

Determination of Long-Range ^{13}C – ^{13}C Dipolar Couplings Using a ^{13}C Labeled Liquid Crystal

Chibing Tan[†] and B. M. Fung*

Department of Chemistry and Biochemistry, University of Oklahoma, Norman, Oklahoma 73019-3051

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A liquid crystal labeled with a single ^{13}C nucleus, 4'-cyano-4-biphenyl hexanoate- I - ^{13}C , has been synthesized for the purpose of measuring long-range ^{13}C – ^{13}C dipolar coupling constants. The proton-decoupled ^{13}C spectrum of this compound gives eleven ^{13}C – ^{13}C dipolar coupling constants for carbon nuclei ranging from one to seven bonds away from the labeled ^{13}C position. In addition, although ^1H – ^{13}C dipolar coupling constants for carboxyl carbons have never been determined from the 2D technique of proton encoded local field spectroscopy using naturally abundant liquid crystals, three such coupling constants were obtained using the ^{13}C -enriched compound 4'-cyano-4-biphenyl hexanoate- I - ^{13}C .

Introduction

The most important characteristic of liquid crystals is the presence of orientational ordering without three-dimensional positional ordering. The orientational ordering for a rigid ellipsoid can be specified by a second-rank order parameter tensor, the elements of which are time-averaged quantities:¹

$$S_{\alpha\beta} = \langle 3 \cos \theta_{\alpha a} \cos \theta_{\beta a} - \delta_{\alpha\beta} \rangle / 2 \quad (1)$$

where $\alpha, \beta = x, y, z$ are coordinates of the ellipsoid, and a is an external axis.

Nuclear magnetic resonance (NMR) spectroscopy is an important technique for the study of liquid crystals; it can provide information on molecular geometry, orientational ordering, and internal dynamics.² A very useful parameter that can be obtained from NMR studies of liquid crystals is the dipolar coupling constant between two nuclei i and j , D_{ij} . When the direction of the magnetic field is taken as the a axis, D_{ij} is expressed by^{1,2}

$$D_{ijaa} = \frac{\gamma_i \gamma_j \hbar}{8\pi^2 \langle r_{ij}^{-3} \rangle} [S_{zz} \langle 3 \cos^2 \theta_{ijz} - 1 \rangle + (S_{xx} - S_{yy}) \langle \cos^2 \theta_{ijx} - \cos^2 \theta_{ijy} \rangle + 4S_{xy} \langle \cos \theta_{ijx} \cos \theta_{ijy} \rangle + 4S_{xz} \langle \cos \theta_{ijx} \cos \theta_{ijz} \rangle + 4S_{yz} \langle \cos \theta_{ijy} \cos \theta_{ijz} \rangle] \quad (2)$$

where γ is the magnetogyric ratio, r_{ij} is the internuclear distance, and $\theta_{ijx}, \theta_{ijy}$, etc., are angles between r_{ij} and one of the molecular axes.

Most liquid crystals contain alkyl chains, which impart flexibility to the molecules to lower the phase transition temperatures. To acquire a detailed understanding of the anisotropic behavior of liquid crystals, it is necessary to consider the complex motions of the flexible alkyl chains. In this case, the observed dipolar coupling constant is the average between

the coupling constants of n conformations:

$$\langle D_{ij} \rangle = \sum_{k=1}^n p_k D_{ij}^{(k)} \quad (3)$$

where p_k is the fraction of the k th conformation. The complexity of the problem increases rapidly with the increase in the number of bonds separating the nuclei i and j . Therefore, long-range dipolar coupling constants are a very good set of experimental parameters for judging the qualities of molecular models involving conformational analyses of the alkyl chains in liquid crystals.

For small solute molecules dissolved in liquid crystalline solvents, the ^1H peaks are usually well-resolved, so that quantitative analyses of the spectra can give ^1H – ^1H dipolar coupling constants.¹ On the other hand, the ^1H spectra of bulk liquid crystals are broad and ill resolved, so that special experimental techniques must be used to obtain the dipolar coupling constants. The earliest work was reported by Emsley and co-workers,³ who studied the ^1H spectrum of polydeuterated 4'-pentyl-4-biphenylcarbonitrile (5CB), in which the chain and its adjacent phenyl ring are deuterated; with ^2H decoupling, the ^1H peaks of the four remaining protons in the second phenyl ring are clearly resolved, and the ^1H – ^1H dipolar coupling constants can be determined. The ^1H spectra are more complicated when fewer protons are replaced by deuterium, but multiple-quantum transition can be used to simplify the spectra.⁴

To study liquid crystals in natural abundance, ^1H – ^{13}C dipolar coupling constants can be determined by using a 2D method called separated local field (SLF) spectroscopy, often in combination with off-magic-angle spinning (OMAS).⁵ A recent technique developed in Pines' group called proton-detected local field (PDLF)⁶ (or alternatively proton-encoded local field, PELF) spectroscopy greatly improves the resolution of the 2D spectra.⁷ Recently, Emsley and co-workers used the PDLF method to obtain ^2H – ^{13}C dipolar coupling constants in perdeuterated 5CB,⁸ and extended this method to a 3D version to study long-range ^1H – ^{13}C dipolar coupling constants.⁹ ^{19}F – ^{13}C dipolar couplings can be observed by using mono- or di-fluorinated liquid

* E-mail: bmfung@ou.edu.

[†] Current address: Department of Biochemistry and Molecular Biology, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73190-0001.

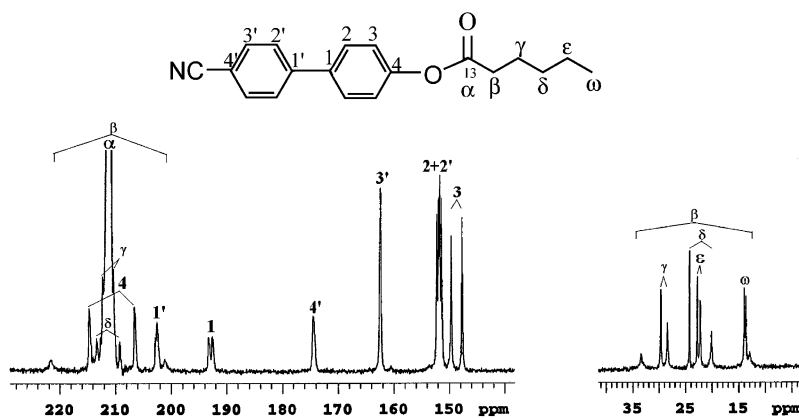


Figure 1. ^{13}C NMR spectrum of 4'-cyano-4-biphenyl hexanoate- I - ^{13}C at 100.58 MHz and 55 °C. The spectrum was obtained with broadband ^1H decoupling sequence using the SPINAL-64 sequence with $\gamma B_2/2\pi = 28$ kHz.

crystals.^{10–14} Using a similar strategy, we have shown that a study of the 1D ^{13}C spectra of monodeuterated compounds can yield many long-range ^2H – ^{13}C dipolar coupling constants.^{15,16}

Long range ^1H – ^{13}C or ^2H – ^{13}C dipolar coupling constants are dependent on the H–C–C bond angles and H–C bond distances, which are difficult to determine accurately for complex molecules. On the other hand, C–C–C bond angles and C–C distances can be determined with good accuracies from X-ray diffraction studies of single crystals. Therefore, ^{13}C – ^{13}C dipolar coupling constants would serve as more direct criteria for judging the success of molecular dynamics simulations and other methods of computer modeling. Using a 2D technique with a large sample and long accumulation times, Sandstrom and Levitt determined 28 ^{13}C – ^{13}C couplings between carbons in the biphenylcarbonitrile moiety of 5CB¹⁷ but were unable to obtain coupling constants involving the carbon nuclei in the alkyl chain. We believed that this type of information could be readily obtained by studying a ^{13}C -enriched liquid crystal and proceeded to carry out corresponding experiments, the results of which are reported here.

Experimental Section

4'-Cyano-4-biphenyl hexanoate- I - ^{13}C was chosen for the present study because of the simplicity in its synthesis. It was prepared by the esterification of 4'-hydroxy-4-biphenylcarbonitrile with hexanoic- I - ^{13}C acid, using dicyclohexylcarbodiimide (DCC) as dehydrating agent and (dimethylamino)pyridine (DMAP) as catalyst.¹⁵ The final product was purified by column chromatograph using CH_2Cl_2 as eluent, followed by recrystallization in hexane. Its nematic range is from 53.7 to 73.0 °C.

The NMR experiments were performed using a Varian INVOA 400 NMR spectrometer. The sample was placed in a 5 mm glass tube in the standard configuration so that the director was aligned parallel to the field; the tube was spun slowly (16 Hz) to improve the spectral resolution. The temperature calibration was made by observing the nematic to isotropic transition. The decoupler power ($\gamma B_2/2\pi$) was 28 kHz for broadband decoupling in both 1D and 2D experiments and 43 kHz for dipolar decoupling in the 2D PELF ^{13}C NMR experiments. The delay time between successive scans was set to 30 s to minimize radio frequency heating.

Results and Discussion

^{13}C – ^{13}C Dipolar Coupling Constants. Using an efficient broadband decoupling sequence called SPINAL-64, sharp ^{13}C peaks can be obtained for liquid crystals with only moderate

decoupler power.¹⁸ As an example, the ^{13}C spectrum of 4'-cyano-4-biphenyl hexanoate- I - ^{13}C at 55 °C is shown in Figure 1. In the spectrum, with the exception of three types of carbons (3', 4', and –CN; the –CN peak is too broad and weak to be observed because the spectrum was obtained with ^1H – ^{13}C cross-polarization), all the peaks of the unlabeled carbons are split into a doublet by the labeled ^{13}C nucleus in the α position. The peak heights of the two halves of some of the doublets are not equal. This may be the result of differential relaxation,¹⁹ but the effect of incomplete decoupling may also have some contribution. The larger splittings are also discernible as satellites of the labeled ^{13}C peak.

In a previous study of a monodeuterated analogue, 4'-cyano-4-biphenyl 2-deuteriohexanoate, ^2H – ^{13}C splittings were also observed for all carbon nuclei in the chain, but extended only to the C3 nucleus in the first phenyl ring. In the present study, we are able to observe splittings as far as the C α –C2' pair, which are separated by seven bonds. The main reason that ^{13}C – ^{13}C dipolar couplings can be detected over a longer range is because ^{13}C has a larger magnetogyric ratio than ^2H (as a comparison, ^{19}F – ^{13}C dipolar couplings up to 12 bonds apart has been observed¹²). The fact that the labeled ^{13}C nucleus is located closer to the phenyl rings is also a contributing factor.

For 4'-cyano-4-biphenyl hexanoate- I - ^{13}C , the larger ^{13}C – ^{13}C splittings ($\Delta\nu$) were directly measured from the spectrum; for peaks with small overlapping, $\Delta\nu$ was obtained by simple spectral deconvolution. When the anisotropy of the scalar coupling constant (J) is negligible, $\Delta\nu$ is related to the dipolar coupling constants (D) and J by

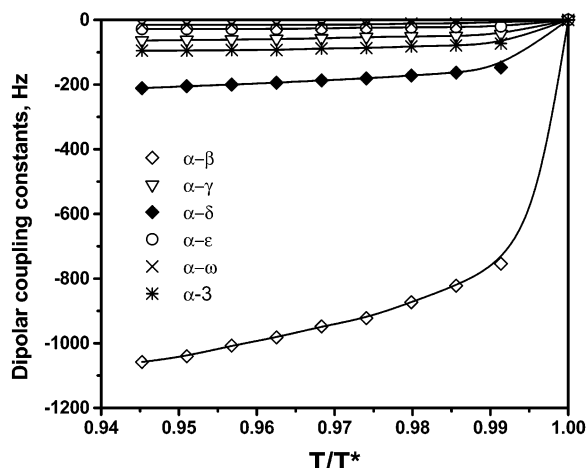
$$\Delta\nu = 2D + J \quad (4)$$

If J^{aniso} is not zero, it would contribute to the dipolar term.¹ Fortunately, the values of J^{aniso} for ^{13}C – ^{13}C couplings are quite small (about 3 Hz for directly bonded carbons)²⁰ compared to D and can be neglected without causing appreciable errors. The values of the isotropic J coupling were determined from the spectrum in the isotropic phase, and only that of the directly bonded pair was nonzero ($J_{\alpha\beta} = 58$ Hz). The signs of $\Delta\nu$ cannot be determined from the spectrum and are assumed to be negative according to geometric considerations. A complete analysis of the results obtained over the whole nematic range has been made, and the data are summarized in Table 1. At higher temperatures, some of the smaller splittings could not be resolved even with spectral deconvolution.

The temperature dependence of the ^{13}C – ^{13}C dipolar coupling constants can be described by an empirical equation¹⁵ which is

TABLE 1: ^{13}C – ^{13}C Dipolar Coupling Constants (Hz) for 4'-Cyano-4-biphenyl Hexanoate- I - ^{13}C at Several Temperatures

T (°C)	α - β	α - γ	α - δ	α - ϵ	α - ω	α -1	α -2	α -3	α -4	α -1'	α -2'
55	-1058	-64	-211	-28	-15	-35	-17	-95	-412	-14	-17
57	-1040	-62	-205	-28	-15	-33	-17	-95	-412	-14	-17
59	-1007	-61	-200	-28	-15	-29	-17	-93	-412	-14	-15
61	-982	-59	-194	-28	-15	-27	-17	-93	-412	-14	-13
63	-948	-57	-187	-26	-15	-23	-16	-88	-412	-14	-11
65	-922	-53	-181	-24	-14			-87	-412		
67	-873	-51	-172	-23	-11			-82			
69	-822	-50	-163	-22	-11			-79			
71	-754	-44	-147	-20				-73			

**Figure 2.** Plot of the ^{13}C – ^{13}C dipolar coupling constants between the α -carbon and various carbons in 4'-cyano-4-biphenyl hexanoate- I - ^{13}C against T/T^* , with $T^* = 347.8$ K. The solid lines were calculated from eq 5.**TABLE 2:** Values of D_0 and F Obtained by Fitting the ^{13}C – ^{13}C Dipolar Coupling Constants in 4'-Cyano-4-biphenyl Hexanoate- I - ^{13}C to Equation 6, with $T^* = 347.8$ K

	D_0	F		D_0	F
α - β	-1911	0.22	α - ϵ	-52	0.22
α - γ	-132	0.24	α - ω	-24	0.24
α - δ	-388	0.22	α -3	-143	0.24

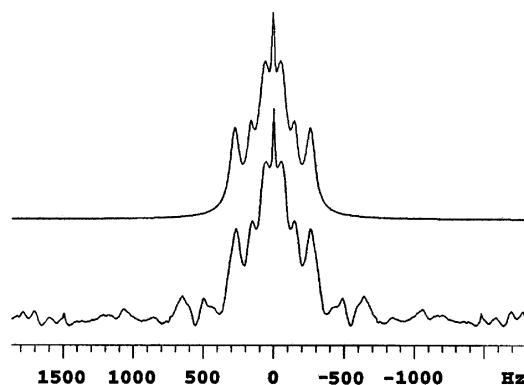
similar to the Haller equation²¹ for the order parameter:

$$D(T) = D_0(1 - T/T^*)^F \quad (5)$$

where D_0 is the limiting value of the dipolar coupling constant, F is a parameter describing how fast this limit is approached as a function of temperature, and T^* is a temperature at which the dipolar coupling constant becomes zero. In the initial step of data fitting, all three parameters were treated as variables; then, the weighted average value of F was used as a fixed parameter in the second round of data fitting. The data for the chain carbons and the C3 carbon are plotted in Figure 2, and the corresponding parameters are listed in Table 2. It is interesting to note that the values of F are slightly different for different pairs of carbon nuclei.

^1H – ^{13}C Dipolar Coupling Constants. In a previous study of unlabeled 4'-cyano-4-biphenyl hexanoate,¹⁵ all one-bond and some two-bond ^1H – ^{13}C dipolar coupling constants were determined by using the 2D PELF/OMAS method. However, the ^1H – ^{13}C splittings involving the carboxyl carbon could not be measured because the signal was too weak. This is now possible by using the ^{13}C enriched compound.

For a quantitative determination of the ^1H – ^{13}C dipolar coupling constants involving the carboxyl carbon in 4'-cyano-4-biphenyl hexanoate- I - ^{13}C , the 2D PELF method was used without OMAS. The ^{13}C spectrum for the α carbon in the $\omega 1$

**Figure 3.** Bottom: α -Carbon spectrum in the $\omega 2$ dimension of a 2D proton-encoded local field (PELF) experiment of 4'-cyano-4-biphenyl- I - ^{13}C hexanoate at 55 °C. Top: Spectrum calculated from deconvoluting the experimental spectrum into three doublets plus an unresolved central peak.**TABLE 3:** ^1H – ^{13}C Dipolar Coupling Constants (Hz; Absolute Value Only) for 4'-Cyano-4-biphenyl Hexanoate- I - ^{13}C at 55 °C

α - β	312
α - γ	180
α - δ	65

dimension at 55 °C is shown in Figure 3, in which three pairs of ^1H – ^{13}C splittings are clearly observed.

In the PELF sequence, a homonuclear dipolar decoupling sequence is used in the evolution period. Therefore, eq 4 is modified by a scaling factor f :

$$\Delta\nu = f(2D + J) \quad (6)$$

The theoretical value of f is 0.424 for the BLEW-48 sequence,²² and the experimental value is 0.414.²³ Unlike the ^{13}C – ^{13}C splittings, the signs of $\Delta\nu$ cannot be assumed to be negative because the flexibility of the chain makes the angle between the C–H vector and the principal axis more uncertain than that for the C–C vector. Fortunately, the J values for nonbonded C–H pairs are small enough to be negligible compared to the corresponding values of D , so that the absolute values of the ^1H – ^{13}C dipolar coupling constants can be readily calculated. These values are 312, 180, and 65, respectively (Table 3). The largest coupling constant is most likely attributable to the $\text{C}\alpha$ – $\text{H}\beta$ pair, but the assignment of the other two values is not immediately obvious. Therefore, another set of experiments was conducted.

In principle, the ^1H – ^{13}C splittings of the enriched compound can be directly observed in the ^1H spectrum provided ^1H – ^1H dipolar couplings can be removed, for example by using the MREV-8 pulse sequence.²⁴ In practice, the resolution is not good enough for quantitative determination (Figure 4, bottom), and spectral deconvolution did not yield definitive and reliable results. Nevertheless, by comparing the ^1H – ^1H dipolar de-

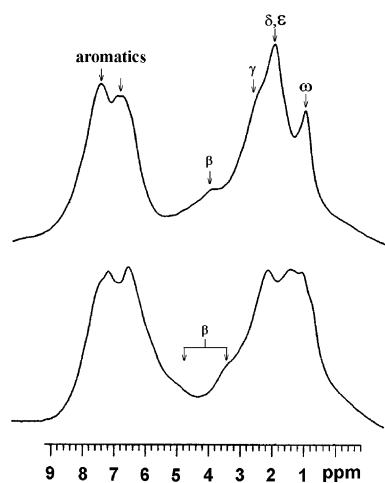


Figure 4. ^1H NMR spectra obtained by using MREV-8 dipolar decoupling at 55 °C. Top: 4'-Cyano-4-biphenylhexanoate; bottom: 4'-cyano-4-biphenyl- ^{13}C hexanoate.

coupled spectrum of the labeled compound with that of the unlabeled one (Figure 4, top), it can be seen that some of the aliphatic protons are split by the labeled ^{13}C , but the difference in the peaks of the aromatic protons is less obvious. Based on this information, it is confirmed that the largest splitting of $|D_{\text{C-H}}| = 312$ Hz determined by the PELF method is indeed due to the $\text{C}\alpha\text{-H}\beta$ pair. The dipolar coupling constant of 180 Hz can now be assigned to the $\text{C}\alpha\text{-H}\gamma$ pair. The assignment of the value of $|D_{\text{C-H}}| = 65$ Hz is not unambiguous, but it is mostly likely due to the $\text{C}\alpha\text{-H}\delta$ coupling instead of the $\text{C}\alpha\text{-H}\epsilon$ coupling. These assignments are listed in Table 3. Because the splittings are expected to decrease with the increase of temperature to cause more spectral overlapping in the ^{13}C spectrum (Figure 3), the 2D study was not performed at higher temperatures; nevertheless, the temperature dependence is expected to be similar to that of the $D_{\text{C-C}}$ values shown in Figure 2 and the $D_{\text{C-H}}$ values of other carbon nuclei in 4'-cyano-4-biphenyl hexanoate, which was reported previously.¹⁵

Conclusion

In conclusion, the study of proton-decoupled 1D ^{13}C NMR of the labeled compound 4'-cyano-4-biphenyl hexanoate- ^{13}C has provided long-range ^{13}C – ^{13}C dipolar coupling constants. In addition, by using the 2D PELF technique to study the α -carbon in this compound, three pairs of ^1H – ^{13}C dipolar coupling constants have been determined. The data reported here would serve as a very useful database for theoretical investigations of the conformational equilibrium of the alkyloyl chain

in this compound, and the method of ^{13}C labeling is applicable to other liquid crystals.

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