or located within the pole gap. The output of the generator is synchronized with the trace along the X axis of an oscilloscope or suitable graphic recorder.

The sample is placed within the pole gap and subjected to the rf alternating magnetic field produced by passing a high-frequency a-c current through the oscillator coil. The detector serves to pick up changes in the magnetization of the nuclei induced by the rf oscillator, and the detector signal is fed to the Y axis of the oscilloscope or graphic recorder. A nuclear resonance spectrogram is thus a plot of detector signal against magnetic field at constant oscillator frequency.
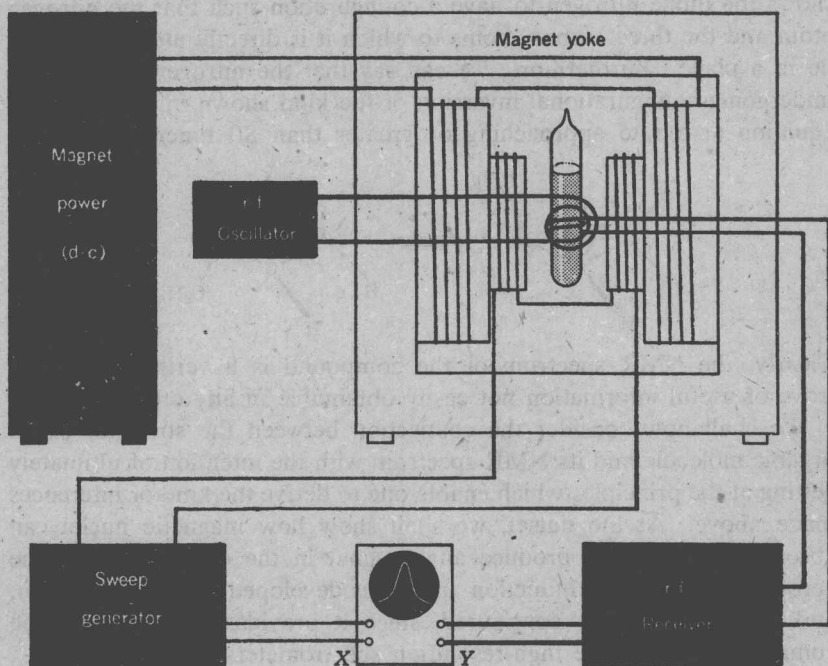
Fig. 1-2. A block diagram showing NMR spectrometer equipped with an electromagnet.

The state of affairs in the immediate vicinity of the sample is shown in Fig. 1-3. It will be seen that the oscillator coil is oriented with its axis perpendicular to the principal magnetic field. The receiver coil is tuned to the oscillator frequency but is oriented with its axis perpendicular to both the direction of the principal magnetic field and the axis of the oscillator coil. This arrangement is used to minimize the overloading of the necessarily sensitive receiver which would result from direct coupling between the oscillator and receiver coils. Therefore, a nuclear resonance signal arises from an indirect coupling between the oscillator and receiver coils produced by the sample itself. The requirements for such coupling can be described more precisely as follows. The magnetic field of the oscillator alternates through the sample along one direction. The receiver coil responds to a magnetic field which alternates perpendicularly to the field produced by the oscillator coil. The signal results from an alternating magnetization which is induced in the sample by the oscillator field in a direction perpendicular to the axis of the oscillator coil.

Fig. 1-3. Arrangement of sample and coils in nuclear induction apparatus.

1-3. Magnetic Properties of Nuclei. Nuclear Spin

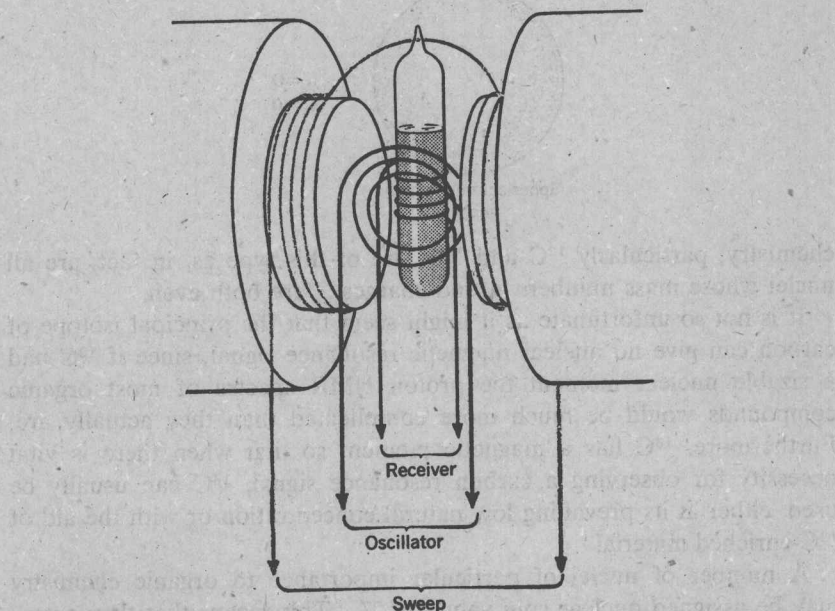Induction of an alternating magnetization in a substance like an organic compound, by an oscillatory magnetic field as described above, can be shown by isotopic substitution procedures to involve certain types of atomic nuclei which act like tiny magnets. In the ensuing discussion of magnetic properties of nuclei, we shall find it convenient to ascribe certain electromechanical properties to nuclei which are gross oversimplifications of the real state of affairs but are nonetheless very helpful in explaining how a nuclear resonance signal can arise.

In some ways, certain nuclei behave as though they are nonspinning spherical bodies with the nuclear charge distributed evenly over their surfaces. This type of nucleus does not have a magnetic moment because there is no circulation of the nuclear charge. We also say that the "nuclear quadrupole moment" is zero because, when a probing electrical charge approaches such a nucleus, it experiences an electrostatic field, the magnitude of which is independent of the direction of approach. These nuclei are said to have their "nuclear spin" value equal to zero and, not having a magnetic moment, they can give no nuclear resonance signal. Many nuclei of considerable importance to organic

$\mu = 0$
$eQ = 0$

Spherical nonspinning
nucleus
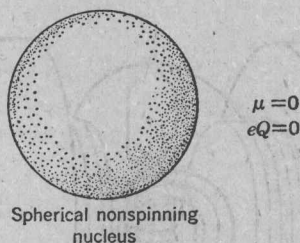
chemistry, particularly ^{12}C and ^{16}O, are of this type as, in fact, are all nuclei whose mass numbers A and charges Z are both even.

It is not so unfortunate as it might seem that the principal isotope of carbon can give no nuclear magnetic resonance signal, since if ^{12}C had a sizable nuclear moment the proton NMR spectra of most organic compounds would be much more complicated than they actually are. Furthermore, ^{13}C has a magnetic moment so that when there is vital necessity for observing a carbon resonance signal, ^{13}C can usually be used, either at its prevailing low natural concentration or with the aid of ^{13}C-enriched material.

A number of nuclei of particular importance to organic chemistry may be assigned nuclear spin values of $\frac{1}{2}$. This means that they act as though they were spherical bodies possessing uniform charge distributions but spinning like tops. A spinning nucleus has circulating charge, and this generates a magnetic field so that a nuclear magnetic moment results. The spherical charge distribution ascribed to nuclei with spin of $\frac{1}{2}$ means that a probing charge approaching them experiences the same electrostatic field regardless of the direction of approach and, therefore, as with the spherical nonspinning nuclei, the electric quadrupole moment is zero. Nuclei with a spin of $\frac{1}{2}$ include ^{1}H, ^{13}C, ^{15}N,

$\mu \neq 0$
$eQ = 0$

Spherical spinning
nucleus
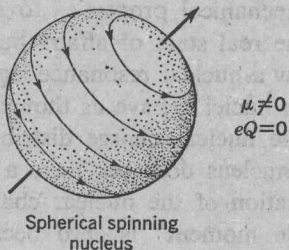
^{19}F, and ^{31}P, and, in general, such nuclei are particularly favorable for nuclear resonance experiments.

A very large number of magnetic nuclei act as though they are spinning bodies with nonspherical charge distributions and are assigned

spin values of unity or larger integral multiples of $\frac{1}{2}$. Often such nuclei are taken to approximate ellipsoids spinning about the principal axis. A charged, elongated (prolate) ellipsoid with the charge uniformly distributed over its surface will present an anisotropic electrostatic field to an approaching unit charge so that the electrostatic work will 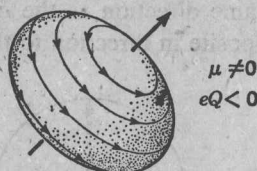be different in bringing up a unit charge to a given distance if the charge approaches along the spin axis or at some angle to it. By convention, the electric quadrupole moment of a nucleus ascribed the shape of a prolate ellipsoid is assigned a value greater than zero. Important examples are ^{2}H and ^{14}N.

$\mu \neq 0$
$eQ > 0$
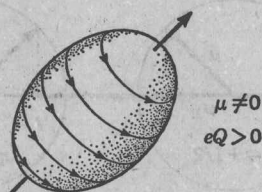
Ellipsoidal (prolate)
spinning nucleus

$\mu \neq 0$
$eQ < 0$

Ellipsoidal (oblate)
spinning nucleus

Nuclei which behave like charged, flattened (oblate) ellipsoids also present an anisotropic electric field to a probing charge and by convention are assigned negative electric-quadrupole-moment values. Nuclei of this type include ^{17}O, ^{33}S, ^{35}Cl, etc. In the ensuing discussion, we shall confine our attention largely to nuclei with a spin of $\frac{1}{2}$, since, as will be seen, complications are often introduced when the electric quadrupole moment is different from zero. These complications are in themselves capable of providing useful chemical information but are not helpful to an understanding of the operation of a nuclear resonance spectrometer.

1-4. Magnetic Quantum Numbers

An important property of spinning nuclei is that their magnetic moment vectors appear to have only certain specified average values

in any given direction, such as along the axis of the principal magnetic field. The permitted values of the vector moment along the direction of interest can be described with the aid of a set of magnetic quantum numbers m, which are derivable from the nuclear spin I and the relation $m = I, (I-1)(I-2), \ldots, -I$. Thus, if I is ½, the possible magnetic quantum numbers are $+½$ and $-½$, and if the magnetic moment is μ, the possible values of the vector components of the moment in the direction of the principal magnetic field H will be $+\mu_H$ and $-\mu_H$, as shown below. If I is unity, then the possible magnetic quantum num-

bers are $+1$, 0, and -1, and the vector along the field direction will have possible values corresponding to the nucleus being oriented so as to have a component in the same direction as the field vector, perpendicular to the field vector, or opposite in direction to the field vector.
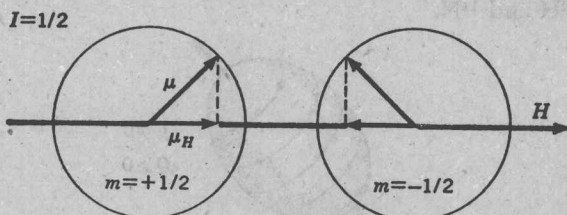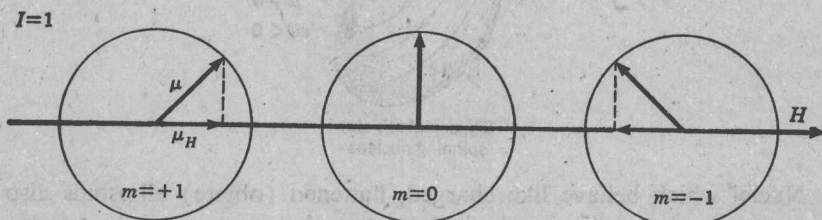
In the absence of a magnetic field there will be no preference for one or the other of the two possible magnetic quantum numbers for a nucleus with I equal to ½. In a large assemblage of such nuclei, there will be then exactly equal numbers with m equal to $+½$ and m equal to $-½$. In a magnetic field, the nuclei will tend to assume the magnetic quantum number $(+½)$ which represents alignment with the field in just the same way as compass needles tend to line up in the earth's magnetic field. Thus, in the presence of a magnetic field, $m = +½$ represents a more favorable energy state than $m = -½$ [provided the gyromagnetic ratio γ (see Sec. 1-5) is positive]. However, the tendency of the nuclei to assume the magnetic quantum number $+½$ is opposed by thermal agitation. The nuclear moment, field strength, and temperature

can be used to calculate the equilibrium percentages of the nuclei in each quantum state by the Boltzmann distribution law. At room temperature, even in rather high magnetic fields such as 10,000 gauss, thermal agitation is so important relative to the energy gained by alignment of the nuclei that only a very slight excess of the nuclei go into the more favorable quantum state, as shown by the following:

$$N = Ap \exp\left(-\frac{\varepsilon}{kT}\right) \quad \text{(Boltzmann equation)}$$

$$\varepsilon = -\mu_H H = -\frac{\gamma h}{2\pi}\, mH$$

For protons at 300°K in a field of 9,400 gauss

$$\frac{N(+\frac{1}{2})}{N(-\frac{1}{2})} = \exp\left(\frac{\gamma h H/2\pi}{kT}\right) = 1.0000066$$

This situation is analogous to an assemblage of compasses on a table subjected to violent agitation. The movements of the table tend to throw the compass needles out of alignment with the earth's magnetic field, so that on the average only a very slight excess of the needles may be actually pointing north.

Nuclear magnetic resonance spectroscopy is primarily concerned with transitions of the nuclei in a magnetic field between energy levels which are expressed by the different magnetic quantum numbers. These energy changes are analogous to electronic and vibrational-rotational energy changes in other forms of spectroscopy. There is no direct magnetic interaction between the nuclei and the electrons which surround them. Thus, a problem is posed with regard to the transfer of energy from the nuclei to and from their surroundings. The energy-transfer problem may be restated in the following way. Consider an assemblage of nuclei in the absence of a magnetic field. As stated before, there will be exactly equal numbers of nuclei with the magnetic quantum numbers $+\frac{1}{2}$ and $-\frac{1}{2}$. In the presence of a magnetic field, this distribution corresponds to an infinitely high temperature because the state with the magnetic quantum number $-\frac{1}{2}$ is now energetically less favorable than the $+\frac{1}{2}$ state and only an infinitely high temperature could produce sufficient thermal agitation to keep the nuclear magnets from having some net alignment in the field direction. In order to achieve the equilibrium distribution of nuclei between the two possible spin states at a lower temperature, it is necessary that energy be lost to the surroundings by nuclear "relaxation." Relaxation is hardly expected to be a simple process, since the nuclei are not easily able to collide with one another or the surrounding electrons and convert their energy due to

an external magnetic field into molecular vibrational, rotational, or translational energy. Transfer of energy back and forth among nuclei in various magnetic quantum states and their surroundings can be achieved with the aid of another property which might be ascribed to magnetic nuclei, called "nuclear precession."

1-5. Nuclear Precession

When a nucleus with a magnetic moment is placed in a magnetic field, it acts as though it were undergoing precession around the field axis at an angular velocity ω_0, which is directly proportional to the magnetic field at the nucleus H_0. This precession is analogous to the precession

$\omega_0 =$ precession
frequency

$H_0 =$ magnetic field at
the nucleus
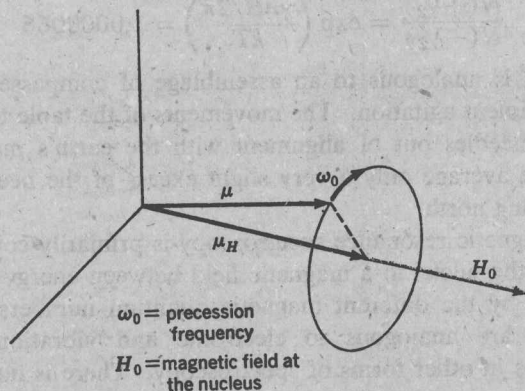
of a spinning gyroscope when allowed to topple in the earth's gravitational field. The direction of precession of a gyroscope depends on the direction of its angular momentum vector, and the angular velocity depends on the magnitude of the angular momentum vector and the strength of the gravitational field to which it is subjected. For nuclei, the proportionality constant γ between the angular velocity of precession and the field strength depends on the angular spin momentum and the magnetic moment of the nucleus. γ is called the "gyromagnetic" ratio or, less commonly, the "magnetogyric" ratio. All nuclei of the same charge and mass number have the same gyromagnetic ratio. Thus, all protons act as though they precess at the same angular velocity when the magnetic field strength *at the nucleus* is the same. γ may be either positive or negative, corresponding to different directions of precession.

1-6. Nuclear Relaxation

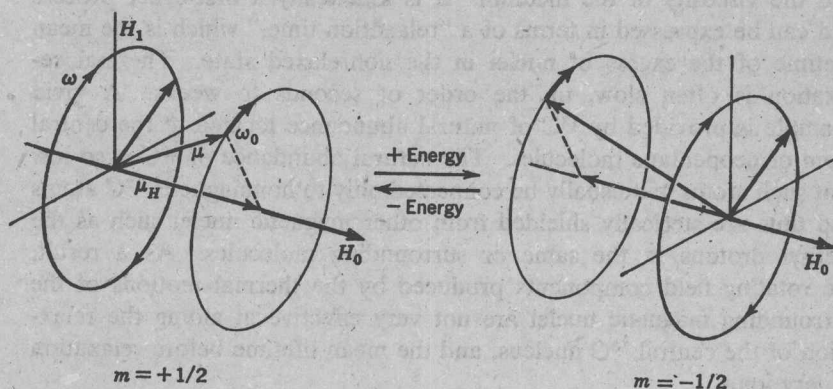The property of magnetic nuclei which corresponds to precession

$m = +1/2$ $m = -1/2$

Fig. 1-4. Interaction between a rotating magnetic vector H_1 and nuclei precessing in an applied magnetic field H_0.

provides a means whereby energy may be transferred back and forth between the nuclei and their surroundings. Consider a magnetic field vector arranged so as to rotate perpendicular to a magnetic field in which are immersed magnetic nuclei precessing at the angular velocity ω_0 (Fig. 1-4). If the rotating vector has a quite different angular velocity from the precessing nuclei, the rotating field vector and the precessing nuclear magnetic vectors cannot remain in phase and there will be no effective interaction between them. On the other hand, if the rotating field vector has the same angular velocity as the precessing nuclear vectors, it will remain in phase with them and can exert a magnetic torque tending to flip over the orientation of the nuclei and thence change their magnetic quantum numbers. Of course, if the nuclear magnetic quantum numbers change, energy is transferred to or from the agency producing the rotating field vector. Thus, an assemblage of nuclear magnets immersed in a magnetic field can come to thermal equilibrium with its surroundings.

An important mechanism for relaxation of a group of nuclei at a nonequilibrium spin temperature utilizes atomic and molecular thermal motions as follows. Suppose a magnetic nucleus is surrounded by others of its type contained in atoms undergoing violent thermal motions. The thermal motions of the nuclei produce random oscillatory magnetic fields which can have frequency components with frequencies equal to the precession frequencies of the relaxing nuclei and can act as a rotating magnetic field vector so as to permit the magnetic orientation energy to be converted to thermal energy. The rate of relaxation by this mechanism depends on the temperature, the concentration of magnetic nuclei,

and the viscosity of the medium. It is kinetically a first-order process and can be expressed in terms of a "relaxation time," which is the mean lifetime of the excess of nuclei in the nonrelaxed state. Thermal relaxation is often slow, on the order of seconds to weeks. A vivid example is provided by ^{13}C of natural abundance located at the central atom of neopentane molecules. The natural abundance of ^{13}C is so low that such atoms will usually be connected only to nonmagnetic ^{12}C atoms and thus are sterically shielded from other magnetic nuclei such as the methyl protons in the same or surrounding molecules. As a result, the rotating field components produced by the thermal motions of the surrounding magnetic nuclei are not very effective at aiding the relaxation of the central ^{13}C nucleus, and the mean lifetime before relaxation is very long.

As might be expected, thermal motions of substances with unpaired electrons are particularly effective in inducing thermal relaxation, and such paramagnetic substances present as impurities may spoil high-resolution spectra by making the relaxation times very short, which, as will be seen later, results in line-broadening.

In summary, transitions between states with various magnetic quantum numbers which have different energies because of an applied magnetic field may be induced by thermal motions of magnetic nuclei or paramagnetic substances or else by an external rotating magnetic field which has a frequency equal or very nearly equal to the precession frequency of the nuclei.

1-7. Longitudinal Relaxation, T_1

It turns out that there are two varieties of relaxation. The first, discussed above, has to do with the establishment of thermal equilibrium between an assemblage of nuclear magnets with different quantum numbers. This is "longitudinal" relaxation, since it results in establishment of an equilibrium value of the nuclear magnetization along the magnetic field axis. Thus, an assemblage of nuclei in a very weak magnetic field, such as the earth's magnetic field, will have essentially no net magnetization of the nuclei along the field axis, since only a few more of the nuclei possess the spin quantum number $+\frac{1}{2}$ as compared with those with the value of $-\frac{1}{2}$. When this assemblage is placed in a magnetic field and relaxation takes place, there is an increase in the sample magnetization along the field axis as more of the nuclei drop into the lower energy state with magnetic quantum number of $+\frac{1}{2}$. The characteristic longitudinal relaxation time is designated as T_1.