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High-Resolution Study of NMR Spin Echoes: "*J* Spectra"*

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The spin-spin relaxation of individual lines in a high-resolution NMR spectrum has been studied by a technique which extracts an essentially "monochromatic" component from the Carr-Purcell spin-echo response by means of a narrow-band filter. The resulting selectivity significantly reduces the complexity of the modulation of the spin-echo amplitude due to homonuclear spin-spin coupling, and further simplification may be achieved by double irradiation experiments. Echo modulation has been used as a precise measure of the 0.051-Hz long-range coupling in 3-bromothiophene-2-aldehyde, normally hidden by magnet inhomogeneity. It is proposed that modulation and spin-spin relaxation effects are best analyzed in the general case by calculating the Fourier transformation of the envelope of the spin-echo peaks. The general term suggested for this new mode of presentation is the "spin-echo spectrum." It consists of a set of resonance responses with widths determined by the relevant spin-spin relaxation times, at frequencies determined by the various modulation components of the spin-echo decay. The present study concentrates on operating conditions (low pulse repetition rate and "first-order" spin coupling) where the resonance frequencies correspond to one-half the sums and differences of the spin coupling constants. This special case of a spin-echo spectrum is called a "*J* spectrum." When the spin-echo response appropriate to a single group of chemically shifted nuclei is observed selectively, the transformation gives a "partial *J* spectrum" which can be used as an aid to the assignment of the full spectrum. *J* spectra are illustrated for a typical first-order three-spin system—the ring protons of methyl furoate.

I. INTRODUCTION

The majority of high-resolution nuclear magnetic resonance spectra are interpreted solely in terms of chemical shifts and indirect spin-spin coupling constants, without regard to the relaxation properties of the nuclei. The reason is that, for most organic substances in the liquid state or in solution, the coupling of the nuclear spins to the thermal reservoir (represented by the inverse of the spin-lattice relaxation time, T_1) and the interaction between nuclear spins (represented by the inverse of the spin-spin relaxation time, T_2) are both so weak that their influence on the observed line-width is masked by instrumental shortcomings, notably the spatial inhomogeneity of the applied magnetic field. Relaxation information about the individual components of a many-line high-resolution spectrum can be obtained through techniques such as saturation recovery,¹ progressive saturation,² or multiple resonance.³ However if conventional pulse techniques for determining relaxation times are applied directly to such spectra, they yield only a composite signal consisting of many different relaxation decays, not readily separable into the individual components. For this reason these pulse methods have tended to be confined to the investigation of molecules of extreme simplicity or high symmetry, for example, water or benzene.

A. High-Resolution Studies of Nuclear Spin Relaxation

Attempts to adapt pulse techniques to measure relaxation of individual lines in a high-resolution NMR spectrum can be divided into two classes. The first method employs a "selective" excitation pulse, where the radio-frequency (rf) level during the pulse is sufficiently weak that only a single line (or in some cases a group of very close lines) is significantly perturbed, all the remaining lines being sufficiently far from resonance

that the pulse is not effective.⁴ The rf level must nevertheless be strong enough to excite the selected line essentially uniformly, and since the pulse width is necessarily several orders of magnitude greater than in conventional spin-echo work, some attention must be paid to the relaxation effects that occur during the pulse. Within these inherent limitations the technique can be used to measure spin-spin and spin-lattice relaxation times of the order of a second or longer. The subject is described in detail elsewhere.⁴

The second technique employs strong rf pulses that excite the entire spectrum of NMR frequencies essentially uniformly, selectivity being confined to the detection scheme. The pulses are narrow and relaxation during the pulse is quite negligible. The basis of the method is that the free nuclear precession signal, although it is normally observable for only a short time, contains all the information available in the corresponding slow-passage spectrum, the two modes of display being related by a Fourier transformation.⁵ The free precession signal is generated by a 90° pulse or by refocussing to form a spin echo, which may be regarded as two free induction decays back to back. The Fourier transform technique can thus produce an entire high-resolution spectrum from a measurement requiring only a very short time interval, typically of the order of one second, and it provides an ideal method for monitoring a spin-lattice recovery curve or a spin-spin relaxation decay curve for relaxation times longer than a few seconds.

The idea was first used by Vold *et al.*⁶ to determine individual spin-lattice relaxation times. A 180° pulse is applied while the spin system is at thermal equilibrium, aligning the nuclear magnetization vectors along the $-Z$ direction in the rotating reference frame. After a short interval t sec the progress of recovery of these vectors towards the $+Z$ direction is monitored by a 90°

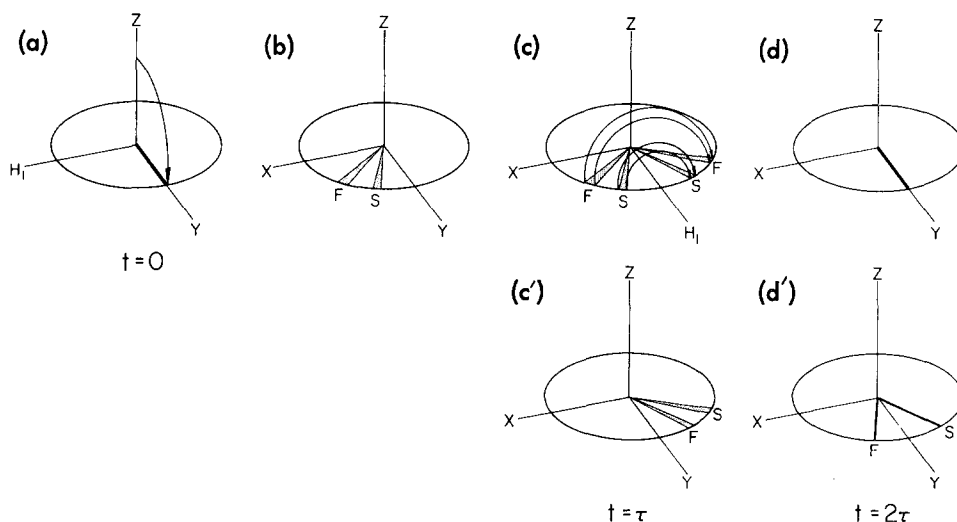


FIG. 1. Vector diagrams illustrating the modulation of the amplitude of Carr-Purcell spin-echo trains. (a) Initial 90° pulse at $t=0$. (b) Spin-spin coupling causes the magnetization to break up into a fast (F) and slow component (S), each exhibiting a spread due to field inhomogeneity. The chemical shift causes a net precession of the mean frequency. (c) At $t=\tau$ a 180° pulse turns all the vectors into new positions that are reflections in the YZ plane. (d) If the coupling is to a *nonresonant* nucleus, a conventional spin echo is formed at $t=2\tau$ with amplitude independent of coupling constant, field inhomogeneity, and chemical shift. (c') If the coupling is to a *resonant* nucleus, the 180° pulse at $t=\tau$ inverts the spin states of that nucleus, interchanging the fast and slow components of the observed nucleus. (d') At $t=2\tau$, chemical shift and inhomogeneity effects are refocused, but spin coupling causes a continued divergence of the fast and slow components, leading to a modulation of the echo amplitude according to $\cos(\pi J\tau)$.

pulse which excites a free induction signal that is recorded and subject to Fourier transformation. After a suitably long interval to re-establish thermal equilibrium for the nuclear spins, the measurement can be repeated at a different value of the interval t , and a series of such measurements yields a series of spectra that may be stacked together to give a three-dimensional diagram. A section across such a diagram at a frequency corresponding to an absorption peak permits the intensity of that line to be followed as a function of t , yielding the individual spin-lattice relaxation time. The method has recently been applied to carbon-13 spectroscopy,⁷ which is particularly well suited to such measurements when all proton-carbon splittings have been removed by incoherent irradiation of the proton resonances.

In practice many relaxation studies concentrate on only two or three lines of interest, and then it becomes acceptable to examine them one line at a time, and a complete Fourier transformation of the free induction signal is no longer required. It may in fact be much simpler to extract the selected resonance frequency by narrow-band filtration, all other resonance frequencies being rejected. One possible realization of this idea employs a low-pass filter following a phase-sensitive detector, the reference frequency of which is set to correspond with the selected resonance line⁸ (as it is carried at an audiofrequency at the output of the NMR receiver).

The present investigation extends these studies to spin-spin relaxation, where information about relaxation of individual lines must be extracted from the

spin-echo response, usually excited by the pulse sequence introduced by Carr and Purcell.⁹ The method of filtration is used rather than complete Fourier transformation. Except in the simple case of an isolated line that is not spin coupled to any other nuclei of the same isotopic species, the well-known " J modulation" of the spin-echo amplitude¹⁰⁻¹⁴ introduces a new complication into the measurement, and this is only partially offset by the use of the highly selective detection scheme. However, it will be shown that this modulation effect can be put to very good use for measuring weak spin coupling constants, and in fact the complex modulating wave can be subjected to Fourier transformation to give a new form of presentation called the "spin-echo spectrum," or under certain limiting conditions, the " J spectrum."

B. Modulation of Spin Echoes Due to Homonuclear Coupling

When a transverse component of nuclear magnetization is created (for example, by a 90° rf pulse) the macroscopic signal normally decays through interference effects resulting from the distribution of nuclear precession frequencies in the inhomogeneous static field. The application of a 180° pulse after a delay τ sec has the effect of reversing the spread of magnetization vectors, causing them to refocus at time 2τ into a spin echo. In a very similar way chemical shifts or heteronuclear spin-spin couplings create groups of precessing vectors that lose phase coherence one with another, but which can be refocused by a 180° pulse.

Consider the simple case of a spectrum containing

two resolved lines of a spin multiplet, e.g., a single proton A spin coupled to a single nucleus X of some other spin- $\frac{1}{2}$ species ("heteronuclear coupling"), and with a "chemical shift" measured with respect to the excitation. The diagrams (a)–(d) of Fig. 1 illustrate this case. The 90° pulse at time zero aligns all vectors along the Y axis of the rotating frame (absorption mode). The two components of the doublet, F (fast) and S (slow), precess at different rates, while within each component there is a spread of vectors due to field inhomogeneity [Fig. 1(b)]. At time τ seconds a 180° pulse is applied about the Y axis¹⁵ turning the individual vectors into new positions that are reflections of the old positions in the YZ plane [Fig. 1(c)]. As each individual vector precesses freely at its own characteristic rate, it comes back into phase with the rest at time 2τ to form a spin echo, the amplitude of which is quite independent of field inhomogeneity, chemical shift, or heteronuclear spin coupling constant [Fig. 1(d)].

A distinctly different behavior is observed if the spin-spin coupling is to a resonant nucleus (one that experiences the effect of the 180° pulses). Suppose that Fig. 1 is now taken to represent the case of coupling to a nucleus of the *same* species (homonuclear coupling), but with a selective detection scheme that is sensitive only to signals of nucleus A. Free precession and loss of phase coherence occur exactly as in the heteronuclear case, but the effect of the 180° pulse is different. Not only are the vectors rotated about the Y axis [Fig. 1(c)] but also the spin states of nucleus X are reversed, causing the fast and slow components of the A nucleus to be interchanged [Fig. 1(c')]. Further free precession for τ seconds then causes a refocussing of the chemical shift and field inhomogeneity effects at time 2τ , but allows the fast and slow J components to continue to diverge at their original rate [Fig. 1(d')]. Although the echo amplitude (the projection on the Y axis) remains independent of the chemical shift and field inhomogeneity, the homonuclear coupling introduces a new factor $\cos(2\pi J_{AX}\tau)$, and if the echoes are studied as a function of τ or if multiple echoes are generated⁹ they will exhibit a modulation of their amplitudes at a frequency $\frac{1}{2}J_{AX}$ Hz superimposed on any damping due to spin-spin relaxation. (This modulation of the echo *amplitude* should be carefully distinguished from the *structure* of the echo, which is a complex waveform containing information about chemical shifts as well as coupling constants.)

Coupling to a "resonant" nucleus is thus the prerequisite for J modulation of the echoes. Modulation is absent for heteronuclear coupling, but could be restored by the application of 180° pulses to the heteronucleus,¹⁰ timed to coincide with the 180° pulses on the observed nucleus. Similarly, echo modulation is not observed in homonuclear cases when the excitation pulses are applied selectively⁴ but it can be re-introduced by the simultaneous application of further sets of selective 180° pulses at resonance for the neighbor nuclei.

Further complications arise if higher-order effects of homonuclear spin-spin coupling are considered. The effect of a 180° pulse on nucleus X can no longer be correctly represented by the interchange of the fast and slow components of the A signal as in Fig. 1(c'), and the modulation of the echo amplitude becomes more complex, containing information about the chemical shift δ between the two nuclei.¹⁰ Abragam¹¹ has outlined the density matrix treatment of such a situation, considering the case of a single spin echo studied as a function of τ , and has concluded that for a strongly coupled two-spin system, two new modulation terms can be observed at frequencies $(\Delta \pm J)/2$ Hz, where $\Delta = (J^2 + \delta^2)^{1/2}$. For a multiple-echo train the treatment is further complicated.^{12–14}

Spin coupling constants are only simply related to the spin-echo modulation frequencies if two conditions are satisfied—the NMR spectrum is accurately described by first-order theory, and the pulse repetition rate is low in comparison with the chemical shift differences ($2\pi|\delta|\tau \gg 1$). Errors are introduced if either condition is violated, and at very high repetition rates the J modulation disappears altogether.^{13,14,16–18} Since the modulating wave is expected to be quite complex in multispin systems even without these two complicating factors, the exploratory experiments presented below have all been carried out on first-order systems at low pulse repetition rates.

High selectivity in the detector greatly reduces the complexity of spin-echo modulation compared with the results for conventional spin-echo operation. This improves the possibilities of separating out the damping due to spin-spin relaxation from the various modulation components. It will be demonstrated below that the introduction of double resonance techniques can be a further aid in disentangling the modulation components. However in the general case, where the modulating waveform is too complex to be decomposed by inspection, this represents an ideal case for the application of the Fourier transform technique.

C. Fourier Transformation of the Envelope of Spin-Echo Peaks

Suppose the Carr-Purcell spin-echo response of a nucleus A is detected selectively, and suppose A exhibits first-order spin coupling to two other nuclei, M and X, that are both subject to the influence of the rf pulses. The only point on the spin-echo profile unaffected by chemical shift and field inhomogeneity effects is the echo peak (at time $2m\tau$), and it is at this point that the signal must be sampled. Let this sampling frequency be $F_s = 1/(2\tau)$ Hz. It follows from the sampling theorem¹⁹ that only frequency components below $F_s/2$ Hz are recoverable after the sampling process, higher-frequency components being "folded back" into the range 0 to $F_s/2$. These discrete points, measured over a total period T sec, define a complex

waveform,

$$S = \cos(\pi J_{AM}t) \cos(\pi J_{AX}t) \exp(-t/T_2) \\ = \frac{1}{2} \{ \cos[\pi(J_{AM} - J_{AX})t] + \cos[\pi(J_{AM} + J_{AX})t] \} \\ \times \exp(-t/T_2). \quad (1)$$

The discrete Fourier transform of this wave may be readily calculated by standard programs²⁰ on a digital computer. The result is a spectrum extending from 0 to $F_s/2$ Hz with sampling points every $1/T$ Hz, containing two resonance responses at $(J_{AM} - J_{AX})/2$ and $(J_{AM} + J_{AX})/2$. Each line has a Lorentz shape with a full width $(\pi T_2)^{-1}$, essentially unaffected by magnet inhomogeneity.²¹

The decomposition into two modulation components and a spin-spin relaxation time is thus achieved in a very convenient fashion. An equivalent procedure can be followed for spin echoes detected nonselectively, yielding a correspondingly more complicated spectrum. It is proposed to describe this method of presenting the data as the " J spectrum," and when selective detection methods are employed, as the "partial J spectrum." This avoids the cumbersome description as the Fourier transform of the envelope of the spin-echo peaks observed in a Carr-Purcell experiment.

Note that the echo modulation due to coupling to several different resonant nuclei is *multiplicative* rather than additive, just as are spin-spin splittings in conventional first-order NMR spectra. This is the reason why sums and differences of spin-coupling constants are observed in the J spectrum rather than the coupling constants themselves. A typical component of a J spectrum would be the absolute value of one of the frequencies, $\frac{1}{2}(\pm J_{AK} \pm J_{AL} \pm J_{AM} \pm \dots)$. For a first-order system of N nonequivalent spins with finite values for all $N(N-1)/2$ coupling constants, the complete J spectrum would contain $N \times 2^{N-2}$ combinations of coupling constants, made up of N partial J spectra of 2^{N-2} combinations each. (Note that when $N=2$, the two partial J spectra are identical.)

There are four basic conditions for observing J spectra.

(a) The measurement must be made in a magnetic field sufficiently intense that the first-order approximation for spin coupling ($|\Delta| \gg |J|$) is valid. Otherwise new modulation components make their appearance on the spin-echo envelope at frequencies involving chemical shifts.^{10,11}

(b) The pulse repetition rate must be sufficiently low in comparison with the smallest chemical shift difference that $2\pi|\delta|\tau \gg 1$. If this condition is violated¹⁶ the resonance responses in the transformed spectrum are shifted from the frequencies defined by half the sums and differences of the spin coupling constants.

(c) The refocussing pulses (that is all pulses after the first) must be accurately adjusted to the 180° condition, otherwise new resonance responses appear

in the transformed spectrum at frequencies involving chemical shifts. An extreme example where this condition is not fulfilled is the experiment treated by Hahn and Maxwell,¹⁰ where the echo amplitude was studied as a function of τ in a $90^\circ\text{--}\tau\text{--}90^\circ$ pulse sequence, and where these new modulation components appear even in the first-order limit. In practice throughout the present work a modification¹⁵ of the Carr-Purcell sequence compensates for small deviations from the 180° condition of the refocussing pulses.

(d) Other possible physical sources of spin-echo modulation should be absent. One such mechanism is the direct dipole-dipole interaction observable in anisotropic liquid phases where there is a net molecular alignment along some preferred axis.²²

When one or more of these restrictive conditions is violated, the Fourier transform of the envelope of spin-echo peaks can be said to fall into a more general class of "spin-echo spectra." This wider area of investigation would appear to have some useful applications, particularly those spin-echo spectra generated by relaxing conditions (a) or (d). For reasons of simplicity the present study has been restricted to the special case of J spectra, and this term has therefore been used almost exclusively throughout.

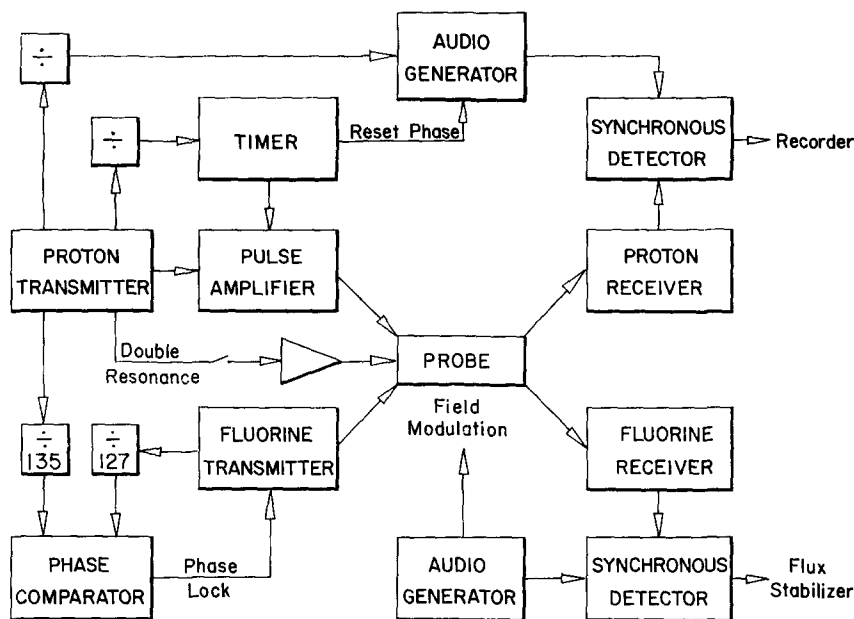
II. EXPERIMENTAL

A. Spin-Spin Relaxation of Individual Lines

To observe a long stable train of spin echoes under high-resolution conditions requires extremely precise regulation of the ratio of the applied radiofrequency²³ to the static magnetic field at the sample. Fortunately, instabilities at frequencies much lower than the pulse repetition rate are corrected to first order by the refocussing effect of the 180° pulses. This greatly relaxes the field/frequency stability requirements in conventional spin-echo work, but since the present experiments employ much lower pulse rates (typically of the order of 10 Hz), they remain susceptible to the frequency range of the instabilities normally encountered in a field/frequency control loop. The critical parameter in this context is the accumulated error in the *phase angle* of a typical nuclear precession, integrated over the interval between 180° pulses. Thus even a momentary deviation from the correct field/frequency ratio can cause a net phase error which, if not corrected, will affect the amplitude of all subsequent echoes.

Experiments were carried out on a modified Varian HR-6F spectrometer. An internal reference signal from the ^{19}F nuclei in a small quantity of hexafluorobenzene was used for regulation of the Larmor condition, the dispersion-mode component being fed as an error signal to the flux stabilizer.²⁴ The rf transmitter coils were tuned at 60 MHz, and the receiver coil was tuned for resonance at both 60 and 56.4 MHz. This servo loop strictly controls only the ratio of *frequency* to applied

FIG. 2. Schematic diagram of the equipment used to observe the spin-echo responses of individual lines in a selective manner.



field, whereas it is the *phase* of the observed nuclear precession that is important. In order to operate as closely as possible as a phase-locking system, the gain and response of the servo loop were adjusted to minimize the integrated frequency excursions, and the synchronization of the proton and fluorine transmitter frequencies employed an integrating circuit that maintained a stable phase relationship between the two oscillators. Figure 2 illustrates how the ratio of the effective fluorine and proton excitation frequencies was determined by the 127/135 division ratio, finely adjusted by the choice of the audiofrequency used to modulate the field (typically about 2 KHz). This field modulation created sideband responses of the fluorine signal, but the modulation index was kept low enough to avoid any perturbation of the proton spin-echo response. Experimental tests indicated that this internal fluorine regulator could be adjusted to maintain phase stability for the observed proton signal comparable with that of a *proton* internal lock loop that derived its error signal directly from the spin-echo response itself.

A train of spin echoes at times $2n\tau$ seconds was excited by an initial 90° pulse followed by a series of 180° pulses at times $(2n-1)\tau$ according to the scheme devised by Carr and Purcell.⁹ The rf field during the pulse was approximately 1 G ($\gamma H_1/2\pi \approx 4$ KHz) which for the illustrative experiments described below was adequate to excite all the proton resonances of interest in an essentially uniform manner. Meiboom and Gill¹⁵ have suggested the introduction of a 90° shift in the relative phase of the 180° pulses as a method of compensating for misadjustment of the 180° condition. In the present equipment a similar compensation was achieved by alternating the phase of the 180° pulses⁴ (in practice a rather simpler expedient).

Up to this point the experiment is nonselective and

the spin-echo response contains signal frequencies from all parts of the proton spectrum. It would be quite feasible to study the spin-spin relaxation rates of all these components separately by subjecting each spin echo response to Fourier transformation. However, as explained in the Introduction, the chosen technique is to select a single component of the proton spectrum for study and to filter its resonance frequency from all others in an audiofrequency phase-sensitive detector. The attainable selectivity (the degree to which the relaxation behavior of the chosen line can be "resolved" from that of a near neighbor) can in principle approach the resolution achieved in the steady-state slow-passage spectrum, essentially limited only by the magnet field inhomogeneity. This selectivity can be varied by changing the output bandwidth of the phase-sensitive detector, and a typical setting might be 1 Hz.

The application of a 180° pulse disrupts the precession phase of a typical signal component by rotation of that particular magnetization vector about the X axis of the rotating coordinate frame. For the chosen resonance line, however, the phase-sensitive detector must always be adjusted for pure absorption mode; hence this phase jump must be compensated by a corresponding jump in the phase of the reference signal. This was accomplished by deriving the reference frequency by subdivision of a much higher frequency²⁵ in a ripple counter, resetting the counter at the end of each 180° pulse. This maintains a given phase; the adjustment to the condition for pure absorption mode was made by maximizing the amplitude of the echo response.

Since the precession of a near-neighbor line would exhibit similar phase discontinuities due to the 180° pulses every 2τ seconds, this will generate appreciable signal components over a band of frequencies²⁶ of the order $1/(2\tau)$ Hz, and some component will appear at

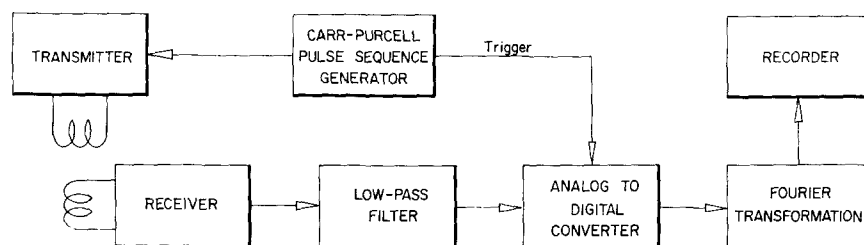


FIG. 3. Schematic diagram of the equipment used to observe J spectra. The internal fluorine field/frequency regulation scheme outlined in Fig. 2 forms part of this equipment but for simplicity is not shown. The transformed spectrum could also be displayed on an oscilloscope while two phase parameters were adjusted.

the frequency of the line chosen for study. The pulse repetition rate can therefore impose a *fundamental* limitation on the attainable selectivity of this experiment, and should be chosen low in comparison with the desired resolving power expressed in frequency units. Typical repetition rates employed in practice ran from 1 to 10 Hz. This automatically precludes operation at high pulse rates where the echo modulation becomes strongly dependent on pulse rate.^{13,14,16-18}

Selective detection of spin echoes makes feasible homonuclear double irradiation experiments where one component of the echo modulation is suppressed by decoupling the neighbor nuclei. Provision was therefore made to introduce a second rf excitation by feeding a continuous-wave 60-MHz signal from the proton transmitter via an isolating amplifier. Irradiation of a chosen resonance involved readjustment of the modulation frequency (which was one of the factors that determined the total applied field), and thus necessitated readjustment of the frequency of the phase-sensitive detector.

The alternation of the sense of the spin echoes observed in this mode of operation can be a complicating factor in observing the echo modulation. It was therefore eliminated by alternating the phase of the reference signal fed to the phase-sensitive detector. In this way, if the pulse repetition rate is sufficiently high in comparison with the inhomogeneity width of the NMR lines, adjacent echoes tend to coalesce and the observed signal corresponds very closely with the *envelope* of the spin-echo peaks. This is evident in the traces shown below for benzene echoes observed with a pulse repetition rate of 10 Hz.

A few experiments were carried out with *selective* pulses to demonstrate the different behavior with respect to homonuclear spin coupling. They were performed on a second spectrometer (Varian HR-60) modified as described elsewhere for the application of weak pulses in the form of modulation sidebands.⁴ A conventional field/frequency regulation scheme employing an internal proton lock was used for these experiments, since the pulses have negligible effect on the lock signal. Double resonance experiments were performed by introducing another field modulation sideband which was also pulse modulated.

B. Equipment for J Spectroscopy

A simplified schematic of the equipment used to observe J spectra is shown in Fig. 3. Field/frequency regulation was achieved by the same internal fluorine

locking scheme described in the previous section, and already illustrated in Fig. 2. Both experiments impose the same requirements on the stability of the *phase* of the Larmor precession; however, the J spectrum mode of presentation appears to be particularly sensitive to any discontinuity in phase that might occur during the acquisition of the spin-echo signals. This can result in a spurious multiplicity of the lines of the J spectrum. Such disturbances are thought to originate in magnetic field fluctuations not entirely compensated by the regulation scheme. Even if a phase excursion is later corrected by an equal and opposite phase shift, the refocussing motion of the nuclear spins can be seriously perturbed if a 180° pulse intervenes. A "quiet" magnetic field can be said to be a necessary (but not sufficient) condition for a good J spectrum.

The experiments described in Sec. II.A used the continuous-wave rf signal as a second irradiation field for spin decoupling. Since no such double resonance experiments were carried out on the J spectra, this restores a degree of freedom in choosing the Larmor condition. The chosen region of the NMR spectrum can therefore be arranged to fall near zero frequency at the output of the receiver by adjusting the applied magnetic field via the fluorine sideband frequency. This permits the use of a simple low-pass filter for achieving selectivity, rather than the phase-sensitive detector scheme described in Sec. II.A. When the bandwidth of this filter encompasses the full chemical shift range, the entire J spectrum is obtained; when narrowed to cover a single chemically shifted group, the result is a partial J spectrum. This is a very simple method of achieving and controlling selectivity, since no phase resetting is required.

The pulse generator for the Carr-Purcell sequence remains unchanged from Sec. II.A, but in addition provides a trigger pulse at time $2n\tau$ sec which instructs the analog-to-digital converter to take one sample of the incoming spin-echo signal. Since some delay is introduced into this signal (mainly by the filter) a corresponding delay must be allowed after the trigger pulse in order that the sample be taken as near as possible to the exact center of the echo, since it is only at this point that the signal is truly independent of chemical shift and field inhomogeneity effects. In practice this adjustment is made by trial and error. It was felt to have an important bearing on the quality of the J spectra.

Another spectrometer in the same laboratory was being used for conventional Fourier transform spectro-

scopy aimed at improving NMR sensitivity for protons and carbon-13. It made use of a small dedicated digital computer and a program based on the fast Fourier transform algorithm.²⁰ With some very minor modifications, this program was adapted for transforming spin-echo envelopes into *J* spectra. After the transformation the program monitors the voltage on two potentiometers to permit manual adjustment of a phase angle and a frequency-dependent phase term, while the spectrum is displayed on an oscilloscope. This interactive loop with the operator greatly facilitates the attainment of a uniform signal mode across the entire *J* spectrum, since the low-pass filter otherwise introduces phase shifts that vary appreciably as a function of frequency.

In these experiments, where no phase-sensitive detector was used, the sense of the spin echoes alternates, but no attempt was made to correct this since it turns out that the resulting change in the *J* spectrum is quite trivial. Suppose the spin-echo envelope has the form

$$S = \cos(\pi J t) \exp(-t/T_2) \quad (2)$$

and is sampled at a rate $F_s = 1/(2\tau)$ Hz. If there were no problem of phase alternation of the echoes, the Fourier transform of this wave would be a spectrum extending from 0 Hz to $F_s/2$ Hz with a single line at $J/2$ Hz. The alternation of the sense of the spin echoes can be expressed by a square-wave modulation at the frequency $F_s/2$ and with the detection system used it is permissible to neglect all harmonics except the fundamental, giving a spin-echo envelope,

$$S_{\text{alt}} = \cos(\pi J t) \cos(\pi F_s t) \exp(-t/T_2) \\ = \frac{1}{2} \{ \cos[\pi(F_s - J)t] + \cos[\pi(F_s + J)t] \} \\ \times \exp(-t/T_2). \quad (3)$$

The process of sampling causes all frequencies above the sampling frequency to appear folded back an equal distance below the sampling frequency. Thus both terms of Eq. (3) will give coincident lines at $(F_s - J)/2$ Hz in the *J*-spectrum. A generalization of this result is that phase alternation of the echoes simply reverses the *J* spectrum left to right, and the problem is simply corrected by instructing the computer to read out the frequencies in reverse (i.e., decreasing) order.

All Fourier transform experiments tend to be sensitive to extraneous frequencies in the input waveform. In order to minimize any possible interference effects from the magnetic field modulation, the pulse repetition rate was synchronized with the modulation frequency in the *J*-spectroscopy experiments; the pulse is then always applied at the same point on the field modulation cycle. As a side effect, the frequency width of the *J* spectra was partly determined by the choice of modulation frequency, and thus changed slightly if the Larmor condition was readjusted. The sample spinning rate was sometimes observed to have a critical effect on the quality of the *J* spectra, but since there was no way to synchronize this frequency, it was adjusted by trial

and error into a range where it no longer produced artifacts in the observed spectrum. Presumably these problems arise if the spinning frequency beats with a harmonic of the pulse repetition rate. In principle, a possible solution would be to turn off the spinner altogether, and in fact *J* spectra have been recorded with a stationary sample, although the lines were somewhat broader than normal. The refocussing effect should be capable of compensating for quite large static field inhomogeneities, in the same way as it compensates large chemical shifts. Unfortunately the spurious decay of spin-echo amplitude from spin diffusion becomes more severe as the magnetic field gradients increase, and since the pulse repetition rate is limited by other considerations, the refocussing process will eventually be defeated by the finite motion of spins through field gradients in the relatively long interval between 180° pulses. The problem would be minimized by restriction of the sample size, and possibly by the introduction of physical barriers to macroscopic motion. In the present experimental arrangement there was a second problem with nonspinning samples—the internal fluorine field/frequency regulation scheme operated less efficiently with the resulting broad fluorine resonance line. Nevertheless it would appear that equipment for *J* spectroscopy could be designed with a stationary sample, breaking the almost universal convention for high-resolution NMR.

III. RESULTS

A. Spin Echoes from Benzene

The first experimental tests of the technique were made on a single line from the protons in a degassed sample of benzene (about 10% in carbon tetrachloride containing about 10% of hexafluorobenzene as an internal lock). The results are shown in Fig. 4. Although this experiment has no bearing on the selectivity of the method, it does establish two important points that prepare the way for later experiments.

First, these results establish that the internal fluorine field/frequency regulation scheme is capable of holding the Larmor precession phase suitably stable that 1000 spin echoes may be recorded (lower trace of Fig. 4). These results were obtained with a spinning sample and good field homogeneity, hence the echoes are quite broad. Note that at a rate of 10 echoes/sec, the individual echoes are no longer distinguishable, and the trace approximates the *envelope* of the spin-echo *peaks*. This proves to be a useful simplification when echo modulation is to be detected.

Second, the measured decay rates at two different pulse repetition rates (1 and 10 Hz) can both be fitted to exponentials with time constants $T_2 = 33 \pm 1$ sec. This lack of sensitivity to the pulse interval is taken as evidence that spin diffusion effects can be safely neglected under these conditions, even at the low pulse repetition rates dictated by the requirements of high selectivity. Conventional spin-echo experiments, which

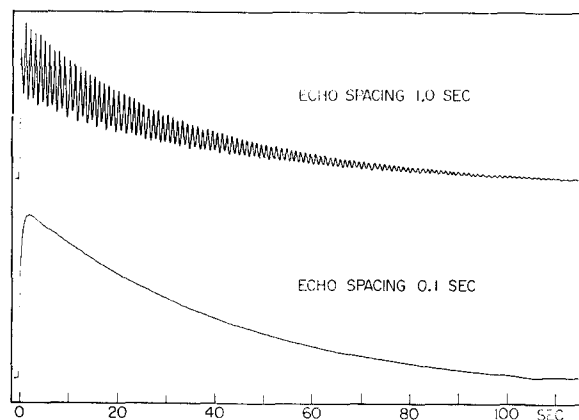


FIG. 4. Spin-echo responses recorded for a degassed spinning sample of benzene (about 10% in carbon tetrachloride, containing about 10% hexafluorobenzene). In the upper trace the individual echoes are clearly distinguishable. In the lower trace the dephasing of isochromats is so small between refocussing pulses that the individual echoes are not resolved. Since both decays can be fitted to exponentials of time constant 33 ± 1 sec, this is taken as evidence that spin diffusion effects are negligible.

are usually carried out in a much less homogeneous magnet without spinning the sample, would normally operate with a much shorter pulse interval to minimize the loss of echo amplitude due to spin diffusion.

B. Applications of Echo Modulation

The introduction of high selectivity methods into spin-echo studies greatly reduces the complexity of the echo modulation observed for molecules with several nonequivalent spins. One promising application of this modulation is in the detection of homonuclear spin-spin couplings that are normally hidden by instrumental effects, notably magnet inhomogeneity.¹² Provided that the modulation frequency due to spin coupling exceeds the natural width of the line, $\frac{1}{2}|J| \geq (\pi T_2)^{-1}$, it should be measurable with high precision. For properly degassed samples the ratio of instrumental width to natural width may often exceed an order of magnitude; consequently the spin-echo technique may open up a wide field of long-range spin couplings. Previous attempts to probe this area have tended to rely on resolution enhancement²⁷ or multiple resonance methods.²⁸

A normally unresolved long-range coupling in 3-bromothiophene-2-aldehyde was chosen to illustrate the method. The high-resolution spectrum and the assignments of the resonance lines are indicated in Fig. 5; note that the A and X lines conceal an unresolved splitting due to the long-range coupling between the aldehyde proton and the ring proton at position 4. A Carr-Purcell spin-echo train adjusted to detect the X resonances selectively gave the response illustrated in the upper trace of Fig. 6. No modulation due to the pulse repetition rate (5 Hz) is apparent in this response since there is negligible dephasing of spin vectors due to inhomogeneity in the 0.1-sec interval between an echo and the next refocussing pulse.

However, two other modulation components are apparent—one at 0.69 Hz ($\frac{1}{2}J_{BX}$) and the other at about 0.025 Hz ($\frac{1}{2}J_{AX}$).

The origin of these modulation components may be readily confirmed by double irradiation experiments where one of the components is eliminated by decoupling. The lower trace of Fig. 6 illustrates the spin-echo response obtained with simultaneous irradiation of the A resonance with a continuous-wave component from the proton transmitter. Only the high-frequency modulation is now observed, making it much easier to evaluate the spin-spin relaxation time of the aldehyde proton, $T_2 = 11.5 \pm 0.5$ sec. A more precise determination of the weak long-range spin coupling constant can now be made by plotting the difference between peak excursions of the spin-echo response under single and double resonance conditions. After normalization to eliminate the exponential decay, these data can be fitted to a cosine wave as illustrated in Fig. 6, giving a measure for the long-range coupling $J_{AX} = 0.051 \pm 0.002$ Hz.

It is instructive to examine the same long-range coupling by means of the "selective pulse" technique.⁴ A Carr-Purcell train of pulses was applied to bromothiophenealdehyde in such a way as to affect only lines A3 and A4 (see Fig. 5), all other resonances being insensitive to the pulses. To achieve this selectivity, the rf level was set very low ($\gamma H_1/2\pi = 0.5$ Hz) which necessitated widths of 1 sec for 180° pulses. The spin echoes occurred at 4-sec intervals; they are illustrated in the upper trace of Fig. 7. Since none of the neighbor nuclei were affected by the 180° pulses, this case is represented by the refocussing sequence (a), (b), (c), (d), of Fig. 1, and no modulation appears on the echo envelope (just as if the couplings had been heteronuclear). The experiment was then repeated with a second set of synchronized 180° pulses applied at the center of the four X lines, with the rf level set high enough to affect all four components essentially uniformly ($\gamma H_2/2\pi = 2.5$ Hz). The refocussing sequence

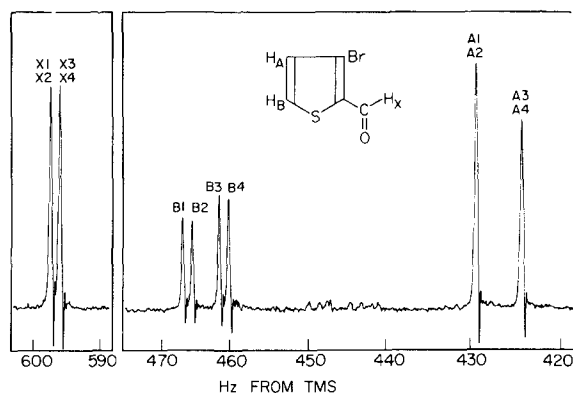


FIG. 5. Assignment of the high-resolution NMR spectrum of 3-bromothiophene-2-aldehyde. There is a weak unresolved long-range coupling between the ring proton A and the aldehyde proton X.

(a), (b), (c), (c'), (d') of Fig. 1 applies to this case and modulation corresponding to the long-range coupling, $J_{AX}/2$, is evident in the lower trace of Fig. 7. The difference in height of the spin-echo peaks observed under single and double resonance conditions was normalized with respect to the unmodulated echoes to eliminate the exponential decay, and fitted to a cosine wave as illustrated in Fig. 7. A good fit is obtained for about two-thirds of a cycle; then the difference becomes too small to measure accurately. (However, it is interesting to note a very weak modulation at about J_{AX} on all the later echoes, presumably a quite different phenomenon.) Because of the finite width of the 180° pulses of H_1 , during which dephasing due to J coupling is inhibited, a correction must be applied to the observed modulation frequency. Since there are seven such pulses in the first half cycle of the cosine wave, the half period must be reduced from 26.6 to 19.6 sec, confirming the previously obtained value for the long-range coupling $J_{AX} = 0.051 \pm 0.002$ Hz.

Wells and Gutowsky¹⁶ have shown that even for first-order spectra, the spin-echo modulation frequency is not exactly equal to half the spin coupling constant unless the condition $2\pi|\delta|\tau \gg 1$ is satisfied by a sufficiently slow pulse repetition rate $F_s = 1/(2\tau)$. The expression for the echo amplitude at time $2n\tau$ for a

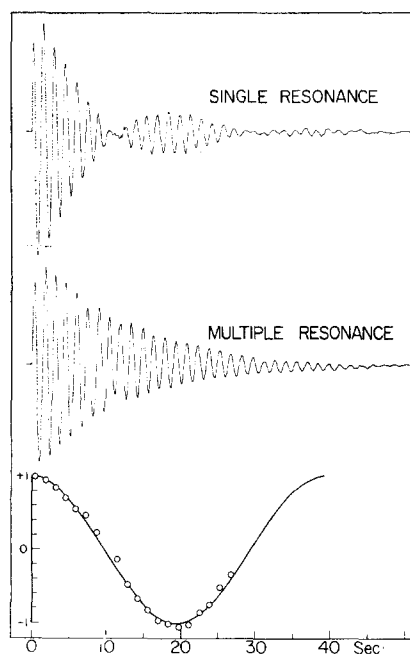


FIG. 6. Spin echoes from the X proton of 3-bromothiophene-2-aldehyde observed selectively under conditions where the individual echoes are not resolved. The upper trace exhibits echo modulation at frequencies equal to $J_{AX}/2$ and $J_{BX}/2$, while in the lower trace, continuous irradiation of the A resonances has decoupled A from X, leaving only one modulation component. The plot is the difference between the peak excursions in the two traces (the exponential decay having been eliminated) and shows a close fit of the low-frequency component to a cosine wave of period 39.2 sec.

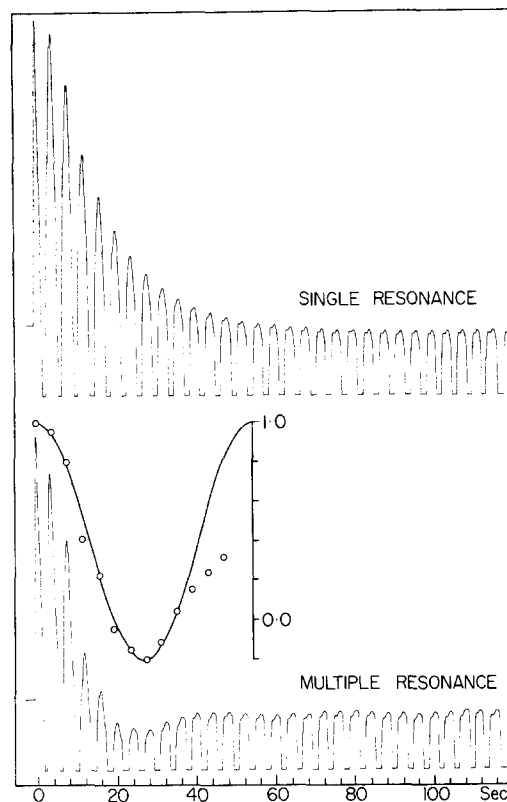


FIG. 7. Spin echoes from the A3 and A4 lines of 3-bromothiophene-2-aldehyde observed by the selective pulse method with a Carr-Purcell-Meiboom sequence. The (truncated) negative spikes are attributed to off-resonance excitation of lines A1 and A2 by the 180° pulses. In the upper trace there is no echo modulation because the pulses do not affect either B or X. In the lower trace a second set of selective 180° pulses has been applied simultaneously to the four X transitions, introducing a modulation component at a frequency $J_{AX}/2$. The difference in spin-echo amplitude between the two traces (after elimination of the exponential decay) gives a good fit to a cosine wave until in the later echoes the relative inaccuracy of the measurements becomes too high.

first-order coupling ($|\delta| \gg |J|$) can be written¹⁸

$$S = \{ \cos 2\pi J n \tau [1 - (\sin 2\pi \delta \tau / 2\pi \delta \tau)] \} \exp(-2n\tau/T_2). \quad (4)$$

However, adequate sampling¹⁹ of the modulation wave requires that the rate at which echoes are generated (which is equal to the pulse repetition rate) must satisfy the condition $F_s \geq |J|$. Thus it is not possible to slow down the pulse repetition rate indefinitely.

In the general case, a group of equivalent nuclei j is coupled to several other groups of nuclei k, l , etc., with homonuclear coupling constants J_{jk} , etc. The highest modulation component observed for this group is half the sum of the absolute values of all these couplings, $\frac{1}{2} \sum_k |J_{jk}|$. (In a nonselective spin-echo experiment there is, of course, a similar summation for each group of nuclei.) The spectrum width $F_s/2$ must therefore be

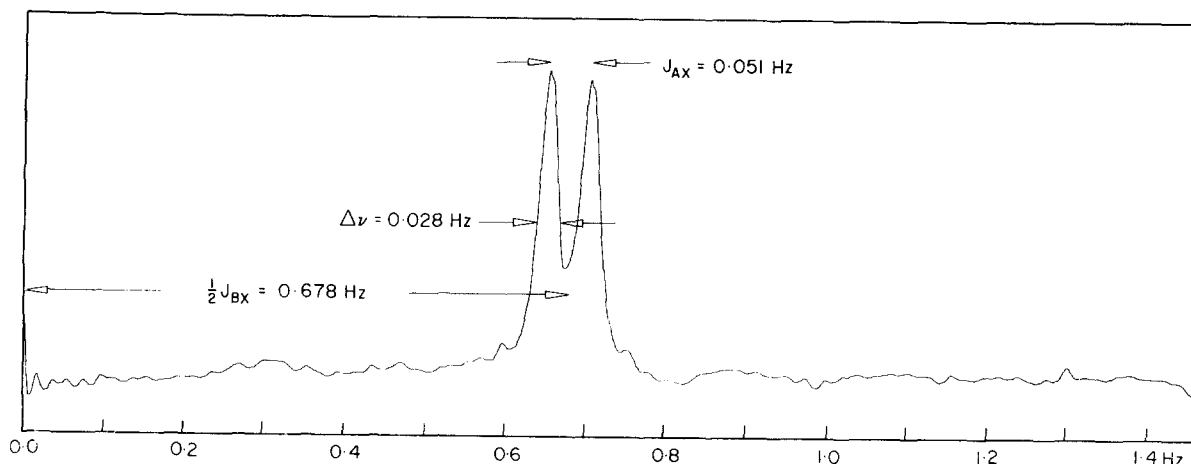


FIG. 8. Partial J spectrum of 3-bromothiophene-2-aldehyde. Carr-Purcell spin-echo responses of the aldehyde proton were detected selectively at a repetition rate of 2.5 Hz (cf. Fig. 6). 150 samples were taken, one at the peak of each echo, and subjected to Fourier transformation in a digital computer. Resonance responses appear at $(J_{BX} - J_{AX})/2$ and $(J_{BX} + J_{AX})/2$ with widths that correspond to a spin-spin relaxation time of 11.2 ± 0.5 sec.

chosen to exceed this frequency, becoming a compromise

$$\pi |\delta| \gg F_s \geq \sum_k |J_{jk}|. \quad (5)$$

For the practical example of 3-bromothiophene-2-aldehyde studied above, the pulse repetition rate was 5 Hz and the approximate chemical shift was 170 Hz. The actual correction to be applied to the modulation frequency depends rather critically on the exact chemical shift, but even at a maximum on the $\sin x/x$ curve would still be less than 1% for the long-range coupling J_{AX} , which is negligible with respect to the experimental error. For the selective pulse experiments, the pulse repetition rate was only 0.25 Hz, hence this correction is correspondingly smaller still.

C. J Spectra

Simple spin systems were chosen to illustrate the first J spectra because of the exploratory nature of the experiment. A particularly simple starting point is the partial J spectrum obtained by selective detection of the spin-echo response of the aldehyde proton (X) of 3-bromothiophene-2-aldehyde. This represents a model of a single nucleus with two spin coupling constants, and affords an opportunity to cross check the parameters derived from the J spectrum with those calculated from the spin-echo envelopes illustrated in Fig. 6.

The pulse repetition rate was set at 2.92 Hz, corresponding to a frequency width of 1.46 Hz for the J spectrum. As in the experiments of Sec. III.B, the high selectivity was achieved through the phase-sensitive detector, and the alternation of the echoes was compensated by alternating the reference phase. Figure 8 illustrates the resulting J spectrum. It consists of two lines at $(J_{BX} - J_{AX})/2$ and $(J_{BX} + J_{AX})/2$ permitting very precise determinations²⁹ of the two coupling constants, $|J_{BX}| = 1.356$ Hz and $|J_{AX}| = 0.051$ Hz, in excellent agreement with the measurements made in

Sec. III.B, and previous double resonance²⁸ and resolution enhancement²⁷ work on the same molecule. The full linewidth at half-height was determined to be 0.028 Hz, corresponding to a spin-spin relaxation time of 11.2 sec, in good agreement with the decay rate observed in the lower trace of Fig. 6. In practice 150 spin-echo peaks were sampled covering a period of about 51 sec, or about 4.6 times T_2 . This emphasizes a very important condition for obtaining an accurate value for T_2 from the linewidth in the J spectrum: the time T for which the echo peaks are sampled should be long compared with T_2 , a good working rule might be³⁰

$$T \geq 4T_2. \quad (6)$$

Otherwise the observed line will be perceptibly broadened and will no longer be a pure Lorentz curve but will acquire some $\sin x/x$ character. In this practical example any appreciable broadening would soon perturb the measurement of the doublet separation and hence affect the determination of the long-range coupling.

Investigation of a first-order three-spin system was the next step, since this provides an opportunity to examine the three partial J spectra that go to make up the complete spectrum. Early experiments on vinyl acetate had given interpretable J spectra, but there were some complications due to the ABX nature of this spin system and some weak long-range couplings. A better model is provided by the ring protons of methyl furoate, an AMX spin system. The sample was made up of roughly 20% methyl furoate (obtained commercially) and 20% hexafluorobenzene in carbon disulphide solution, and was degassed by several freeze-pump-thaw cycles. The conventional NMR spectrum gave $\delta_{AM} = 34.2$ Hz, $\delta_{MX} = 29.4$ Hz, $J_{AM} = \pm 3.4$ Hz, $J_{AX} = \pm 1.7$ Hz, and $J_{MX} = \pm 0.8$ Hz. The protons were assigned on the basis of shifts and coupling constants, as illustrated in Fig. 9.

The field/frequency regulator was adjusted to the condition where the proton transmitter frequency corresponded approximately to the resonance condition for the M proton. The resulting pulse repetition rate was 5.92 Hz which corresponds to a frequency width of 2.96 Hz for the J spectrum. A delay of about 10 msec was introduced into the process of sampling the echoes so as to compensate some instrumental delays. Filtering was accomplished with a commercial band-pass filter,³¹ which when set to pass frequencies up to 60 Hz, gave the complete J spectrum with responses from all three nuclei (see the top trace of Fig. 9). This is in fact a six-line spectrum with accidental overlap of two lines near the center of the spectrum. Reduction of the bandwidth of the filter to 6 Hz, with other conditions unchanged, suppressed the A and X responses while displaying the partial J spectrum due to the M nucleus, with lines at $(J_{AM} - J_{MX})/2$ and $(J_{AM} + J_{MX})/2$ (see the third trace of Fig. 9). In a similar way the A and X responses were recorded selectively by maintaining the 6-Hz bandwidth but displacing the Larmor condition by 32 Hz upfield and downfield, respectively. (Note that this entailed a slight perturbation of the frequency width of the J spectra since the pulse repetition rate was synchronized to the fluorine sideband frequency.) Apart from these very slight changes in the frequency scale, the partial J spectra show very good correspondence with the complete spectrum.

It is apparent that not all lines have the same width, even within a partial J spectrum, and these linewidth variations appeared to be reproducible. One possible explanation is that the couplings in this molecule are not strictly first order, particularly the coupling between A and M. Tokuhira and Fraenkel¹⁸ have given explicit expressions for the spin-echo modulation frequencies to be expected in an ABX spin system, and it is interesting to note that one X response is predicted at *exactly* $(J_{AX} + J_{BX})/2$, whereas the other is *near* $(J_{AX} - J_{BX})/2$ but is dependent on the AB shift to a certain extent (just as are the corresponding separations in the conventional NMR spectrum). Note that in the lowest trace of Fig. 9, the response at $(J_{AX} + J_{MX})/2$ is markedly narrower than the response at $(J_{AX} - J_{MX})/2$. It is tempting to speculate that such a difference might originate in a very weak long-range coupling of proton M to the methyl group, creating four slightly different effective chemical shifts between A and M.³² There are other possible mechanisms for linewidth variations in a J spectrum, and further work is planned on this aspect. One of the narrowest lines, the response at $(J_{AM} + J_{AX})/2$ in the selective (A) spectrum, has a full width at half-height of 0.032 Hz, corresponding to a spin-spin relaxation time of at least 10 sec.

Another problem associated with the finite chemical shifts is the introduction of errors in the derived spin-spin coupling constants, since according to Wells and Gutowsky¹⁶ a fractional error of $\sin 2\pi\delta\tau / 2\pi\delta\tau$ can occur even in a first-order spectrum. These errors turn out

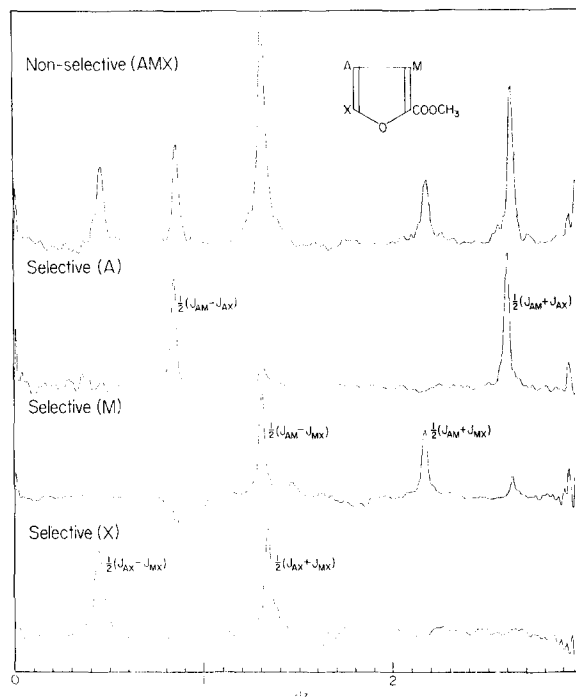


Fig. 9. J spectra of the AMX spin system of methyl furoate. In the top trace the envelope of the spin-echo peaks from all three groups of nuclei was recorded using a detector bandwidth of 60 Hz. Fourier transformation gives the complete J spectrum of six lines, with an accidental degeneracy of the third and fourth lines. This spectrum can be assigned (in terms of sums and differences of spin coupling constants) through the three partial J spectra obtained by tuning the detector to each chemical shift in turn with a restricted bandwidth of 6 Hz. This required ± 32 -Hz frequency displacements to detect the partial J spectra of A and X (second and fourth traces), resulting in a slight perturbation of these frequency scales because of an incidental instrument effect.

to be quite significant for the coupling constants derived from Fig. 9. Owing to the uncertainty in the chemical shift values, the extreme values of the errors, $\pm(2\pi\delta\tau)^{-1}$ have been calculated, the actual errors would of course tend to be smaller.³³ These measurements yield values of the three spin coupling constants,

$$J_{AM} = \pm 3.47 \pm 0.19 \text{ Hz,}$$

$$J_{AX} = \pm 1.77 \pm 0.05 \text{ Hz,}$$

$$J_{MX} = \pm 0.87 \pm 0.06 \text{ Hz.}$$

Clearly for accurate determination of spin coupling constants it would be preferable to operate at the highest available magnetic fields. Other perturbations on the derived values of coupling constants are not ruled out (for example, the imperfect nature of the pulses), and it is planned to look into these problems further.

Partial J spectra are clearly valuable aids to assigning a complete J spectrum as can be appreciated from Fig. 9. However, in a situation where highly selective measurements are not available, there are certain frequency rules that can be applied to help analyze the

J spectrum. For example, in a three-spin system, two pairs of lines must be centered on the same mean frequency, equal to half the largest coupling constant (in absolute magnitude). Two pairs of lines must also have identical separations, equal to the smallest coupling constant (in absolute magnitude). Correspondingly more complex frequency relations apply to higher spin systems.

Certain artifacts are evident in the J spectra of Fig. 9, and more serious interference has been observed in the exploratory experiments. These spurious effects tended to fall into four main categories:

- (a) Broadening or fine structure on all the lines.
- (b) Lines "reflected" left to right (see lowest trace of Fig. 9).
- (c) Partial J spectra with "ghost" lines from other nuclei (see third trace of Fig. 9).
- (d) Spikes at the extreme ends of the spectrum (0 Hz and $F_s/2$ Hz).

Further instrumental work will be required to eliminate these problems. However, it was observed that certain experimental parameters were particularly critical in determining the quality of the spectra—the stability of the field/frequency lock, the spinning rate, the timing of the sampling process to correspond with the center of the echo, and the adjustment of the pulses to the 90° and 180° conditions.

IV. DISCUSSION

Spin-spin relaxation of individual high-resolution lines can be studied by extracting a chosen band of frequencies from a Carr-Purcell spin-echo train using a narrow-band filter. If the magnetic isotope under investigation occurs in low natural abundance (for example ^{13}C), there are no homonuclear couplings in the majority of molecules and the determination of the individual spin-spin relaxation times is consequently straightforward. Otherwise, and in particular for the important nuclei ^1H and ^{19}F , homonuclear coupling modulates the amplitude of the spin echoes and complicates the determination of T_2 . If high selectivity is to be preserved, this imposes a rather severe upper limit on the pulse repetition rate, and it is not possible to eliminate the modulation by pulsing rapidly.¹³ However, the complexity of the modulation can be reduced by detecting the response of one chemically shifted group selectively, and it may be further simplified by spin decoupling experiments.

The proposed general solution to this problem is to perform a Fourier transformation of the envelope of spin-echo peaks. The resulting frequency response is called a " J spectrum." For first-order spectra, this consists of resonance responses at frequencies equal to one-half the sums and differences of spin coupling constants, having the Lorentz shape and natural linewidths unaffected by magnet inhomogeneity (provided that spin diffusion can be neglected). In principle the

individual spin-spin relaxation times can be read off from the linewidths, and in practice the results obtained for 3-bromothiophene-2-aldehyde show excellent agreement between the observed spin-echo decay rate and the linewidths in the partial J spectrum. The principal application of this new mode of presenting NMR data thus appears to be in studies of spin-spin relaxation of high-resolution spectra.

In addition this can be an extremely precise method of determining homonuclear spin coupling constants,¹² particularly useful for very weak spin couplings normally hidden by field inhomogeneity effects. In the future it can be anticipated that much of the routine interpretation of high-resolution NMR spectra will be accomplished automatically by computer. One of the first steps in such an interpretation would be to distinguish frequency differences due to chemical shifts from those due to spin coupling, and this would typically be attacked through a trial-and-error search for repeated spacings. The J spectrum provides an attractive alternative if the spectrometer field is high enough to ensure first-order spectra, for this would provide the computer with precise supplementary information on the spin coupling constants.

When NMR spectra are studied in liquid crystal mesophases, dipole-dipole coupling effects (which average to zero in isotropic media) combine with the indirect spin-spin coupling to give new splittings which can be interpreted to give internuclear distances, absolute signs of spin-spin coupling constants, and the degree and direction of the molecular orientation.³⁴ These important splittings should be measurable from the Fourier transform of the envelope of spin-echo peaks.²² If comparably high accuracy could be attained, this would be particularly important for studies of molecular geometry.

These preliminary experiments suggest the features that would be desirable in a spectrometer designed specifically for J spectroscopy. The requirements for first-order spin coupling and accurate J values favor the highest available magnetic field, if possible a superconducting solenoid since field homogeneity is probably not critical. Small spherical nonspinning samples might be used to avoid artifacts associated with the spinning frequency. The present scheme of internal field/frequency control through a heteronuclear lock might be retained, or alternatively an internal homonuclear lock could be devised where the error signal would be a suitable unmodulated component extracted from the spin-echo response itself by means of a narrow-band filter. (This would entail a conventional modulation sideband lock to hold the field/frequency condition until the spin-echo train is initiated.) A crossed-coil probe configuration would ensure high homogeneity in the transmitter field over the effective volume of the receiver coil. Considerable improvement in the power available from the pulsed transmitter would be advisable in order to obtain an essentially uniform effect

across the entire range of chemical shifts; pulsewidths of a few microseconds would probably be adequate for proton work. The pulse repetition rate would be determined by the largest (absolute) sum of *J* couplings to be investigated, and the echo peaks would be sampled for a period at least four times the longest spin-spin relaxation time. Thus for many proton experiments a 1000-channel storage device would be adequate. Since the pulse repetition rate constitutes the calibration of the frequency scale of *J* spectra, it should be derived by subdivision of a suitable frequency standard.

Throughout the present investigation, particular emphasis has been placed on the simplification to be obtained in Carr-Purcell spin-echo spectra if the spin-spin coupling obeys first-order theory, if the pulse repetition rate is sufficiently low, and if spin-echo modulation effects other than spin-spin coupling are absent. This was dictated by the interest in the special case of *J* spectra, but it should not be construed to rule out the study of spin-echo spectra under more general conditions, e.g., where the conventional continuous-wave NMR spectrum is complex, or where dipole-dipole effects contribute to spin-echo modulation. The additional theoretical complexity should not constitute an insurmountable barrier to the exploitation of these kinds of spin-echo spectra. Further work is planned in this area.

ACKNOWLEDGMENTS

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* A preliminary description of *J* spectra was given at the Eleventh Experimental NMR Conference held at the Mellon Institute, Pittsburgh, Penna., on April 22, 1970.

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²¹ In many cases this would correspond to the natural linewidth that would be observed in a continuous-wave experiment in a "perfect" magnet. However, if the correlation spectrum contains very low-frequency components (for example, as a result of chemical exchange), there will be an additional contribution to the continuous-wave natural linewidth, but this will be partially removed in the *J* spectrum by the refocusing effect of the 180° pulses. See Z. Luz and S. Meiboom, *J. Chem. Phys.* **35**, 366 (1963).

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²³ Although the rf is only applied to the sample in the form of very short pulses, it still influences the frequency of the detected signal between pulses through the heterodyne action in the receiver.

²⁴ H. Primas, 5th European Congress on Molecular Spectroscopy, Amsterdam, 1961 (unpublished); R. Freeman and D. H. Whiffen, *Proc. Phys. Soc. (London)* **79**, 794 (1962); W. A. Anderson (unpublished work).

²⁵ In practice the frequency of the proton transmitter was used, as shown in Fig. 2, but synchronization with the rf phase is not essential to the experiment.

²⁶ This is analogous to the finite frequency width of a resonance response obtained by Fourier transformation of a free induction signal observed for only a restricted time.

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³⁰ Similar conditions apply in Fourier transformation of free precession signals. The numerical factor is, of course, arbitrary—for example, a factor 3 has been suggested by R. R. Ernst, *Advances in Magnetic Resonance* (Academic, New York, 1966), Vol. 2, p. 112.

³¹ Krohn-Hite Corporation, Cambridge, Massachusetts, Model 330-A.

³² Note that if this is the correct explanation of the broadening, this assigns the narrow response to $(J_{AX} + J_{MX})/2$, and thus establishes that J_{AX} and J_{MX} have like signs.

³³ In principle the errors could be eliminated by measuring the *J* spectrum at various settings of the pulse repetition rate, covering at least one cycle of the $\sin x/x$ function.

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