

Simplification of ^{19}F NMR Spectra of Liquid Crystalline Samples by Multiple-Pulse COSY Experiments

Philippe Lesot,^{*,1} James W. Emsley,^{*} Jean-Michel Ouvrard,[†] and Eirian Curzon[‡]

^{*}Department of Chemistry, University of Southampton, Southampton, SO17 1BJ, United Kingdom; [†]Laboratoire de Chimie Structurale Organique, URA no. 1384, Université de Paris-sud, 91405 Orsay Cedex, France; and

[‡]Bruker Spectrospin, Banner Lane, Coventry, CV4 9GH, United Kingdom

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A general method is presented of converting second-order fluorine-19 spectra of liquid crystalline samples into first-order spectra. This is achieved by recording a ^{19}F COSY spectrum with a multiple pulse dipolar reducing sequence (MPS) operating in the t_1 period, leading to a F_1 projection which is first order. The method is illustrated by recording spectra on a sample of 1,3-dichloro-4-fluorobenzene dissolved in the nematic solvent ZLI 1167. Experiments have been done in which the MPS is either the MREV-8 or Flip-Flop-16 sequence. The first-order F_1 projections are analyzed to give reduced total ^1H - ^{19}F couplings, $K_{CS}T_{ij}^{\text{HF}}$ and the reduction factors, K_{CS} , are obtained by comparison with the T_{ij}^{HF} available from an analysis of the ordinary 1D spectrum. The reduction factors are compared with values predicted by average Hamiltonian theory (AHT). The reasons for the differences found between observed and predicted values of K_{CS} have been investigated by performing numerical simulations of the 2D MPS COSY experiments. © 1998 Academic Press

Key Words: liquid crystalline samples; NMR; average Hamiltonian theory; heteronuclear total spin-spin coupling; multiple pulse sequence; and reduction factor.

INTRODUCTION

The NMR spectra of liquid crystal samples are a rich source of information on the structure, conformation, and orientational order of molecules, but the data are often inaccessible because the spectra defy analysis. The development of methods for simplifying such spectra, therefore, is a central task in order to apply NMR usefully to these samples. The spectra of molecules containing a single group of chemically equivalent ^{19}F nuclei in the presence of several protons should be easier to analyze than the same spin system but containing only protons since the ^{19}F spectrum is observed separately from the complex proton spectrum. However, even with this simplification the spectra may still be difficult, or impossible, to analyze. The main reason for the complexity of the ^{19}F spectrum in these spin systems is that the protons are usually strongly coupled to each other, thus giving a second-order ^{19}F spectrum. The ^{19}F spectrum can, in principle, be simplified by proton decoupling,

but this removes the ^1H - ^{19}F dipolar couplings, whose measurement is the main objective of the spectral analysis. The only methods advanced to date to simplify these ^{19}F NMR spectra is to partially deuterate the molecule, followed by deuterium decoupling. This method works very well, but the deuteration can be chemically difficult to perform. Another possibility would be to rotate the liquid crystalline sample about an axis which makes an angle θ with the magnetic field (I). This reduces all the dipolar couplings by the factor $(3 \cos^2\theta - 1)/2$, which may lead to the fluorine spectrum becoming first order. However, this method is restricted to nematic samples and requires a special probe (I).

We present here a more general method for reducing second-order ^{19}F spectra to first-order spectra, which are then easily analyzed to give the ^1H - ^{19}F total spin-spin couplings T_{ij}^{HF} . The method uses multiple-pulse sequences (MPS) and is analogous to those which have been used to simplify ^{13}C spectra in order to extract ^1H - ^{13}C dipolar couplings, i.e., separated local field spectroscopy, and for the case of ^{19}F coupled to ^1H consists of the class of experiments illustrated in Fig. 1a (2–4).

The MPS is a multiple-pulse sequence applied to the protons which effectively removes the interproton dipolar interaction term from the total spin Hamiltonian, \mathcal{H} , acting during t_1 . Thus, \mathcal{H}_{tot} changes to being an effective average Hamiltonian at zero order, $\mathcal{H}_{\text{eff}}^{(0)}$, of the form (5)

$$\bar{\mathcal{H}}_{\text{eff}}^{(0)} = K_{CS}(\mathcal{H}_{ZI} + \mathcal{H}_{TIS}) + K_D\mathcal{H}_{DII} + \mathcal{H}_{III} + \mathcal{H}_{ZS} + \mathcal{H}_{TSS}. \quad [1]$$

\mathcal{H}_{ZI} and \mathcal{H}_{ZS} are the Zeeman interaction terms for the unobserved (protons) and observed (fluorine) nuclei; thus

$$\mathcal{H}_{ZI} = -\sum_i \nu_i^p I_{iz} \quad [2]$$

$$\mathcal{H}_{ZS} = -\sum_i \nu_i^s S_{iz} \quad [3]$$

where I_{iz} and S_{iz} are the components of the nuclear spin angular momentum operators along the direction of the applied magnetic field for the unobserved and observed nuclei, respec-

¹ Present address: Laboratoire de Chimie Structurale Organique, URA no. 1384, Université de Paris-sud, 91405 Orsay Cedex, France.

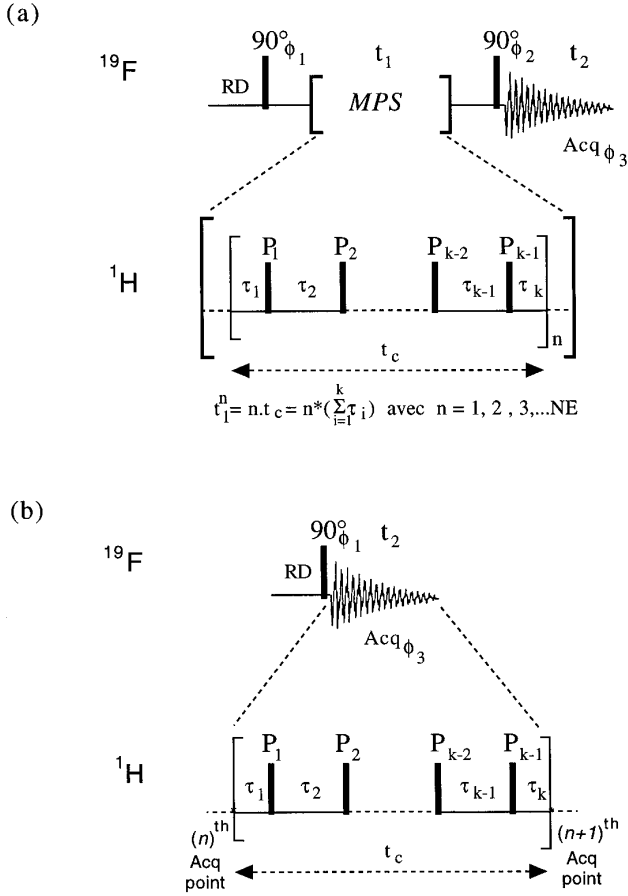


FIG. 1. The multiple pulse COSY experiment with the multiple pulse sequence applied during t_1 (a) and t_2 (b).

tively. In Eq. [1], \mathcal{H}_{TIS} and \mathcal{H}_{TSS} are the total, spin-spin coupling terms,

$$\mathcal{H}_{TIS} = \sum_{i < j} T_{ij}^{IS} I_{iz} S_{jz} \quad [4]$$

$$\mathcal{H}_{TSS} = \sum_{i < j} T_{ij}^{SS} S_{iz} S_{jz} + 1/2 (J_{ij}^{SS} - D_{ij}^{SS}) (S_i^+ S_j^- + S_i^- S_j^+), \quad [5]$$

where

$$T_{ij} = 2D_{ij} + J_{ij}, \quad [6]$$

D_{ij} and J_{ij} being the direct and the indirect spin-spin coupling constants, respectively. The two remaining terms in Eq. [1], \mathcal{H}_{DII} and \mathcal{H}_{III} , are

$$\mathcal{H}_{DII} = \sum_{i < j} D_{ij}^{II} [I_{iz} J_{jz} - 1/2 (I_i^+ I_j^- + I_i^- I_j^+)] \quad [7]$$

and

$$\mathcal{H}_{III} = \sum_{i < j} J_{ij}^{II} [I_{iz} J_{jz} + 1/2 (I_i^+ I_j^- + I_i^- I_j^+)]. \quad [8]$$

Finally, the reduction factors K_{CS} and K_D depend on the particular MPS scheme applied to the protons.

We shall demonstrate in this paper the effectiveness of two multiple-pulse sequences, the MREV-8 and Flip-Flop-16 (FF-16) sequence. MREV-8 is a well-known sequence designed for use with solid samples; it employs 90° pulses, as shown in Fig. 2a, and for ideal, infinitely short pulses is predicted by average Hamiltonian theory (AHT) when taken to first order to have $K_D = 0$ and $K_{CS} = 0.471$ (6, 7). Flip-Flop-16 is a MPS introduced recently and was specifically designed to be used with liquid crystalline samples (8, 9). This sequence, which is shown in Fig. 2b, has the particular advantage that K_{CS} and K_D can be adjusted by a suitable choice of the pulse flip angle, α , and the pulse intervals, τ_λ and τ_η .

For monofluorinated molecules, the normal 1D ^{19}F spectrum of a liquid crystalline sample is second order primarily because the D_{ij}^{HH} are large compared with $\Delta\nu_{ij}^H$, the proton chemical shift differences. The scalar couplings J_{ij}^{HH} are also much smaller than D_{ij}^{HH} , and they may be anywhere in the range $\Delta\nu_{ij}^H < J_{ij}^{HH} \ll D_{ij}^{HH}$ or $\Delta\nu_{ij}^H > J_{ij}^{HH} \ll D_{ij}^{HH}$.

The point of using either MREV-8 or FF-16 in a heteronuclear experiment is that when $K_D = 0$ the fluorine reduced spectrum is certainly first order when $\Delta\nu_{ij}^H \gg J_{ij}^{HH}$. In practice, this spectrum may also be first order for $\Delta\nu_{ij}^H \approx J_{ij}^{HH}$ because the effect on the proton spectrum of spin coupling to fluorine is to change the effective chemical shifts difference to

$$\Delta\nu_{ij}^{\text{eff}} = \Delta\nu_{ij}^H + K_{CS} m_{^{19}\text{F}} (T_{i^{19}\text{F}}^{\text{HF}} - T_{j^{19}\text{F}}^{\text{HF}}), \quad [9]$$

where $m_{^{19}\text{F}} (\pm 1/2)$ is the magnetic quantum number of the ^{19}F nucleus. The total spin-spin coupling constants are usually such that

$$K_{CS} m_{^{19}\text{F}} (T_{i^{19}\text{F}}^{\text{HF}} - T_{j^{19}\text{F}}^{\text{HF}}) \gg \Delta\nu_{ij}^{\text{eff}} \quad [10]$$

when $\Delta\nu_{ij}^H \approx J_{ij}^{HH}$.

In principle the 1D NMR experiment shown in Fig. 1b should produce a first-order ^{19}F spectrum. In practice this experiment is more sensitive to imperfections in the pulses and the interval timings, and is more difficult to implement for a ^{19}F - ^1H experiment. Consequently, it is advantageous to introduce the MPS during the t_1 period of a COSY experiment as presented in Fig. 1a (8, 9).

The reason for using a 2D MPS COSY experiment is to obtain the scaled couplings $K_{CS} T_{ij}^{IS}$, and from them to obtain T_{ij}^{IS} . To do this it is necessary to know K_{CS} , which will be possible if it is a characteristic property of the MPS sequence and does not depend on the particular spin system being studied. In practice, even if this criterion is satisfied there will be imperfections in the MPS sequence which may lead to K_{CS} being different from that predicted by theory. To test whether

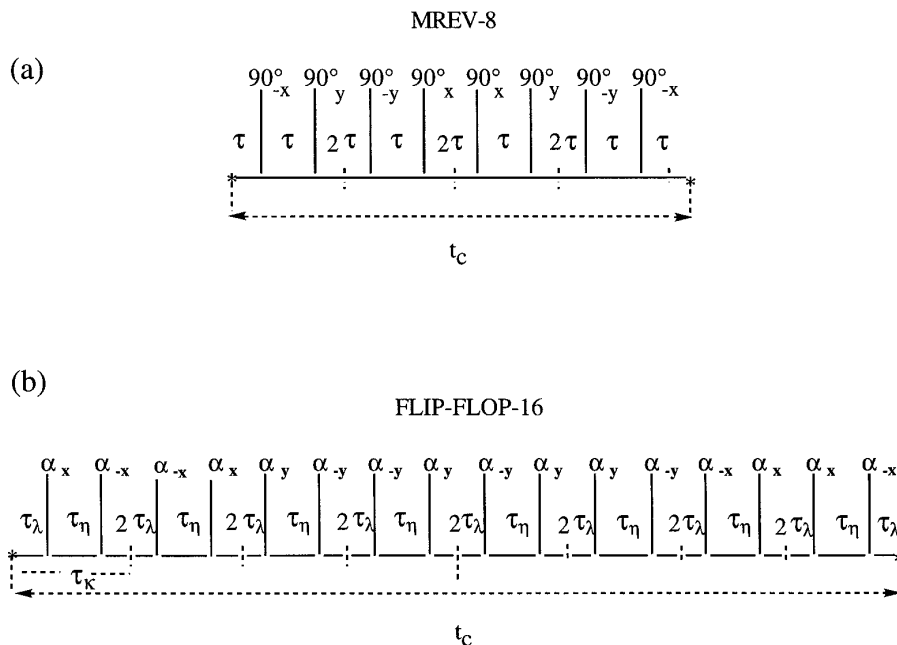


FIG. 2. The MREV-8 (a) and the FF-16 (b) multiple-pulse sequences; α is the pulse angle and τ is the interpulse spacings.

the T_{ij}^{IS} can be obtained by the 2D MPS-COSY heteronuclear experiment we have applied this method to the case of a solute dissolved in a liquid crystalline solvent. The 1D spectrum of this solute was chosen such that it has a spectrum which could be easily analyzed to give all the NMR parameters so that the values of $K_{CS}T_{ij}^{HF}$ obtained from the 2D experiment can be compared with the measured values of T_{ij}^{HF} , and experimental values of K_{CS} derived. These can then be compared with values of K_{CS} predicted by average Hamiltonian theory for ideal MPS. Possible reasons for the differences found between observed and predicted values of K_{CS} have been explored by performing numerical simulations of the 2D MPS COSY heteronuclear experiments.

EXPERIMENTAL

The solute, 1,3-dichloro-4-fluorobenzene (DCFB), was purchased from the Aldrich Chemical Company, and the liquid crystalline solvent, ZLI 1167, from Merck, Ltd. Note that ZLI 1167 has a negative anisotropy of the magnetic susceptibility and so the liquid crystal directors align uniformly in the plane perpendicular to the applied magnetic field. The spectra were recorded on a sample contained in a 5-mm-o.d. tube with a Bruker DRX 400 spectrometer equipped with a X-QNP output switch box. The probe (QNP probe) was double tuned to ^1H and ^{19}F , and the 90° pulse widths were $15.7 \mu\text{s}$ for ^{19}F and $13.5 \mu\text{s}$ for ^1H . The time to switch the transmitter output between 376.45 and 400.13 MHz, the two resonance frequencies, was $20 \mu\text{s}$. The spectra were recorded with sample spinning at 40 Hz, the temperature was controlled at 310 K, and there was no field-frequency lock. A recycle delay of 3 s was used. This is

required because the MPS sequences have duty cycles of the order of 50% and so can produce sufficient sample heating to broaden the lines unless a delay between cycles is used which allows sample cooling to occur. The t_1 period must be incremented in steps of t_c , the total duration of the MPS cycle, which therefore sets the spectral width in F_1 . The number of increments in t_1 used was 256. The signal was acquired into 2 k of computer memory, and 16 free induction decays were added for each t_1 increment. Note that the phases in the MPS are those shown in Fig. 2. The normal phase cycling of the COSY sequence was used (10). The spectral appearance of the F_1 projection was improved by applying a forward linear prediction algorithm to the data in the t_1 domain. The t_1 domain was zero-filled to 1 k of data points, giving a final 2D matrix before Fourier transforming of $1 \text{ k} \times 2 \text{ k}$.

RESULTS AND DISCUSSION

Figure 3 presents the ^1H and ^{19}F 1D spectra of the sample of DCFB dissolved in ZLI 1167, which were analyzed using the PANIC program (11) to yield the data in Table 1. The absolute signs of the dipolar couplings have been chosen on the basis of the expected orientational order in ZLI 1167 of a substituted benzene. The scalar couplings were obtained by analysis of the ^1H spectrum of a sample dissolved in chloroform. Under these conditions, the root mean square error (rms) of the fit was 0.2 Hz.

MREV-8 as the Multiple Pulse Sequence

The experimental 2D MREV-8 COSY spectrum is presented in Fig. 4a, and this shows a second-order spectrum in F_2 , but

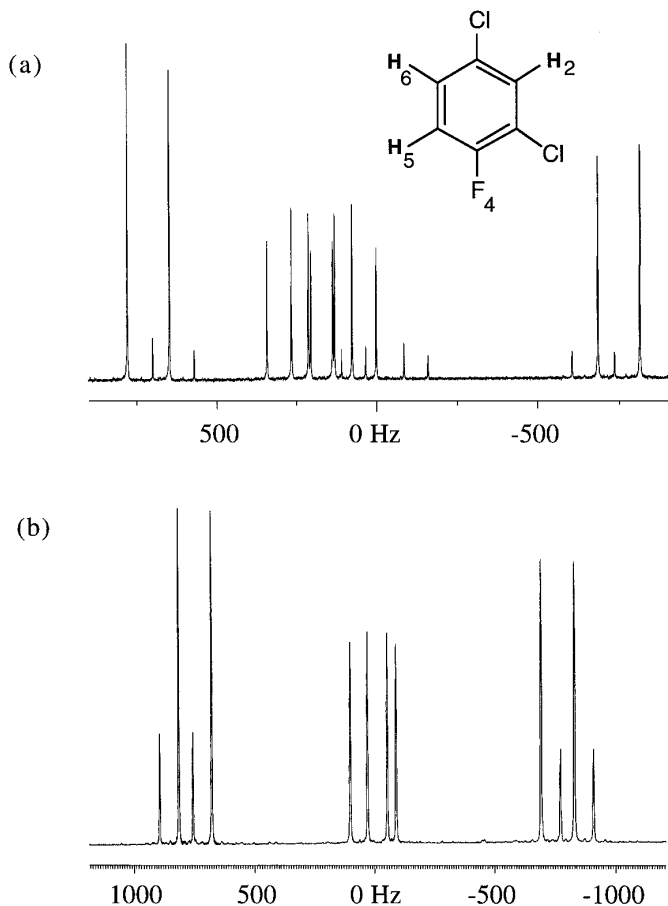


FIG. 3. The 400.13-MHz proton spectrum (a) and the 376.45-MHz fluorine spectrum (b) of a sample of 1,3-dichloro-4-fluorobenzene dissolved in the nematic solvent ZLI 1167 at 310 K.

a first-order one in F_1 , except for some low intensity lines in the center.

Analysis of the eight strong lines in F_1 as a first-order spectrum gives the reduced values of T_{ij}^{HF} , denoted hereafter $(T_{ij}^{\text{HF}})^{\text{red}}$, shown in Table 2, which are compared with the data listed in Table 1 to yield experimental values of the

reduction factors K_{CS} . A MREV-8 sequence with pulses of negligible duration compared with the interpulse spacings, and producing exact 90° rotations for all the protons, is predicted from average Hamiltonian theory to have $K_{CS} = 0.471$ for all the couplings (7). Experimentally, when the pulse widths, t_w , are not negligible, the K_{CS} scaling factor of the experiment is given by (6)

$$K_{CS} = \frac{\sqrt{2}}{3} \left[1 + \frac{t_w}{2\tau'} \left(\frac{4}{\pi} - 1 \right) \right], \quad [11]$$

where τ' is the time between the beginning of the first and the second pulse ($\tau' = \tau + t_w$).

The value predicted by Eq. [11] in the present case is 0.493. The experiment, however, finds a variation in the K_{CS} for the three couplings, with the value obtained from T_{46}^{HF} being in closest agreement with theory (4% too small), and those derived from T_{24}^{HF} and T_{45}^{HF} being worse (11 and 8% too small). The agreement between the observed and ideal F_1 projection is therefore good but not perfect. The imperfections are the presence of the small peaks in the center of the observed spectrum, and the variation in the values of K_{CS} . These imperfections could arise because in the real experiment the nuclei do not experience exact 90° pulses because of the presence of small chemical shifts (offset effects) and pulse errors (phase errors and amplitude variations during the pulse) (10). Thus, the most important effects of nonperfect pulses are to render the symmetric cycle of the multiple pulse sequence nonsymmetric and to destroy the cyclic property of the MPS (10). Furthermore, there could be a more general reason for the imperfections in that MREV-8, even with perfect pulses, does not completely eliminate higher order terms in the average Hamiltonian (6).

To test these possibilities we have simulated the effect of the 2D MREV-8 COSY experiment on the DCFB spin system with the NMR parameters set at their experimental values. The simulation was carried out with the program NMRSIM, which allows for the finite lengths and B_1 amplitude of the pulses, and

TABLE 1
Spectral Parameters and Total Spin-Spin Couplings of DCFB Dissolved in ZLI 1167
Obtained by Analysis of the 1D Spectra Reported in Fig. 3

| ^1H Chemical shifts in Hz | | Scalar and dipolar couplings in Hz | | | Total couplings in Hz | |
|------------------------------------|--------------------|------------------------------------|---------------|-----------------|-----------------------|----------------------|
| i | ν_i^{H} | i, j | J_{ij}^a | D_{ij} | T_{ij}^{HH} | T_{ij}^{HF} |
| 2 | 86.1 ± 0.2 | 2, 4 | 6.3 ± 0.1 | 65.0 ± 0.2 | | |
| 5 | -14.9 ± 0.2 | 2, 5 | 0.0 ± 0.1 | 29.9 ± 0.3 | 59.8 ± 0.6 | |
| 6 | 0.0 ± 0.2 | 2, 6 | 2.6 ± 0.1 | 73.6 ± 0.2 | 149.8 ± 0.5 | |
| | | 4, 5 | 8.6 ± 0.1 | 608.4 ± 0.2 | | 1225.4 ± 0.5 |
| | | 4, 6 | 4.1 ± 0.1 | 135.5 ± 0.3 | | 275.1 ± 0.7 |
| | | 5, 6 | 8.7 ± 0.1 | 685.6 ± 0.2 | 1379.9 ± 0.5 | |

^a Values were obtained from analysis of the spectrum of a sample dissolved in chloroform and kept fixed in the analysis.

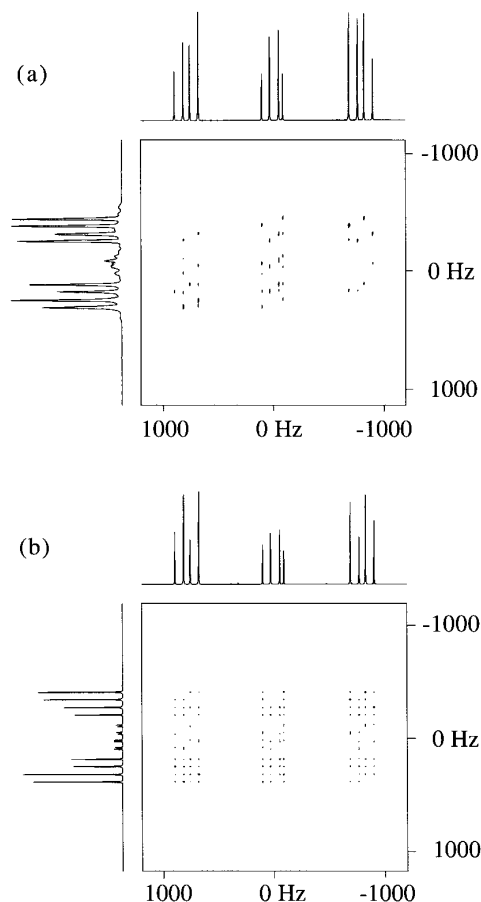


FIG. 4. The 376.45-MHz ^{19}F MREV-8 COSY spectrum (magnitude mode) of DCFB dissolved in ZLI 1167. (a) Experimental spectrum recorded at 310 K with $\tau = 25.8 \mu\text{s}$ and $t_w = 13.5 \mu\text{s}$. (b) Simulated spectrum using the NMRSIM program.

the result is shown in Fig. 4b (13). The F_1 projection of this simulated spectrum is in agreement with experiment in having weak center peaks, which are not, therefore, caused by imperfections in the phases of the pulses or in the homogeneity of the B_1 field. Moreover, these peaks remain when the simulation is repeated but with the J_{ij}^{HH} all set to zero, and so they do not stem from residual second-order effects specific to the present sample. They probably arise from nonzero higher order terms in the average Hamiltonian.

In Table 2 we give also the result of analyzing the eight strong lines in the F_1 projection shown in Fig. 4b as a first-order spin system. The reduction factors K_{CS} are then obtained in the same way as for the experimental spectrum, and these are also given in Table 2. Now the reduction factors obtained from the three couplings are identical within 1.5% and are in good agreement with the value predicted by Eq. [11]. It is probable, therefore, that the deviation of the observed K_{CS} from the value predicted by Eq. [11] is a consequence of using nonideal pulses and phases. We can conclude that the F_1 projection produced by a 2D MREV-8 COSY experiment is a very good approximation of that expected of a first-order spin

system and can be used to obtain values of T_{ij}^{HF} with an average precision of about 8%. This is ample precision to be able to predict good starting values for an analysis of the 1D second-order proton and fluorine spectra.

The FF-16 Sequence

The two reduction factors produced by the FF-16 sequence in the 2D experiment shown in Fig. 2b, if the pulse widths are assumed to be negligible, are predicted by average Hamiltonian theory taken to zeroth order to be (8, 14)

$$K_{CS} = \frac{2\tau_\lambda + \tau_\eta \cos \alpha}{2\tau_\lambda + \tau_\eta} \quad [12]$$

and

$$K_D = 1 - \frac{3}{2} \left(\frac{\tau_\eta \sin^2 \alpha}{2\tau_\lambda + \tau_\eta} \right). \quad [13]$$

The dependence of K_D and K_{CS} on the pulse intervals and the flip angle α allows different combinations of these two reduction factors to be obtained (8, 9). It has been shown that K_D and K_{CS} vary with the pulse angle, α , and the timing ratio, $R = \tau_\eta / (2\tau_\lambda + \tau_\eta)$, assuming instantaneous ideal pulses (8).

A 2D FF-16 COSY experiment on DCFB with $\alpha = 90^\circ$ and a timing ratio $R = 2/3$ was performed, and the result is shown in Fig. 5a. The F_1 projection comprises the eight lines with the regular spacings expected for a first-order spin system, with only very weak extra lines. Analysis of the spectrum as a first-order system gives the values of $(T_{ij}^{\text{HF}})^{\text{red}}$ shown in Table 3, which also lists the experimental reduction factors K_{CS} obtained from the observed values of T_{ij}^{HF} given in Table 1. Table 3 also shows values of K_{CS} calculated by four methods.

The first method uses Eq. [12], which assumes infinitely short, ideal pulses, and yields $K_{CS} = 0.333$. Clearly the observed K_{CS} are in poor agreement (12–35%) with that predicted in this way. The second method makes an allowance for the finite pulse width, t_w , by replacing τ_λ and τ_η in Eqs. [12] and [13] by the real space between the middle of pulses

TABLE 2
Reduced Coupling Constants $(T_{ij}^{\text{HF}})^{\text{red}}$ and Values of K_{CS} Obtained by Analysis of the F_1 Projection of the Experimental and Simulated 2D ^{19}F MREV-8 COSY Spectra Using the Parameters Listed in Table 1

| i, j | From the analysis of the experimental 2D spectrum | | From the analysis of the simulated 2D spectrum | |
|--------|---|-------------------|--|-------------------|
| | $(T_{ij}^{\text{HF}})^{\text{red}}/\text{Hz}$ | K_{CS} | $(T_{ij}^{\text{HF}})^{\text{red}}/\text{Hz}$ | K_{CS} |
| 2, 4 | 60.0 ± 0.5 | 0.441 ± 0.017 | 67.0 ± 0.5 | 0.493 ± 0.005 |
| 4, 5 | 556.2 ± 1.0 | 0.454 ± 0.002 | 599.3 ± 0.7 | 0.489 ± 0.001 |
| 4, 6 | 129.8 ± 1.0 | 0.473 ± 0.008 | 136.4 ± 0.4 | 0.496 ± 0.005 |

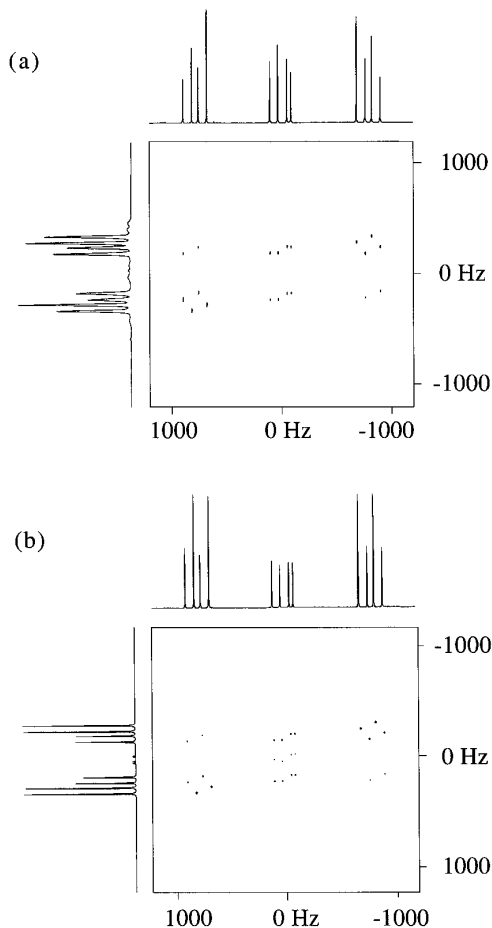


FIG. 5. The 376.45-MHz ^{19}F FF-16 COSY spectrum (magnitude mode) of DCFB dissolved in ZLI 1167. (a) Experimental spectrum recorded at 310 K with $\tau_\lambda = 4.2 \mu\text{s}$, $\tau_\eta = 16.8 \mu\text{s}$ and $t_w = 13.5 \mu\text{s}$. (b) Simulated spectrum using the NMRSIM program.

$$\tau'_\lambda = \tau_\lambda + \frac{t_w}{2} \quad [14]$$

and

$$\tau'_\eta = \tau_\eta + t_w, \quad [15]$$

thus giving K'_{CS} and K'_D (8). This gives $K'_{CS} = 0.419$, which is much closer to the observed values, but there is still a significant difference between theory and experiment (+8 to -11%). A part of this discrepancy arises because allowing for the finite pulse width also affects the value for K'_D predicted by Eq. [13]. In fact K'_D is calculated to be 0.129 rather than zero, and this means that the protons are more strongly coupled. In the present case, when all the NMR parameters are known, the effect that a nonzero K'_D has on the F_1 projection can be calculated, and this leads to the third method of determining the shift reduction factor, leading to values K''_{CS} . These values do show a dependence on T_{ij}^{HF} but not in the same way as those observed and there is no overall improvement in the agreement with experiment.

The fourth and last method of calculating the reduction factors does so by taking into account the finite pulse width, t_w , as discussed by Mehring (8, 15). The calculation obtains a new average Hamiltonian at zeroth order with reduction factors equal to

$$K'''_{CS} = \frac{2\tau_\lambda + \tau_\eta \cos \alpha + 2t_w(\sin \alpha/\alpha)}{2\tau_\lambda + \tau_\eta + 2t_w} \quad [16]$$

and

$$K'''_D = 1 - \frac{3}{2} \left(\frac{\tau_\eta \sin^2 \alpha + t_w(1 - \sin 2\alpha/2\alpha)}{2\tau_\lambda + \tau_\eta + 2t_w} \right), \quad [17]$$

where τ_λ and τ_η are the space between pulses. For $\alpha = 90^\circ$, these give $K'''_{CS} = 0.505$ and $K'''_D = 0.129$ for the present experiment. The effect of a nonzero dipolar coupling reduction factor is small and is neglected. The agreement between K'''_{CS} and the observed values is worse than for K''_{CS} , which is based on an approximate allowance for the finite pulse duration.

A numerical simulation of the 2D FF-16 COSY experiment has been done, using the NMRSIM program, to determine whether the discrepancies between the K_{CS} predicted by the

TABLE 3
Reduced Coupling Constants ($T_{ij}^{\text{HF}}{}^{\text{red}}$) and Values of K_{CS} Obtained by Analysis of the F_1 Projection of the Experimental and Simulated 2D ^{19}F FF-16 COSY Spectra Compared with Predicted Values

| i, j | $(T_{ij}^{\text{HF}})^{\text{red}}/\text{Hz}$ | From the analysis of the experimental 2D spectrum ^a | | | | | From the analysis of the simulated 2D spectrum | |
|--------|---|--|----------|-----------|------------|-------------|--|-------------------|
| | | K_{CS}^{exp} | K_{CS} | K'_{CS} | K''_{CS} | K'''_{CS} | $(T_{ij}^{\text{HF}})^{\text{red}}/\text{Hz}$ | K_{CS} |
| 2, 4 | 60.5 ± 2.5 | 0.444 ± 0.045 | 0.333 | 0.419 | 0.420 | 0.505 | 53.6 ± 0.1 | 0.382 ± 0.001 |
| 4, 5 | 552.7 ± 4.0 | 0.451 ± 0.007 | 0.333 | 0.419 | 0.407 | 0.505 | 467.8 ± 0.2 | 0.393 ± 0.001 |
| 4, 6 | 103.3 ± 3.5 | 0.375 ± 0.037 | 0.333 | 0.419 | 0.418 | 0.505 | 95.7 ± 0.1 | 0.348 ± 0.001 |

^a K_{CS} was obtained from Eq. [12], while K'_{CS} used Eqs. [14] and [15] with [12], K''_{CS} made an allowance for a nonzero value of K_D , and K'''_{CS} is calculated from Eq. [16].

four methods and those observed are caused by pulse imperfections or by the neglect of higher order terms in the average Hamiltonian. The simulated 2D spectrum is presented in Fig. 5b, and the F_1 projection is seen to resemble closely that obtained experimentally in that there are eight strong lines, and only weak extra peaks. Analysis of the eight strong lines as a first-order system yielded the scaled total couplings and the values of K_{CS} listed in Table 3. The values of K_{CS} derived by the simulation are consistently smaller by about 10% than those observed, which can be attributed to imperfections in the pulses used in the experiment. The simulation does produce the same kind of dependence of K_{CS} on T_{ij}^{HF} as that observed, and this probably stems from higher even order terms in the average Hamiltonian being nonzero (8, 9).

CONCLUSION

Both 2D MPS COSY experiments, that employing MREV-8 and that using FF-16, are successful in producing a first-order spectrum in the F_1 dimension. They are both useful experiments, therefore, as a stage in analyzing the 1D spectrum, rather than being the only method for obtaining the dipolar couplings. The analysis of the 1D spectrum is always the preferred route to obtaining the dipolar couplings for a fluorocarbon. This is because the second-order spectra yield the magnitudes of the D_{ij} to a higher precision than do the first-order spectra, and in addition they give the relative signs. However, it is not always possible to analyze the 1D spectra, and the 2D MPS COSY spectrum might be the only route to determine the D_{ij} . In this case the full couplings must be obtained from the reduced couplings by division by a theoretical value of K_{CS} . The precision on the predicted values of D_{ij}^{HF} obtained in this way will depend on pulse imperfections and consequently on the quality of the B_1 field (in terms of phase errors and amplitude variation during the pulse) in a particular spectrometer. The results obtained for DCFB with a Bruker DRX 400 spectrometer suggest that on spectrometers of this type, with high resolution, saddle-coil probes, the values of D_{ij}^{HF} can be obtained within an error of the order of 4% too small for MREV-8 and $\pm 5\%$ for FF-16. To obtain greater precision on the predicted dipolar couplings, it would be nec-

essary to calibrate the spectrometer by recording 2D MPS COSY spectra on a spin system whose parameters are known, as done here. However, without doing this calibration it is possible to obtain $^1\text{H}-^{19}\text{F}$ dipolar couplings from a 2D MPS COSY experiment which provide good starting values for an accurate analysis of the high-resolution 1D spectrum.

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