Efficient Method to Analyze NMR Spectra of Solutes in Liquid Crystals: The Use of Genetic Algorithm and Integral Curves

Hiroshi Takeuchi,* Kaori Inoue, Yuta Ando, and Shigehiro Konaka
Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo 060-0810

(Received August 4, 2000; CL-000752)

A new approach is proposed for the analysis of complex NMR spectra of solutes in liquid crystals. In the analysis, NMR spectra are transformed to integral curves and spectral parameters are refined by means of genetic algorithm. The ^{1}H-NMR spectra of ethanol, *trans*-azobenzene and tolan in ZLI 1132 were successfully analyzed by this method.

NMR spectroscopy of molecules dissolved in liquid-crystal solvents provides valuable information on structures, conformations and orientational order parameters.[1] To derive the information, spectral parameters, chemical shifts and dipolar coupling constants, must be determined after assigning observed spectral lines to calculated ones. However, the assignment is a formidable task for many spin systems because it needs approximate parameter values, which are not easily estimated from complex NMR spectra.[2–5] A few experimental methods have been reported to simplify complicated spectra.[2] On the other hand, automatic analyses which need no assignment have been proposed, where spectral intensities and frequencies are used to determine spectral parameters.[3–5] However, false solutions are often found when spectral parameters are determined by least-squares calculations.

In the present study, an efficient method is proposed for automatic analysis. It differs from the previous methods[3–5] in the following respects. (1) NMR spectra are transformed to integral curves. (2) Spectral parameters are determined by means of genetic algorithm (GA).[6]

To illustrate the merit to use integral curves, we show synthetic spectra in Figure 1A. *R* values[7] were calculated by varying the chemical shift of the theoretical spectrum. The result derived from spectra shows four local minima and one global minimum on the curve of *R* value (see a solid curve in Figure 1B). However, four local minima disappear when integral curves are used. The use of integral curves generally reduces the number of local minima without affecting the position of a global minimum.

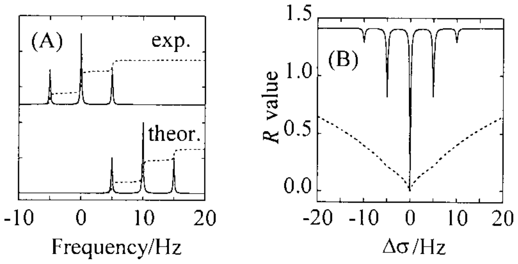

Figure 1. (A) Experimental and theoretical NMR spectra composed of the triplet with a coupling constant of 5 Hz. The dotted curves are integral ones. (B) A comparison of the *R* values obtained for the spectra (-) and integral curves (…): Δσ denotes the difference between chemical shifts of experimental and theoretical spectra.

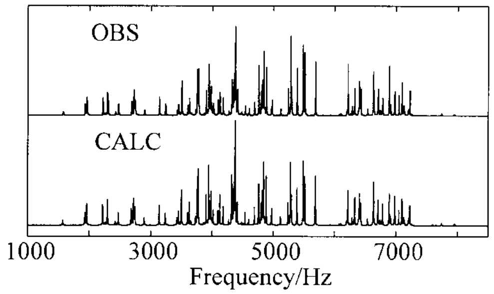

Figure 2. Observed and calculated ^{1}H-NMR spectra of ethanol dissolved in ZLI 1132. The observed spectrum has been corrected for the background due to ZLI 1132.

In the case of ethanol described below, the least-squares analysis of integral curves gives a false minimum because the spectrum is complicated as shown in Figure 2. In the present study, we have found that GA[6] for real parameter optimization is efficient to search an approximate solution close to a global minimum.

The procedure adopted in the analysis is as follows:
1) A run starts with *n* sets of spectral parameters, where *n* is a predetermined number. The reasonable ranges of spectral parameters are set and parameter values are chosen at random within the ranges. 2) Spectral parameters are used to calculate spectra, integral curves and *R* values for integral curves. 3) Two sets are chosen at random. The set with smaller *R* value is selected for the next step. This is repeated *n* times to select *n* sets of parameters. 4) From the sets of the parameters selected in step 3, new sets of the parameters are produced by the operation of one-point crossover and mutation.[6] 5) A run stops when steps 2 to 4 are repeated T_{max} times. T_{max} is the maximum number of generation. The parameters used in GA[6] are as follows: crossover rate; 0.8 (50% linear crossover and 50% real crossover), mutation rate; 0.3, mutation size; 0.1. In spectral analysis, a few runs were performed with different random numbers.

The method was applied to the analysis of a ^{1}H-NMR spectrum of ethanol in ZLI 1132 (see Figure 2).[8] This molecule was selected because the analysis was reported to be difficult.[9]

At first, chemical shifts σ_i and order parameters $S_{\alpha\beta}$ were refined by GA to estimate initial values of dipolar coupling constants. The numbers of *n* and T_{max} were arbitrarily set to 40 and 200, respectively. The structural parameters of *trans*-ethanol were taken from the r_s structure.[10] The existence of *gauche* form was not taken into account in this stage of analysis. The ranges of the parameters were: 2800 Hz $\leq \sigma_i \leq$ 6800 Hz and

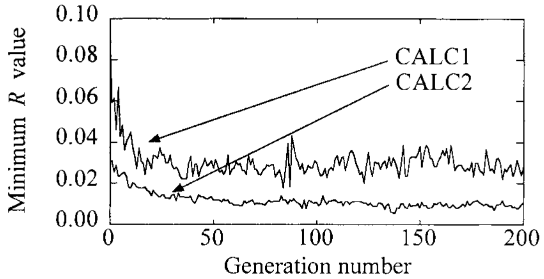

Figure 3. The results of analysis for ethanol. The minimum R value in each generation is plotted against the generation number. See text for CALC1 and CALC2.

$-0.2 \le S_{\alpha\beta} \le 0.2$. The minimum R value, 0.018, was obtained at the generation number of 84 in a run, CALC1. The result is shown in Figure 3.

In the second stage of analysis, chemical shifts and dipolar coupling constants were refined by GA. The range of the i-th parameter P_i was restricted to be: $(P_{i,\mathrm{CALC1}} - 200)$ Hz $\le P_i \le$ $(P_{i,\mathrm{CALC1}} + 200)$ Hz, where $P_{i,\mathrm{CALC1}}$ denotes the value obtained by CALC1. Figure 3 shows the best result as CALC2. The minimum R value in CALC2, 0.0055, was obtained at the generation number of 138. The calculated spectrum was similar to the experimental one and many transitions could be assigned.

The relative errors of transition intensities are larger than those of transition frequencies.[3,11] Therefore, in the final stage of analysis, spectral parameters were determined by the conventional method, i.e., least-squares calculations on frequencies.[1] The calculated spectrum is shown in Figure 2. The R value, 0.0042, obtained finally is smaller than that in CALC2. The final parameter values agree with those obtained in CALC2 within 13 Hz.[12]

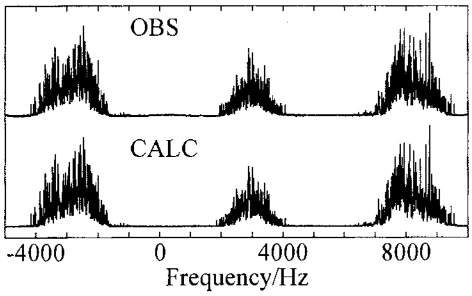

Figure 4. Observed and calculated ^{1}H-NMR spectra of tolan dissolved in ZLI 1132. The observed spectrum has been corrected for the background due to ZLI 1132.

The spectral analyses of 10-spin systems, *trans*-azobenzene (Ph–N=N–Ph) and tolan (Ph–C≡C–Ph), in ZLI 1132 were also carried out.[13] The spectral parameters obtained by GA were further refined by the conventional method. Figure 4 shows good agreement between the observed and calculated spectra of tolan.

The procedure proposed in the present study enables us to analyze complex NMR spectra of solutes in liquid crystals automatically and quickly. This is applicable to NMR spectra of molecules in isotropic solvents.[3a,4b]

References and Notes

1 J. W. Emsley and J. C. Lindon, "NMR Spectroscopy Using Liquid Crystal Solvents," Pergamon, New York (1975).

2 M. Longeri and G. Celebre, in "Encyclopedia of Nuclear Magnetic Resonance," ed. by D. M. Grant and R. K. Harris, John Wiley & Sons, Chichester (1996), p. 2774.

3 a) P. Diehl, S. Sýkora, and J. Vogt, *J. Magn. Reson.*, **19**, 67 (1975). b) P. Diehl and J. Vogt, *Org. Magn. Reson.*, **8**, 638 (1976).

4 a) D. S. Stephenson and G. Binsch, *J. Magn. Reson.*, **37**, 395 (1980). b) D. S. Stephenson and G. Binsch, *J. Magn. Reson.*, **37**, 409 (1980). c) D. S. Stephenson and G. Binsch, *Org. Magn. Reson.*, **14**, 226 (1980).

5 a) G. Celebre, F. Castiglione, M. Longeri, and J. W. Emsley, *J. Magn. Reson. A*, **121**, 139 (1996). b) F. Castiglione, G. Celebre, G. De Luca, and M. Longeri, *J. Magn. Reson.*, **142**, 216 (2000).

6 A. H. Wright, in "Foundations of Genetic Algorithms," ed. by G. J. E. Rawlins, Morgan Kaufmann, San Mateo (1991), p. 205.

7 R value is defined by $\{\Sigma_i(I_i^{\mathrm{obs}} - I_i^{\mathrm{calc}})^2/\Sigma_i(I_i^{\mathrm{obs}})^2\}^{1/2}$ where I_i denotes the intensity at a point i.

8 The sample was dissolved at 25 mol% in nematic liquid crystal Merck ZLI 1132. A ^{1}H-NMR spectrum was recorded on a JNM EX400 spectrometer at 25 °C.

9 J. W. Emsley, J. C. Lindon, and J. Tabony, *Mol. Phys.*, **26**, 1485 (1973). They recorded the ^{1}H-NMR spectra of ethanol in EBBA and reported that the success of the analysis is achieved only by measuring the spectra of partially deuterated samples. These ^{1}H-NMR spectra are quite different from those measured in the present study, indicating that it is difficult to estimate spectral parameters of ethanol in ZLI 1132 from their results.

10 J. H. Callomon, E. Hirota, K. Kuchitsu, W. J. Lafferty, A. G. Maki, and C. S. Pote, in "Landolt–Börnstein," ed. by K. -H. Hellwege and A. M. Hellwege, Springer Verlag, Berlin (1976), New Series, Group II, Vol. 7, p. 203.

11 A. E. Derome, "Modern NMR Techniques for Chemistry Research," Pergamon, Oxford (1987), Chap. 7.

12 The final values of chemical shifts and dipolar coupling constants (in Hz) are: σ_{CH3} = 4526.15(7), σ_{CH2} = 5536.55(10), σ_{OH} = 4215.91(13), D_{CH3} = 664.00(4), $D_{\mathrm{CH3,CH2}}$ = −232.89(3), $D_{\mathrm{CH3,OH}}$ = −201.66(5), D_{CH2} = 642.46(13) and $D_{\mathrm{CH2,OH}}$ = −72.86(7). The values of the corresponding parameters obtained by CALC1 are 4618, 5467, 4206, 684, −211, −165, 647 and −162 Hz, respectively. The values from CALC2 are 4532, 5549, 4218, 658, −230, −198, 649 and −74 Hz, respectively.

13 K. Inoue, Doctoral Thesis, Hokkaido University, Sapporo, 2000.