JOURNAL OF MAGNETIC RESONANCE 79, 369–376 (1988)

Bayesian Analysis of Time-Domain Magnetic Resonance Signals

G. LARRY BRETTHORST, CHI-CHENG HUNG, D. ANDRÉ D'AVIGNON, AND JOSEPH J. H. ACKERMAN

Department of Chemistry, Washington University, St. Louis, Missouri 63130

Received March 29, 1988; revised April 15, 1988

Although the discrete Fourier transform remains the dominant means of processing NMR data (*1–4*), other methods of analyzing time-domain signals exist (*5*), and there has been recent interest among magnetic resonance scientists in applying alternative analysis techniques in an effort to improve signal-to-noise and resolution of the resulting frequency-domain spectrum. Recently, Bretthorst (*6*) and Jaynes (*7*) introduced a novel approach to the general time-domain signal analysis problem utilizing the techniques of Bayesian probability theory. Their approach is particularly suited to the class of time-domain signals characteristic of pulsed magnetic resonance spectroscopy, namely, a sum of decaying sinusoids. An especially attractive feature of Bayesian spectrum analysis lies in its ability to integrate out of the parameter-optimization-search procedure many of the parameters that define the model (so-called "nuisance" parameters). This greatly reduces the complexity of the optimization-search process. These nuisance parameters, such as sinusoid amplitude and phase, are then readily estimated, if needed, once the primary model parameters (e.g., frequencies and decay rates) are found via standard optimization-search algorithms. In this communication we demonstrate the application of Bayesian spectrum analysis to a time-domain (Bloch decay) ^{13}C NMR signal from a standard ASTM reference sample of 1,4-dioxane in benzene-d_6.

Generally, a substantial amount of *prior information* is available regarding the "true" signal resulting from an NMR experiment. Making use of this information ought to improve our results. However, simply taking the Fourier transform of the data affords no way to take it into account. This information can be incorporated advantageously into the time-domain analysis, yielding a more powerful parameter determination. In the Bayesian spectrum-analysis and parameter-estimation technique, one analyzes the data in terms of some model which expresses the prior information. The data are fitted to the model using probability theory to obtain the "best" estimated parameters. The residuals are then reviewed to see if there is any coherent characteristic that has not been accounted for in the model. If there is, the model is updated and the entire process repeated until all coherent characteristics are removed from the residuals, that is, until the data accurately map onto the model.

The Bayesian analysis gives a simple and elegant interpretation to the model-fitting problem and places the discrete Fourier transform in a new light. When fitting data to a model, the data may be thought of as a vector in an N-dimensional vector space

0022-2364/88 $3.00

and the "best" (in the sense of most probable) values of the model parameters (e.g., the frequencies and decay rates) are those for which the projection of the data vector onto the model vector is a maximum.

The analysis shows that taking the Fourier transform of the data is equivalent to postulating a simple single-harmonic-frequency model and then looking for the single frequency which bests fits the data. Obviously, when the signal has more structure than a single stationary frequency, the single-frequency model cannot be fitted to the data well. Models which take on more of the characteristics of the real signal will do better (in the sense of more precise estimates) in determining the frequencies and decay rates. This was to be expected, but the amount of improvement thus obtained was at first surprising.

The Bayesian spectrum analysis begins by postulating a model for the time-series data. The obvious model for solution-state NMR is a sum of exponentially decaying sinusoids; thus, the model used is

$$f(t) = C + \sum_{j=1}^{r} (B_j \cos \omega_j t + B_{j+r} \sin \omega_j t) e^{-\alpha_j t}, \qquad [1]$$

where B_j and B_{j+r} are effectively the amplitude and phase of the jth sinusoid, ω_j is the frequency, α_j is the decay rate, and r is the total number of sinusoids or resonance frequencies. A powerful consequence of the Bayesian analysis is the elimination of the amplitudes $\{B\}$ and reformulation of the problem in terms of the frequencies ω_j and decay rates α_j only. In the case under study herein, all parameters but the four frequencies ω_j and four decay rates α_j were eliminated from the final analysis. The analogous least-squares analysis would have had eight additional amplitudes and a noise variance to determine.

Although the full details of the analysis theory are beyond the scope of this communication (but may be found elsewhere) (*6–8*) a brief overview is given. In the language of probability theory, we seek those model parameters $\{\omega, \alpha\}$ which have the highest "posterior probability" given the data, D, and the prior information, I. This probability, $P(\{\omega, \alpha\} \mid D, I)$, is given by

$$P(\{\omega, \alpha\} \mid D, I) \propto \left[1 - \frac{m\overline{h^2}}{N\overline{d^2}}\right]^{(m-N)/2}, \qquad [2]$$

where $m = 2r + 1$ is the total number of amplitudes (including C) appearing in Eq. [1], $\overline{d^2}$ is the mean square of all N digitized data values d_i,

$$\overline{d^2} \equiv \frac{1}{N} \sum_{i=1}^{N} d_i^2,$$

and $\overline{h^2}$ is a "sufficient statistic" for making inferences about the frequencies and decay rates. The sufficient statistic is the mean-square projection of the data onto a set of orthonormal model functions and is given by

$$\overline{h^2} \equiv \frac{1}{m} \sum_{j=1}^{m} h_j^2, \qquad [3]$$

where h_j is the projection of the data onto one of the orthogonal model functions and is defined as

$$h_j \equiv \sum_{i=1}^{N} d_j H_j(t_i). \qquad [4]$$

The orthonormal model functions H_j are defined as

$$H_j(t) \equiv \lambda_j^{-1/2} \sum_{k=1}^{m} \mathbf{e}_{jk} G_k(t). \qquad [5]$$

The orthonormal model is given in terms of new amplitudes $\{A\}$ (linear combinations of $\{B\}$ in Eq. [1]),

$$f(t) = \sum_{j=1}^{m} A_j H_j(\{\omega, \alpha\}, t). \qquad [6]$$

The orthonormal model functions are constructed from the nonorthogonal model functions, Eq. [1], through the eigenvalues λ_j and eigenvectors $\mathbf{e}_{jk}$ of the real, symmetric, square matrix

$$g_{jk} \equiv \sum_{i=1}^{N} G_j(t_i) G_k(t_i) \qquad (1 \leqslant j \leqslant m), \qquad [7]$$

where $\{G\}$ is essentially the set of $2r + 1$ functions multiplying the amplitudes $\{B\}$ and the constant C in Eq. [1]. The method is called "Bayesian" because Eqs. [2]–[7] result from application of Bayes' theorem of probability theory (*9*).

Figure 1 illustrates the final time-domain result of applying Bayesian spectrum analysis to the ^{13}C–$\{^1H\}$ free induction decay (FID, 75.43 MHz) of an ASTM sample of 40% 1,4-dioxane and 60% benzene-d_6. [IUPAC NMR spectral reporting convention is followed throughout (*10*).] In Fig. 1A is shown an expanded partial portion of the experimentally obtained FID data. The posterior probability (Eq. [2]) for the model function (Eq. [1]) is then successively optimized (maximized) in terms of its parameter set (ω_j and α_j) for a successively greater number of resonance sinusoids (i.e., $r = 1, 2, 3 \cdots$) until a model is found that leaves no coherent characteristics in the residuals, or until any such coherent characteristics are reduced to a sufficiently small level. For the FID shown in Fig. 1A, only four sinusoid components ($r = 4$) were required to fit the data well. Figure 1B shows the resulting optimized model; the residuals are shown in Fig. 1C (note the change in scale).

Frequency-domain results of both discrete Fourier transformation and Bayesian spectrum analysis are compared in Fig. 2. In Fig. 2A the result of FT analysis of the initial 4096 complex time-domain data points is shown. A triplet arising from benzene-d_6 is found centered at 128.0 ppm and a singlet arising from 1,4-dioxane, at 67.2 ppm. If the same 4K complex time-domain data points are analyzed via Bayesian spectrum analysis and the optimized four-frequency decaying sinusoid model (*vide supra*) is Fourier transformed over the same time interval, the identical absorption spectrum results (Fig. 2B).

Of course, since the Bayesian spectrum analysis yields resonance frequencies ω_j, amplitudes $\{B\}$, and decay rate constants α_j directly, there is no reason to convolute

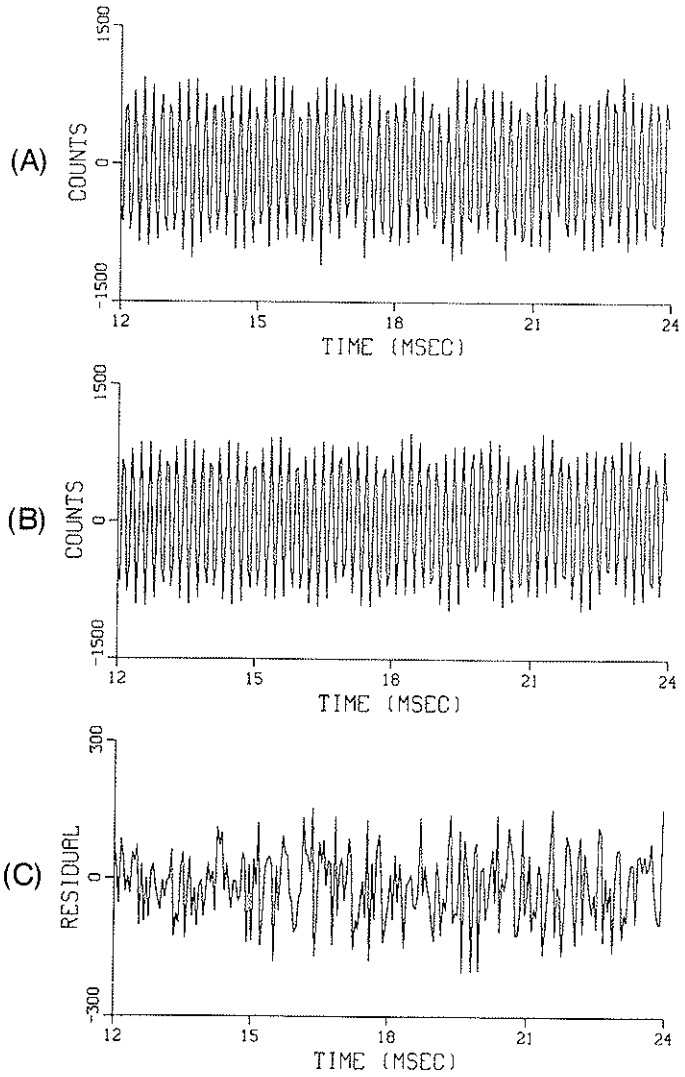

FIG. 1. (A) Expanded partial section (256 data points) of one channel of the $^{13}C-\{^{1}H\}$ free induction decay from a 40% 1,4-dioxane/60% benzene-d_6 sample. (B) The four-frequency, four-decay-rate model (Eq. [1], $r = 4$) resulting from Bayesian spectrum analysis expanded over the same time interval. (C) The residuals resulting from the difference between the real signal (A) and the optimized model (B).

these parameters through Fourier transformation, especially in cases of poor signal-to-noise and overlapping resonance lines. Furthermore, in many instances the resonance linewidth or time-domain decay-rate constant is of little fundamental interest as it typically is reflective of static magnetic field inhomogeneities. The line amplitude in the Bayesian analysis, $(B_j^2 + B_{j+r}^2)^{1/2}$, is equivalent to the integrated intensity in the Fourier presentation and its accurate measurement, along with that of ω_j, is of primary import in quantifying NMR spectra. These line amplitudes are plotted in

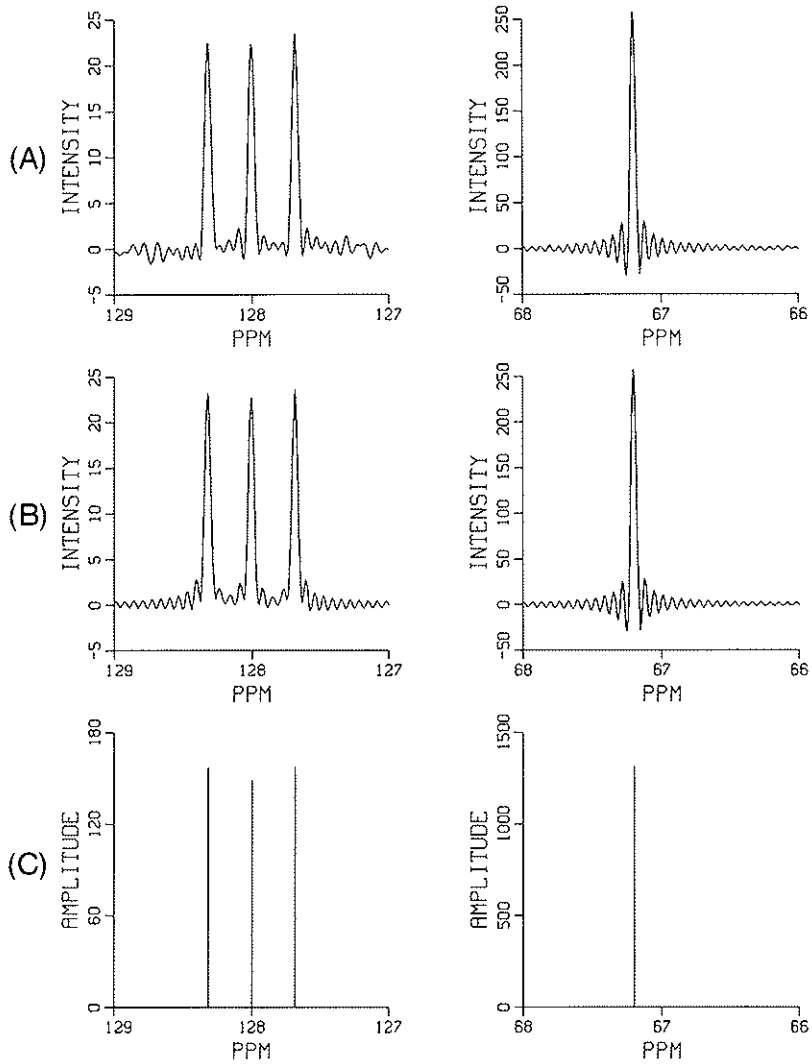

FIG. 2. (A) Expanded portions of the Fourier transformation (4096 complex points) of the free induction decay shown in Fig. 1A. A triplet, $J_{CD} = 24$ Hz, centered at 128.0 ppm, is found for benzene-d_6 and a singlet at 67.2 ppm for 1,4-dioxane. (B) An equivalent presentation of the Fourier transformation (over the same time interval) of the optimized four-frequency, four-decay-rate model shown in Fig. 1B resulting from Bayesian spectrum analysis. (C) The line spectrum of the Bayesian model. The model's parameters are plotted such that the line amplitudes, $(B_j^2 + B_{j+r}^2)^{1/2}$, which are equivalent to the integrated resonance areas in the absorption spectrum, are given as line height. Lines are positioned at each estimated ω_j with uncertainty approximately ±0.01 Hz (2 SD). Lineshapes (not resolved on this scale) are Gaussian with breadth indicative of the precision of the frequency estimates.

Fig. 2C for each resonance where the width of each line represents the uncertainty in frequency estimation, ±0.01 Hz (2 SD). Although determined more precisely than their Fourier counterparts, the resonance frequencies derived from Bayesian spec-

trum analysis of 4K complex time-domain points agree exactly with those from Fourier analysis on a Varian spectrometer within the limits imposed by the fast Fourier transformation of 16K points (after zero-filling to 48K, 0.8 Hz per point) and "Lorentzian" linewidths of about 1–4 Hz.

The above demonstration shows the consistency of the Fourier and Bayesian analyses when resonance frequencies are well separated relative to their decay-rate constants and signal-to-noise is substantial. However, the strength of probability analysis lies in its ability to provide reliable model parameter estimates under conditions of

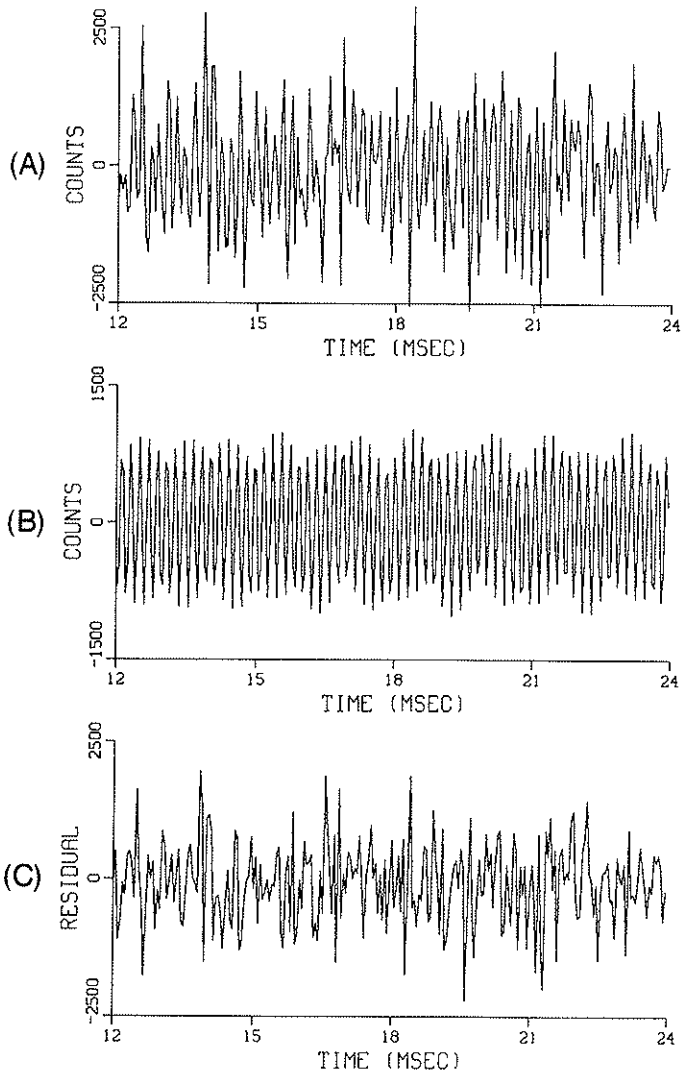

FIG. 3. Presentation equivalent to that of Fig. 1. White (Gaussian) noise has been added to the identical free induction decay described earlier to greatly reduce signal-to-noise.

limited signal "quality" (e.g., poor signal-to-noise, resonance frequency separations comparable to decay-rate constants, and data acquisition periods less than about $2\text{–}3T_2^*$). To demonstrate this, the same time-domain signal employed in Figs. 1 and 2 was mixed with white (Gaussian) noise to provide a simulated data set with the same spectral characteristics, but with greatly diminished signal-to-noise. Figure 3 shows a portion of this low signal-to-noise time-domain data. As before, both Fourier and Bayesian spectrum analyses were applied to this "new" time-domain data set. The results are shown in Figs. 3 and 4.

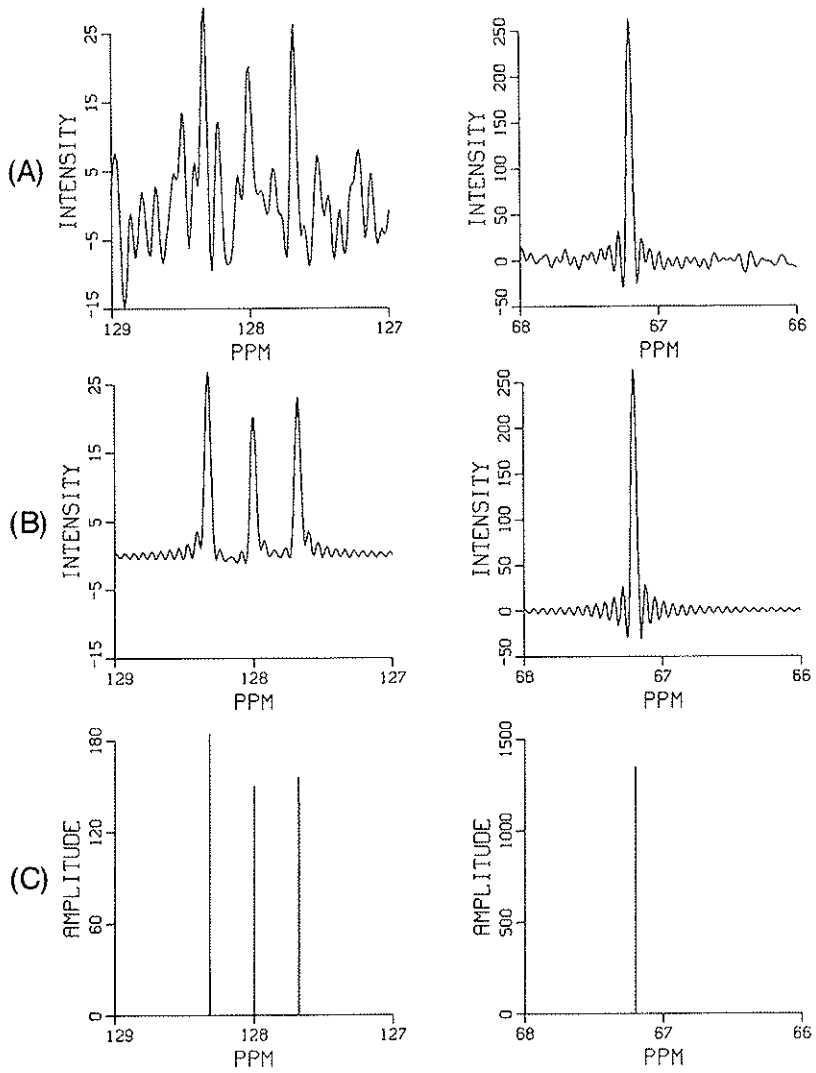

FIG. 4. Presentation equivalent to that of Fig. 2. The Fourier analysis of the "new" low signal-to-noise data is significantly compromised (A) while Bayesian analysis (B, C) yields results similar to those obtained with the previous high signal-to-noise data.

Analysis by discrete Fourier transform, Fig. 4A, yields evidence for the more intense singlet resonance of 1,4-dioxane while the triplet resonance due to benzene-d_6 is almost lost in the noise. Bayesian spectrum analysis, however, again finds four dominant frequencies and Fourier transformation of the resulting model (Fig. 3B) yields the absorption spectrum shown in Fig. 4B. This spectrum appears equivalent to those seen in Fig. 2A or 2B. Actually, because of the decreased signal-to-noise, the parameter estimates are less precise by a factor directly related to the change in signal-to-noise, but negligibly so compared to the washout of the Fourier analysis. The line amplitudes are plotted in Fig. 4C and are similar to those found with greater signal-to-noise (Fig. 2C).

As with other time-domain analysis alternatives to the Fourier transformation, the price for improved spectral quantification is computation time and assumption of an accurate (reasonable) model. The Bayesian analysis presented herein used software with which no real effort at efficiency optimization has yet been made; computation times were on the order of one CPU hour on a DEC VAX 11/780. We speculate that by incorporating more efficient search routines and operating-system-specific software commands, the computation time could be reduced to a few minutes. Computation time is expected to grow approximately as the square of the number of resonance sinusoids in the model function. Given the substantial improvement in spectral analysis and the ever increasing power of research computers, this does not appear to be an impediment to widespread use.

ACKNOWLEDGMENTS

Helpful discussions with Edwin T. Jaynes are gratefully acknowledged as is the assistance of the Washington University High Resolution NMR Service Facility sponsored in part by NIH BRS Shared Instrument Grant RR-02004 and a gift from the Monsanto Company. This work was supported by a gift from Nabisco Brands, Inc., and NIH Grant GM-30331.

REFERENCES

1. I. J. LOWE AND R. E. NORBERG, *Phys. Rev.* **107,** 46 (1957).
2. R. R. ERNST AND W. A. ANDERSON, *Rev. Sci. Instrum.* **37,** 93 (1966).
3. J. W. COOLEY AND J. W. TUKEY, *Math. Comput.* **19,** 297 (1965).
4. J. C. LINDON AND A. G. FERRIGE, *Prog. NMR Spectrosc.* **14,** 27 (1980).
5. S. L. MARPLE, JR., "Digital Spectral Analysis with Applications," Prentice–Hall, Inc., Englewood Cliffs, New Jersey, 1987.
6. G. L. BRETTHORST, "Bayesian Spectrum Analysis and Parameter Estimation," Ph.D. thesis, Department of Physics, Washington University, St. Louis, Missouri, August, 1987.
7. E. T. JAYNES, *in* "Maximum-Energy and Bayesian Spectral Analysis and Estimation Problems," (C. R. Smith and G. J. Erickson, Eds.), p. 1, Reidel, Dordrecht, Holland, 1987.
8. G. L. BRETTHORST, "Bayesian Spectrum Analysis and Parameter Estimation," Springer-Verlag, New York, in preparation.
9. J. H. JUSTICE, (Ed.), "Maximum Entropy and Bayesian Methods in Applied Statistics," Cambridge Univ. Press, London/New York, 1986.
10. IUPAC Recommendations on NMR Spectra, *Pure. Appl. Chem.* **45,** 219 (1976).