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Publication Date

1980-10-01

Lawrence Berkeley Laboratory

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Materials & Molecular Research Division

Submitted to the Journal of Chemical Physics

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October 1980

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EXPERIMENTS ON SELECTIVE EXCITATION OF
MULTIPLE-QUANTUM TRANSITIONS IN NMR SPECTROSCOPY

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Abstract

By irradiating a spin system with an appropriate sequence of phase shifted pulses only certain orders of multiple-quantum transitions can be excited. Using such sequences in preparation and detection produces a large signal/noise enhancement for the high multiple-quantum spectra over non-selective excitation, as predicted from theory. In a previous paper the theory was presented in detail. In this paper some aspects of the theory are first outlined briefly. Experimental results are then presented demonstrating 4-quantum, 6-quantum and A-symmetry selection in oriented benzene and 8-quantum selection in oriented 1-bromobutane. A 6-quantum selective sequence applied to benzene with non-equilibrium initial reduced density matrix proportional to I_x produces 1- and 5-quantum spectra. The n-quantum signal/noise enhancements are obtained and the selectivity is measured as a function of pulse sequence parameters. The behavior is that expected if one assumes that the limit to selectivity is determined by leading nonselective terms in an average Hamiltonian expansion.

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I. Introduction

The observation of normally forbidden ($\Delta M \neq 1$) NMR transitions has been shown to be of great value in extracting information from complex molecules.¹⁻⁸ Because the number of different transitions decreases as ΔM increases, multiple-quantum ($\Delta M > 1$) spectra are always simpler than the normal single-quantum spectrum. Thus, multiple-quantum spectra can be interpreted even when the normal spectrum contains many unresolvable transitions. Wideband nonselective excitation of multiple-quantum transitions, which permits the simultaneous observation of transitions with all possible values of ΔM , is relatively straightforward and requires only a few pulses and delays. However, wideband excitation leaves most of the spectral intensity in the single-quantum and low multiple-quantum spectra because these spectra have the most transitions. As a result, the simple high multiple-quantum spectra are weak.

One alternative approach is to selectively excite transitions which correspond to only a few values of ΔM . From the viewpoint of perturbation theory this appears impossible without detailed knowledge of the form of the Hamiltonian since a multiple-quantum transition occurs only with irradiation which also excites lower quantum transitions. Thus, aside from even-odd selection due to the bilinear form of certain spin operations⁹ and selection in small systems where the Hamiltonian is completely known⁸ no general method of selective excitation has been proposed. In a previous letter,¹⁰ we demonstrated that selective excitation of multiple-quantum transitions is possible, and that arbitrarily high orders can be selected without prior knowledge of the exact Hamiltonian. A theory of selective excitation, some examples of highly selective sequences, and the potential signal gain from selectivity were also presented.^{11, 12} In this paper, we first present some aspects of the theory and then we present the results of experiments on two molecules, benzene and n-butyl bromide, which show that selective excitation is generally feasible and that large signal gains can be achieved.

II. Theory of Selective Multiple-Quantum NMR

A. General Theory of Selective Excitation

The general theory of selective excitation of multiple-quantum coherences was described in reference (12). In this subsection we briefly summarize this theory. In the next subsection we discuss practical pulse sequences for selective experiments which compensate for inevitable pulse errors (inhomogeneity, finite duty cycles, and the like).

To understand how selective excitation works, we consider first the nonselective pulse sequences in Figure 1, and assume that we apply them to dipole-coupled nuclear spins in a large magnetic field. The Hamiltonian is then:

$$H_z = \sum_{i>j} D_{ij} (3I_{zi} I_{zj} - \vec{I}_i \cdot \vec{I}_j) + \sum_{i>j} J_{ij} (\vec{I}_i \cdot \vec{I}_j) + (\sum_i \sigma_i I_{zi} + \Delta\omega I_z)$$

$$\equiv H_{zz} + H_J + (H_{cs} + \Delta\omega I_z) \quad (1)$$

where typically $\|H_{zz}\| \gg \|H_{cs}\|$, $\|H_J\|$. The simplest pulse sequence for producing nonselective wideband multiple-quantum spectra is shown in Figure 1(a).^{4-6,8} The first two pulses, separated by a delay τ such that $\|H_{zz}\tau\| \sim 1$, constitute the preparation sequence. The initial (equilibrium) reduced density matrix is $\rho_0 = -\beta I_z$. At the end of the second pulse, the reduced density matrix is:

$$\rho = -\beta \exp(-i\pi I_y/2) \exp(-iH_z \tau) \exp(i\pi I_y/2) I_z \exp(-i\pi I_y/2) \exp(iH_z \tau) \exp(i\pi I_y/2)$$

$$\equiv -\beta \exp(-iH_x \tau) I_z \exp(iH_x \tau) \quad (2)$$

$$H_x = \sum_{i>j} D_{ij} (3I_{xi} I_{xj} - \vec{I}_i \cdot \vec{I}_j) + \sum_{i<j} J_{ij} (\vec{I}_i \cdot \vec{I}_j) + \sum_i \sigma_i I_{xi} + \Delta\omega I_x \quad (3)$$

In general H_x will contain 0-quantum, 1-quantum and 2-quantum operators, and the complex exponential gives ρ matrix elements corresponding to all multiple-quantum orders. After the preparation sequence, the system evolves under H_z for a time t_1 , called the evolution period. Multiple-quantum coherences do not correspond to oscillating magnetization, so they cannot be directly detected, and a third pulse plus a delay t_2 (called the mixing sequence) are needed to partially transfer them into the observables $\langle I_x \rangle$ and $\langle I_y \rangle$. The sequence is repeated with different values of t_1 , Fourier transformed, converted to a magnitude spectrum,

and averaged with spectra corresponding to different values of t_2 or τ to produce the nonselective spectrum.

Inspection of H_z reveals that the n -quantum spectrum is centered at $n\Delta\omega$, so different values of n will be completely separated if $\Delta\omega > \|H_z\|$. However, static inhomogeneity broadens the n -quantum transitions n times more than the single-quantum transitions. This broadening can be eliminated by echo pulses in t_1 , but in this case the sequence in Figure 1(a) will center all of the multiple-quantum spectra at $\omega=0$. The sequence in Figure 1(b) overcomes this problem by the method of time proportional phase incrementation^{5,6} (TPPI). In this experiment, whenever t_1 is incremented by Δt_1 , the phases of all the pulses in the preparation period are incremented by $\Delta\phi=(\Delta\omega')\Delta t_1$. The incrementation modulates the n -quantum coherences by $\exp(-in\Delta\omega't_1)$, so that the n -quantum spectrum is centered at $n\Delta\omega'$.

There is actually a great deal of similarity between the preparation and mixing portions of this pulse sequence, which is hidden by the experimental need to measure $\langle I_x \rangle$ or $\langle I_y \rangle$ even though the initial density matrix is proportional to I_z . If instead we imagine that $\langle I_z \rangle$ can be measured, as in Figure 1(c), an additional pulse is needed at the end of t_2 . The sequences in parts (b) and (c) would always give the same spectra, but in part (c) the symmetry between preparation and mixing is apparent (if $\tau = t_2$ they are identical except for a phase shift). For this reason we will develop the theory as if $\langle I_z \rangle$ were detected. The experimental pulse sequences will always include one additional pulse immediately before detection, to sample $\langle I_x \rangle$ or $\langle I_y \rangle$.

It can be shown that the signal is maximized for $\tau = t_2$, and in this case is equal to the expectation value of the equilibrium magnetization. There are 4^N density matrix elements in a system with N spins-1/2, and the signal is divided up among all of these elements in the nonselective experiment. If the mixing and preparation sequences selectively produce only a small fraction of the allowed coherences, the signal associated with each coherence can be much larger. For

example, a N -quantum selective sequence in a N -spin system can transfer magnetization from the two states with $M=\pm N/2$ directly into N -quantum coherence, and the potential signal gain relative to totally nonselective excitation is N^2 .¹²

To perform a selective wideband excitation we use a sequence of the type illustrated schematically in Figure 2(a). This sequence can replace the nonselective preparation, the nonselective mixing, or both. We can start with an arbitrary cyclic sequence of pulses and delays. This sequence, which we will call a subcycle, has a total duration of $\Delta\tau_p$ and generates a propagator U_o . Average Hamiltonian theory^{13,14,15} allows us to write the propagator as $U_o = \exp(-iH_o\Delta\tau_p)$, where the effective Hamiltonian H_o is given by a Magnus expansion of the product of the propagators for each piece of the sequence. The subcycle is then repeated, except all the pulses are phase shifted by an angle ϕ . This creates a new subcycle with a new (rotated) effective Hamiltonian:

$$H_\phi = \exp(i\phi I_z) H_o \exp(-i\phi I_z) \quad (4)$$

$$(H_\phi)_{ij} = \exp(i(M_i - M_j)\phi) (H_o)_{ij}$$

which is also allowed to evolve for $\Delta\tau_p$. If $\phi = 2\pi/n$, coherences with $\Delta M = nk$ ($k=0, \pm 1, \pm 2, \dots$) are unaffected, but all other coherences are multiplied by a phase factor of $\exp(i2\pi(\Delta M)/n)$. This process is repeated to make a total of n phase shifts. The propagator after n subcycles is

$$\begin{aligned} U &= \prod_{q=0}^{n-1} \exp(-iH_{\phi=2\pi q/n} \Delta\tau_p) \\ &= 1 - i\Delta\tau_p \left(\sum_{q=0}^{n-1} H_{\phi=2\pi q/n} \right) + O(\|H_\phi \Delta\tau_p\|^2) \end{aligned} \quad (5)$$

If $\|H_\phi \Delta\tau_p\| \ll 1$, the last term can be neglected. Combining equations (4) and (5) to first order in $\Delta\tau_p$ we can write

$$\begin{aligned} U_{ij} &\approx \delta_{ij} - i\Delta\tau_p \left(\sum_{q=0}^{n-1} \exp(i2\pi q(M_i - M_j)/n) \right) (H_o)_{ij} \\ &\quad - i\Delta\tau_p (H_o)_{ij} \delta((M_i - M_j) - nk) \end{aligned} \quad (6)$$

Thus U will only induce transitions between states with $\Delta M = nk$, to first order in $\Delta\tau_p$. We call this a zero-order nk -quantum selective sequence because the zero-order average Hamiltonian is a nk -quantum selective operator, but all higher-order terms are nonselective. Sequences can be designed which are selective to arbitrarily high order in the average Hamiltonian expansion; these sequences are described in references (11) and (12).

B. Pulse Sequences for Multiple-Quantum NMR

Equation (6) implies that U cannot contain multiple-quantum operators unless H_0 does, and it can be shown that, no matter what the actual pulse sequence is for H_0 , it cannot contain substantial contributions from multiple-quantum operators unless $\|H_z \Delta\tau_p\| \gg 1$. For this reason the pulse sequence for H_0 must be constructed such that $\|H_0\| \ll \|H_z\|$, or terms nonlinear in $\Delta\tau_p$ will ruin the selectivity. One particularly convenient way to do this is to use dipolar time reversal sequences as illustrated in Figure 2(b). A pulse sequence with an effective Hamiltonian H_p is applied for a time T such that $\|H_p T\| \gg 1$. After a short delay $\Delta\tau_p'$ another pulse sequence, with an effective Hamiltonian H_p' , is applied for a time T' such that $H_p' T' = -H_p T$. We can then write

$$U_0 = \exp(-iH_0 \Delta\tau_p) \exp(-H_p' T') \exp(-iH_z \Delta\tau_p') \exp(iH_p T) \quad (7)$$

$$H_0 = (\Delta\tau_p' / \Delta\tau_p) \exp(-iH_p T) H_z \exp(iH_p T) \quad (8)$$

and if $\Delta\tau_p' \ll \Delta\tau_p$, $\|H_0\| \ll \|H_z\|$, yet H_0 can have multiple-quantum coherences.

H_p was produced for all of the experiments in this paper by the sequence $(\tau/2 - 90_x - \tau' - 90_x - \tau - 90_x - \tau' - 90_x - \tau - 90_x - \tau' - 90_x - \tau - 90_x - \tau' - 90_x - \tau/2)$ repeated several times. The pulses have a finite width t_p , and we set $\tau' = 2\tau + t_p$. This sequence affects each of the three parts of H_z in equation (1) differently. The dipolar term H_{zz} has a zero-order average of

$$\bar{H}_D^{(0)} = 1/3(2H_{xx} + H_{zz}) = 1/3(H_{xx} - H_{yy}) \quad (9)$$

$$H_{\alpha\alpha} = \sum (3I_{\alpha i} I_{\alpha j} - \vec{I}_i \cdot \vec{I}_j) D_{ij} \quad (\alpha=x, y, \text{ or } z)$$

$\bar{H}_D^{(0)}$ is purely a two-quantum operator, which means that a phase shift of 90° multiplies it by -1 ; this can also be seen by substituting $I_x \rightarrow I_y$, $I_y \rightarrow -I_x$, $I_z \rightarrow I_z$ in equation (9). If the pulse sequence is run with y and $\bar{y}$ pulses instead of x and $\bar{x}$ pulses, the zero-order average of the dipolar Hamiltonian is inverted so with this modification the sequence for H_p was also used for H_p' . $(H_{cs} + \Delta\omega I_z)$ is cancelled to lowest order by this sequence, and H_J is unaffected. In the cases we will consider, $||H_{zz}||$ is several orders of magnitude larger than $||H_J||$, so $\bar{H}_D^{(0)}$ dominates when $||H_z\tau|| \ll 1$, and very good time reversal is possible.

This sequence compensates for several common pulse errors. Static inhomogeneity would force $\Delta\omega$ to be written as $\Delta\omega(\vec{r})$, but the zero-order average vanishes. Similarly, rf inhomogeneity, which can be represented by a pulse flip angle of $90-\epsilon$, does not appear in $\bar{H}_D^{(0)}$ to order ϵ . The largest nonvanishing error term in $\bar{H}^{(0)}$ should be the cross term between static and rf inhomogeneity, which is minimized by making $\Delta\omega \sim 0$.

This sequence is symmetric for the dipolar Hamiltonian, so $\bar{H}_D^{(1)} = 0$. Under ideal experimental conditions, this means that the ultimate limitations to time reversal come from $\bar{H}_D^{(2)}$ and H_J , and these terms will make $||H_o\Delta\tau_p|| > ||H_z\Delta\tau_p'||$. Fortunately, one feature of the selective experiment is that perfect time reversal is unnecessary; imperfections will merely cause $||H_o||$ to be larger than in the ideal case. If this presents a problem, $\Delta\tau_p'$ can be reduced.

III. Experimental Apparatus

All experiments were performed on a homebuilt spectrometer with a superconducting 43kG magnet, giving a proton resonance frequency of 182 MHz. A microprocessor-based pulse programmer produced the pulse sequences. To ensure good rf isolation, switching was done once at 30 MHz (the IF frequency) and once at 182 MHz. Two phases (corresponding to x and $\bar{x}$) were generated by hybrids at the IF frequency and all phase shifts were generated by a Daico 100 DO 898 shifter.

The phases were checked with a Hewlett-Packard 8405A vector voltmeter and found to be stable, reproducible, and within $\pm 1^\circ$ of the digital setting at all times. However, the VSWR of the phase shifter depended on the phase setting. To eliminate fluctuations from this effect and from switching transients, the pulses were amplified to $\sim 3V_{pp}$ and passed through a series pair of crossed PIN diodes followed by a pair of crossed PIN diodes to ground. The first pair eliminates small components which are out of phase with the main pulse, and the second pair reduced fluctuations in the output voltage. The pulses were then filtered, amplified, and sent to the probe.

The probe had a single-tuned 8mm I.D. x 25mm solenoidal coil. All of the samples were nematic liquid crystals, so heating effects had to be minimized. Fortunately, the selective experiment does not require signal sampling in short windows in the pulse sequence, so a high-Q circuit and low power ($\sim 50W$) pulses were used. Samples were sealed in 6mm O.D. x 15mm Pyrex tubes, which were suspended in the center of the coil to minimize rf inhomogeneity and heating effects. A temperature-regulated air stream focused on the sample was used to further decrease heating. Even with these precautions, relatively long delays (as much as 10 seconds) were sometimes required between successive shots.

IV. Experimental Results

A. Oriented Benzene

i. Four-Quantum Selection

The high (D_{6h}) symmetry of benzene produces many different irreducible representations for the eigenstates (Figure 3). This reduces the number of allowed transitions; for example, there is only one pair of five-quantum transitions, instead of the six pairs of five-quantum transitions in an unsymmetrical six spin system. All six protons are equivalent, so we can set $\sigma_i = 0$ for all i in equations (1) and (3). This molecule is small enough to be studied by non-selective sequences, and all of the theoretically allowed transitions have been observed.^{4,5,9}

Figure 4(a) shows the nonselective (pulse sequence of Figure 1(b)) multiple-quantum spectra at 24.0°C of a sample with 14wt% benzene dissolved in Eastman liquid crystal #15320. The same sample was used for all of the benzene experiments. For this experiment $\Delta\omega = 500\text{ Hz}$, and spectra corresponding to $t_2 = \tau = 4.0\text{ msec}$, 6.0 msec , 8.0 msec and 10.0 msec were averaged together. The individual lines are resolvable even in the single-quantum spectra,¹⁶ and the three dipolar coupling constants D_{12} , D_{13} and D_{14} have been shown to be consistent with hexagonal symmetry. Figure 4(b) shows, on the same scale, the averaged results of four spectra with 4k-quantum selection ($\phi = \pi/2$ in figure 2), and different values of T and τ . The four-quantum transitions are significantly enhanced (the integrated intensity is increased by a factor of 3.83) and their positions are unaffected. The nonselected orders are almost entirely under the noise level.

In Figures 5 and 6 we present individual spectra (not averaged over any parameters in the pulse sequence) to calculate selectivity and maximum signal gains. Each of the spectra in Figure 5 was taken with $\phi = \pi/2$, $t_p = 3.8\mu\text{sec}$, $\tau = 5.0\mu\text{sec}$, $T = 1.5\text{ msec}$, and 8 subcycles (the zero-order sequence was applied two consecutive times) to make a 4k-quantum selective sequence. The sequence was used in both the preparation and mixing periods. Immediately before detecting $\langle I_x \rangle$ and $\langle I_y \rangle$, a single additional pulse was applied as explained in Section II.A. The only parameter which was varied was $\Delta\tau_p'$.

The selective terms in the average Hamiltonian are linear in $\Delta\tau_p'$. Higher order terms are nonselective, so the spectra with large values of $\Delta\tau_p'$ are expected to have substantial two-quantum and six-quantum intensity (H_0 still has the form in equation (8), so no odd-quantum operators are present in the propagator). Figure 5e confirms this result. If $\Delta\tau_p'$ is very small and the time reversal is good, even the linear term is small, and very little coherence is produced. Thus, there should be an optimal value (or at least an optimal range) for $\Delta\tau_p'$ to produce four-quantum coherences. One interesting feature of Figure 5

is that the value which optimizes the central four-quantum line is much longer than the value which optimizes the side peaks. There is no reason why the optimal values should be the same; the side peaks are all A_1 transitions, whereas the central peak has contributions from every irreducible representation. In addition, diagonalizing the Hamiltonian shows that $\|H_z\|$ is larger for the A_1 states than for any other representation, so from equation (8) we expect that, if we averaged over all possible operators H_p , the A_1 transitions would peak at the smallest values of $\Delta\tau_p'$. However, this need not be true for each possible H_p .

ii. Signal Gains from Selectivity

The maximum observed signal gain for the side peaks relative to totally nonselective excitation is the gain of 5.6 in Figure 5b. The delay between successive shots was 4 seconds, and was determined by heating effects; the nonselective experiment can be run with a slightly shorter delay (2.5 seconds). The true maximum gain may be larger than this, since a small change in $\Delta\tau_p'$ from 34 usec might produce a larger value. The maximum theoretical gain may be estimated by dividing up the total available intensity (which is the same as the equilibrium magnetization, $\beta\text{Tr}(I_z^2)$) equally among all of the pumped density matrix elements in the A_1 manifold. There are 13 A_1 states, so there are 169 matrix elements, but time-reversal symmetry in the $M=0$ manifold forces all 6 zero-quantum transitions in that manifold plus the three populations to vanish in the nonselective experiment.^{17,18,19} A four-quantum selective propagator will transfer some of $\beta\text{Tr}(I_z^2)$ from ten of the populations ($M=\pm 3, \pm 2, \pm 1$) to the fourteen four-quantum coherences using only terms linear in $\Delta\tau_p'$. Only 24 matrix elements are involved, and if they are all roughly equal, the expected gain is $160/24 \sim 6.7$.

However, it is clear from the spectra in Figure 5 that some zero-quantum coherences are also produced. This is to be expected because four-quantum operators proportional to $\Delta\tau_p'$ in the propagator imply zero-quantum and four-quantum operators proportional to $(\Delta\tau_p')^2$. There are 12 zero-quantum coherences which can be pumped, and if these are pumped as strongly as the four-quantum coherences the maximum gain falls to 4.4.

The largest enhancement observed for the four-quantum center line is the factor of 19 in Figure 5(c). This gain cannot be readily compared to the theoretical gain because this peak corresponds to six different transitions in the different irreducible representations. In addition, the TPPI method of separating the different orders of coherence can produce artifact peaks if the phase shifts are imperfect. In this experiment, the TPPI increment was $\pi/8$ (this means that each pulse in the preparation period had its phase incremented by $\pi/8$ every time t_1 was incremented, so that the initial phase setting was incremented by $\pi/2$ after four points were taken in t_1). A phase shift of $\pi/2$ does not affect populations, zero-quantum coherences, or four-quantum coherences, so it does not affect the density matrix if the selectivity is good. Thus, phase shift inaccuracies would slightly modulate these coherences with a period of four points, producing small satellite peaks with an apparent ΔM of 0, ± 4 , or ± 8 . The largest peak by far in the selective experiment is at $\omega = 0$ (corresponding to populations which cannot be transferred into four-quantum coherence), so the only observable effect of these imperfections is to distort the intensity of the central four-quantum peak (and produce a small central peak corresponding to $\Delta M = 8$, which does not overlap with the benzene spectrum). The central four-quantum peak has no dipolar information so a distorted intensity does not affect the analysis.

Figure 5(f) shows an ensemble averaged nonselective experiment (using the pulse sequence in Figure 1(b)) with $\Delta\omega=0$. H_x has only even-quantum coherences,⁹ so a partially selective spectrum is produced. Comparison of parts (a)-(e) with part (f) shows that the selective experiment does not distort lines positions. Residual pulse errors increase the noise level of the selective experiment, but the signal-to-noise ratio of the four-quantum lines in parts (a) and (b) is still substantially better than could be achieved nonselectively in equal time.

iii. Suppression of Nonselective Operators

The first nonselective term in the effective Hamiltonian for a zero-order selective sequence is proportional to $(\Delta\tau_p')$. If $\Delta\tau_p'$ is cut in half but the number of subcycles is doubled, this term will be cut in half. The selective term will be unaffected. Thus, the selectivity of a zero-order sequence can be made arbitrarily good by making $\Delta\tau_p'$ small and repeating the sequence many times. This is illustrated in Figures 6(a)-(c). In this experiments $t_p=5.9$ usec, $\tau=6.0$ usec, $\tau'=18.2$ usec, and $T=576$ usec, so H_0 is different from the sequences in figure 5. The selective term should be identical for each of the three spectra, and this is confirmed in parts (a) and (b). The four-quantum regions are virtually identical for these two spectra (this particular choice of pulse sequence parameters happens to pump two of the pairs more strongly than the third) except that the four-quantum transitions are slightly weaker in part (b) as the reduced selectivity produces some two-quantum transitions. In part (c) the selectivity has almost disappeared.

Figures 4, 5, and 6 show that suppression of two-quantum coherences is substantially easier than suppression of six-quantum coherences. This result is expected if the phase shifts are imperfect.¹² If the phase of the i^{th} subcycle is $\phi_i + \epsilon_i$ instead of the ideal value ϕ_i , a nonselected coherence ($\Delta M \neq nk$) is multiplied by $(\sum \exp(i(\Delta M)(\phi_i + \epsilon_i)))/n$ instead of 0. If $\epsilon_i \ll 1$ this is approximately equal in magnitude to $(\Delta M) \langle \epsilon_i^2 \rangle^{1/2} / n^{1/2}$, so the error term is three times worse for $\Delta M=6$ than for $\Delta M=2$. Fortunately, most of the allowed coherences correspond to small values of ΔM and are relatively insensitive to phase errors.

iv. Six-Quantum Selection

A 6k-quantum selective sequence can be generated by setting $\phi=2\pi/6$ in Figure 2(a). If this sequence is applied to benzene at equilibrium (initial density matrix proportional to I_z), it connects only the states with $|M|=3$ and creates an effective two level system. The six-quantum spectrum which is generated has only one transition, as illustrated in Figure 7(a). However, if the initial density matrix

is made proportional to I_x by adding one pulse before the selective sequence begins, a 6k-quantum selective propagator will produce only one-quantum and five-quantum coherences. These coherences can be detected by the same 6k-quantum selective sequence if the final pulse of the sequence is removed, and the spectrum is shown in Figure 7(b).

The residual nonselective coherences are not completely suppressed for 6k-quantum selection, because the phase shifter described earlier can only produce shifts in exact multiples of $2\pi/256$. A zero-order sequence was approximated by ϕ values of $(0, 43\pi/128, 85\pi/128, \pi, 171\pi/128, 213\pi/128)$ instead of $(0, \pi/3, 2\pi/3, \pi, 4\pi/3, 5\pi/3)$. This approximation leaves a small amount of non-6k-quantum selective operators in the zero-order term. However, the figure shows that even with this approximate sequence fairly good selectivity can be achieved.

The six-quantum signal produced from one cycle of 6k-quantum selection as a function of $\Delta\tau_p'$ is shown in Figure 8. If the time reversal and selectivity are perfect the six-quantum signal should follow a $\sin^2$ pattern, since the six-quantum selection creates an effective two-level system.¹² Figure 8 deviates from this pattern for large values of $\Delta\tau_p'$ (where the selectivity is poor) and very short values of $\Delta\tau_p'$ (because imperfect time reversal makes $||H_0|| \neq 0$ even if $\Delta\tau_p' = 0$).

The pulse sequence parameters were $\tau = 4.5 \mu\text{sec}$, $t_p = 2.5 \mu\text{sec}$, and $T = 672 \mu\text{sec}$; with $t_p = 4.5 \mu\text{sec}$ the time reversal was clearly worse, and the maximum signal was observed with $\Delta\tau_p' = 0$. Since these pulse sequence parameters are very similar to those used for four-quantum selection it may be concluded that perfect time reversal is not needed for good selectivity and signal gains.

The single six-quantum coherence in benzene has A_1 symmetry, as does the single N-quantum transition in any N-spin system. Therefore, a 6k-quantum selective

sequence applied to an equilibrium density matrix perturbs only A_1 states; all other representations are unaffected. If a single pulse is applied immediately after the selective sequence, A_1 transitions corresponding to all possible values of ΔM are produced, but non- A_1 appear only if $\Delta M=1$, since the density matrix in all other representations is proportional to I_x or I_y . Such a sequence therefore selectively prepares A_1 multiple-quantum transitions, and at the end of the evolution period, a single pulse followed by a 6k-quantum selective sequence selective detects A_1 transitions. The resulting spectrum is shown in Figure 9. One pair of non- A_1 transitions is visible in the three-quantum spectrum; this pair corresponds to two nearly degenerate sets of transitions from the E_1 and E_2 manifolds, and is fairly intense in the nonselective spectrum. Except for this pair, all of the observed lines correspond to known A_1 transitions.

We conclude that 4k-quantum selection, 6k-quantum selection, and A_1 selection can be readily demonstrated in oriented benzene. Nonselective terms can be made very small, and the signal gain from selectivity is approximately equal to the theoretical predictions. The behavior as $\Delta\tau_p$ or the number of cycles is varied is consistent with predictions from average Hamiltonian theory for a zero-order selective sequence.

B. Oriented N-Butyl Bromide

i. Eight-Quantum Selection

Benzene is a small and highly symmetric molecule, so nonselective multiple-quantum spectra are perfectly adequate. However, the signal available for any individual transition in the absence of molecular symmetry is proportional to 4^{-N} , where N is the number of spins in the molecule. Thus, an unsymmetrical seven-spin molecule requires 16 times as many signal measurements as does an unsymmetrical six-spin molecule to achieve the same signal-to-noise ratio.

This problem is illustrated in Figure 10 with the nonselective multiple-quantum spectra of n-butyl bromide (1-bromobutane). The seven-quantum and eight-quantum

spectra of this nine-spin system are expected to reflect internal motion of the chain.^{19,20} However, these spectra are essentially unobservable, since there are many more transitions in the one-quantum and two-quantum spectra. Extensive averaging of nonselective spectra has verified that these transitions are weak.

There are 144 states with A_1 symmetry in n-butyl bromide^{19, 20} (2 with $|M| = 9/2$, 8 with $|M| = 7/2$, 26 with $|M| = 5/2$, 46 with $|M| = 3/2$, and 62 with $|M| = 1/2$). This distribution produces four pairs of eight-quantum transitions and 19 pairs of seven-quantum transitions (simple symmetry arguments²¹ show that there are three more pairs of seven-quantum transitions in the other representations). Nonselective excitation divides the total signal among $144^2 = 20736$ matrix elements. By contrast, ideal eight-quantum selective excitation would involve only 16 eight-quantum coherences, the populations of the ten states with $|M| = 9/2$ or $|M| = 7/2$ (no other states are connected by eight-quantum operators) and 24 zero-quantum coherences for a total of 50 matrix elements. The available signal is the fraction of $\beta \text{Tr}(\mathbf{I}_z^2)$ in the ten selected populations, which is 33% of the total. The net result is a predicted maximum signal gain of 137, which reduces the signal accumulation time by a factor of 18,700. This tremendous gain would probably require high-order selective pulse sequences and suppression of zero-quantum coherences, as explained in reference (12). Nonetheless, even a zero-order selective sequence should give a large enhancement.

Figure 11 shows the results of averaging only four 8k-quantum selective spectra ($\phi = \pi/4$ in Figure 2). The TPPI increment is $\pi/16$ for these spectra so that inaccurate phase shifts are expected to produce a large central spike in the eight-quantum region. At least three of the four expected pairs can be seen. The chain has many allowed conformations, so very little information can be extracted from these few lines, and the seven-quantum spectrum will also be required. This spectrum can be obtained in two fundamentally different ways. A seven-quantum selective propagator can be designed by setting $\phi = 2\pi/7$ in Figure 2(a). Since H_0 in Figure 2(b) is even-quantum selective, some change has to be made in

the sequence; one possibility would be to put a 45° pulse immediately before $\Delta\tau_p'$, and another 45° pulse with opposite phase immediately after $\Delta\tau_p'$. This sequence would pump all 22 pairs of seven-quantum lines. An alternative approach would be to use an eight-quantum selective pulse sequence starting with a density matrix proportional to I_x instead of I_z . Since only the A_1 representation can have eight-quantum operators, only the 19 pairs of A_1 seven-quantum transitions, the single nine-quantum transition, and one-quantum transitions will be produced. The first approach will probably give the larger signal gain.

IV. Conclusions

Selective excitation sequences have been presented for four-, six-, and eight-quantum transitions. These sequences produce large signal enhancements and make multiple-quantum NMR a practical technique for a wide range of hitherto inaccessible molecules. The effects of changing pulse sequence parameters agree with predictions based on average Hamiltonian theory, which suggests that more sophisticated pulse sequences selective to higher order will be able to provide further signal enhancement.

We wish to thank Gary Drobny for his help with the n-butyl bromide experiment and for construction of the phase box controller, and Kathleen Warren for typing the manuscript. This work was supported by the Division of Materials Sciences, Offices of Basic Energy Sciences, U.S. Department of Energy under contract No. W-7405-Eng-48. W.S.W. holds a National Science Foundation Graduate Fellowship.

FOOTNOTES

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only connects gerade to ungerade in the $M=0$ manifold, so no zero-quantum
coherences are produced. If $M \neq 0$, there is no time reversal symmetry.

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Figure Captions:

- Figure 1. Several common nonselective pulse sequences for producing multiple-quantum NMR spectra. In each sequence the density matrix after the first two pulses has multiple-quantum coherences if τ is greater than the reciprocal of a typical dipolar energy level difference.
- Figure 2. General form for zero-order selective sequences. In part a) H_0 is an arbitrary cyclic sequence of pulses and delays. All of the pulses are phase shifted by $\phi = 2\pi/n$ to produce H_0 . To lowest order, only n k-quantum coherences ($k = 0, \pm 1, \pm 2, \dots$) survive after n shifts. Part b) is a possible sequence for H_0 which uses dipolar time reversal to give H_0 multiple-quantum operators yet keep $||H_0 \Delta\tau_p||$ small.
- Figure 3. Energy level diagram for benzene oriented in a liquid crystalline solvent. The assumed symmetry is D_{6h} . There is also a time reversal symmetry operation (flipping all spins) in the $M = 0$ manifold which is not shown. This symmetry operation affects only zero-quantum transitions.
- Figure 4. Multiple-quantum ensemble averaged spectra of oriented benzene. The width of the four-quantum spectrum is 5470 ± 25 Hz. Part (a) is the nonselective spectrum (sequence of Figure 1(b)). Part (b) is 4k-quantum selective (sequence of Figure 2).
- Figure 5. The effects of varying $\Delta\tau_p'$ (see Figure 2) in 4k-quantum selective sequences on oriented benzene. When $\Delta\tau_p'$ is long the selectivity has disappeared. The optimum value of $\Delta\tau_p'$ is expected to be longer for the central peak than for the side peaks (see text). The largest observed gains are 5.6 for the side peaks and 19 for the central peak. Pulse sequence parameters are given in the text.

Figure 6. The effects of increasing the cycle time and reducing the number of cycles. Average Hamiltonian theory predicts that this will not change the selective terms but will increase the nonselective terms. Pulse sequence parameters are given in the text.

Figure 7. Spectra with 6k-quantum selection on oriented benzene. If the initial density matrix is at equilibrium, as in part (a), only the six-quantum coherence is produced. If the initial density matrix is made proportional to I_x by one pulse as in part (b), one-quantum and five-quantum coherences are produced.

Figure 8. Six-quantum signal as a function of $\Delta\tau_p'$. If the time reversal in H_p and H_p' is perfect then the signal should follow a $\sin^2$ pattern. There are substantial deviations, yet good selectivity can still be achieved.

Figure 9. A_1 symmetry selection on oriented benzene. 6k-quantum selection produces a density matrix which is at equilibrium in all manifolds except for A_1 , so one additional pulse gives only single-quantum coherences in these manifolds, but multiple-quantum A_1 coherences.

Figure 10. Nonselective multiple-quantum spectra of 1-bromobutane. The signal intensity for the large values of ΔM is extremely small.

Figure 11. The effects of 8k-quantum selection on 1-bromobutane. The signal scale is the same as in Figure 10. At least three of the four expected pairs are visible above the noise level.

XBL 8010-12245

Figure 1

BENZENE ENERGY LEVELS

Figure 3

Oriented Benzene
n-Quantum Spectra

Nonselective

4k-Quantum Selective

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Figure 4

Figure 5

Figure 6

Oriented Benzene
6k-Quantum Selection

a) Initial Condition I_z

b) Initial Condition I_x

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Figure 7

Theoretical A_1 transitions ($n=0, 2, 3, 4, 5$)

Figure 8

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Figure 9

**n-Quantum Spectra
1-Bromobutane**

Figure 10

8k-Quantum Selection
1-Bromobutane

5 kHz

XBL 808-11262

Figure 11