ASSIGNMENT OF DIPOLAR COUPLINGS AND ESTIMATION OF CONFORMATIONAL PROBABILITIES IN PARTIALLY ORIENTED HEXANE

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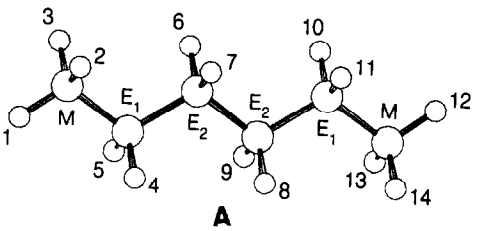
The dipole coupling constants in partially oriented *n*-hexane, determined previously by two-dimensional spectroscopy, are assigned to hydrogen pairs on the molecule using multiple-quantum spectra. Conformational probabilities are estimated assuming statistical independence of conformational dynamics and ordering.

1. Introduction

Magnetic dipolar couplings are a sensitive probe of molecular structure and are valuable in studies of solute conformations and solvent interactions in liquid crystals [1]. Unfortunately, dipolar spectra of molecules containing more than about eight protons are usually complex and unresolved. Recently, we described a method for the determination of dipole coupling constants of intermediate-sized molecules oriented in liquid crystals [2]. As an example, we considered *n*-hexane with 14 hydrogens. The material was statistically deuterated to a high level so that a considerable fraction of molecules was left with only a few protons on the chain. The molecules containing two protons were observed by multiple-quantum filtration [3] and two-dimensional NMR in a nematic liquid crystal to give 16 different AB spectra corresponding to the 16 unique dipole-coupled pairs in *n*-hexane. Thus, it was possible to determine the absolute values of the dipole coupling constants $\langle D_{ij} \rangle$. A general site assignment was made to methyl (M), and methylene (E_1 and E_2) positions of the hexane molecule (A), based on the chemical shifts. The observed dipole coupling constants $\langle D_{ij} \rangle$ are given by



A

$$\langle D_{ij} \rangle = \langle -(h\gamma^2/4\pi^2 r_{ij}^3)(3\cos^2\theta_{ij} - 1) \rangle , \qquad (1)$$

where r_{ij} is the distance between protons i and j, θ_{ij} the angle their internuclear vector makes with the z axis and the angular brackets indicate an average over all molecular motions. From the experiment described above, the signs of the $\langle D_{ij} \rangle$ and their assignment to specific protons i and j on the molecule (A), a prerequisite for structural analysis, cannot be established. In this paper, we describe further work to determine the signs and assignments of the couplings and to estimate the conformational probabilities.

2. Experimental

Samples used were 22 mole% *n*-hexane-1,1,1,6,6,6-d_6 dissolved in the nematic EK 11650 (*p*-pentyl-

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phenyl-2-chloro-4-(*p*-pentylbenzoyloxy)-benzoate) for the multiple-quantum studies, and a 23 mole% solution of 81% randomly deuterated *n*-hexane in EK 11650 for the deuterium spectrum. NMR experiments were carried out on a 360 MHz home-built spectrometer equipped with a parallel data channel interface to a VAX 11/730 computer. All two-dimensional data manipulations and multiple-quantum simulations were carried out on the VAX.

The multiple-quantum spectra were recorded using time proportional phase incrementation (TPPI) [4]. The chemical shift was echoed during t_1. The multiple-quantum preparation time was $\tau = 11.706$ ms for even quanta and $\tau = 12.000$ ms for odd quanta and the two absolute value spectra were added. The spectra were taken using double-quantum deuterium spin decoupling. 8192 points were recorded in t_1 and 1024 points in t_2. Total spectral width for 16 orders was 250 kHz in ω_1 and, for the single-quantum spectrum, 20 kHz in ω_2. Different multiple-quantum orders were separated by a phase increment of 22.5°. Six shots were averaged per t_1 point with a recycle delay of 4.5 s.

3. Assignment of the couplings

Table 1 and molecule (A) should be referred to in following the arguments below. A number of assignments of the $\langle D_{ij} \rangle$ can be made readily. For example in E_2E_2, the coupling constant 4487 which is much larger than the rest, is assigned to the close vicinal pair (6, 7). In general, proximity is not the only factor in determining the magnitude of $\langle D_{ij} \rangle$, because of the angular dependence; in this case, however, it may be used because of the alignment of the (6, 7) vector along the hexane C_2 axis, and hence the assurance that it does not lie close to the magic angle axis. The angular factor is also taken into account in assigning the two largest E_1E_2 coupling constants to the proton pairs (4, 8) and (5, 8) which have their internuclear vector along the chain direction, again far from the magic angle. Similarly, signs can be easily allocated to some of the $\langle D_{ij} \rangle$. By the definition in eq. (1), $\langle D_{ij} \rangle$ will be positive along the C_2 axis and negative perpendicular to it, for hexane molecules aligned with their long axis in the direction of the field. Thus, geminal coupling constants will, for example, all be positive, while a coupling constant that extends along the length of the chain will be negative.

Table 1
Magnitudes and assignments of the dipolar couplings in *n*-hexane

Site [a]	*i*–*j*	$\langle D_{ij} \rangle$(meas) [b]	$\langle D_{ij} \rangle$(model)
MM	1–2	1876(28) [c]	1895
MM	1–12	−206(13)	−181
ME_1	1–4	−386(15)	−414
ME_1	1–10	−322(14)	−291
ME_2	1–6	−1034(25)	−1003
ME_2	1–8	−598(15)	−602
E_1E_1	4–5	3974(34)	3959
E_1E_1	5–10	−713(18)	−772
E_1E_1	4–10	−609(14)	−612
E_2E_2	6–7	4487(34)	4489
E_2E_2	7–8	−190(12)	−187
E_2E_2	6–8	43(12)	98
E_1E_2	4–8	−1616(25)	−1642
E_1E_2	5–8	−1086(27)	−1043
E_1E_2	4–6	186(14)	157
E_1E_2	5–6	81(12)	54

[a] From chemical shift assignments (ref. [2]).
[b] All values are in Hz; the ambient temperature was 28°C, with decoupling 52 ± 3°C.
[c] The numbers in parentheses indicate the approximate error margin, given by the half width at half height of the NMR peaks in the 2-D spectra of ref. [2].

The assignments which cannot be deduced in this way are those of the vicinal coupling constants between ethyl groups. Both the sign and the decision of which coupling is trans and which is cis are uncertain. These couplings are very sensitive to the molecular conformation. To determine the signs and assign the $\langle D_{ij} \rangle$, we used model calculations and multiple-quantum NMR.

3.1. The (n−2)-quantum spectrum

The multiple-quantum NMR spectra are sensitive both to the signs of the dipole coupling constants and to their assignments. At the same time, the high-order $(N-1)$- and $(N-2)$-quantum spectra are well resolved and the frequencies can be easily determined. Strong dipolar coupling of all protons implies a complex coupling pattern with every vertex (atom) coupled to every other. Each $(N-2)$-quantum tran-

sition incorporates the environment of all except two of the vertices and is sensitive to any change such as switching of couplings, except for a complete interchange of two identical vertices under which the Hamiltonian is invariant.

The experimental 6QT and 7QT spectra of hexane-d_6 are shown in fig. 1. The spectra were simulated using existing programs [5] for different possible assignments of ambiguous coupling constants. Fig. 2 shows the expected 6QT and 7QT spectra for various cases, compared to the experimental spectrum. Figs. 2b and 2c give identical 7QT spectra and very similar 6QT spectra, except for the two inner lines, which are split by 25 Hz for assignment 2b (model I), but by 97 Hz for assignment 2c (model II). This line splitting does not appear in the experimental spectrum with a digital resolution of 30 Hz and at the current linewidth of 50 Hz. It is noted that the splitting changes with 10–15% variation of the magnitudes of $D_{4,6}$ and $D_{5,6}$, indicating that the accuracy of interpretation of the 6QT spectrum depends on the accuracy of the measured $\langle D_{ij} \rangle$. Model I is considered more probable at the present level of accuracy and the corresponding assignment of the $\langle D_{ij} \rangle$ is given in table 1.

The following permutation leaves the Hamiltonian invariant: Interchange the E_1E_2 vicinal couplings (i.e. (4, 6) with (4, 7); (5, 6) with (5, 7); (8, 11) with (9, 11); (8, 10) with (9, 10) and the E_1E_2 couplings across three carbon atoms (i.e. (4, 8) with (4, 9); (5, 8) with (5, 9); (6, 10) with (7, 10); (6, 11) with (7, 11)). This corresponds to a permutation of vertices (atoms) 6 and 7 and vertices 8 and 9 (or of vertices 4 and 5 and vertices 10 and 11). This permutation is considered a less appropriate solution because of model calculations which indicate that (4, 8) should be larger than (4, 9).

3.2. Model calculation

We have shown that the $(N-2)$-quantum spectrum of an N-spin system can be used to determine the assignment of dipole coupling constants, up to a restricted number of possible permutations. The success of this technique relies on previous knowledge of the dipole coupling constants, since, although the

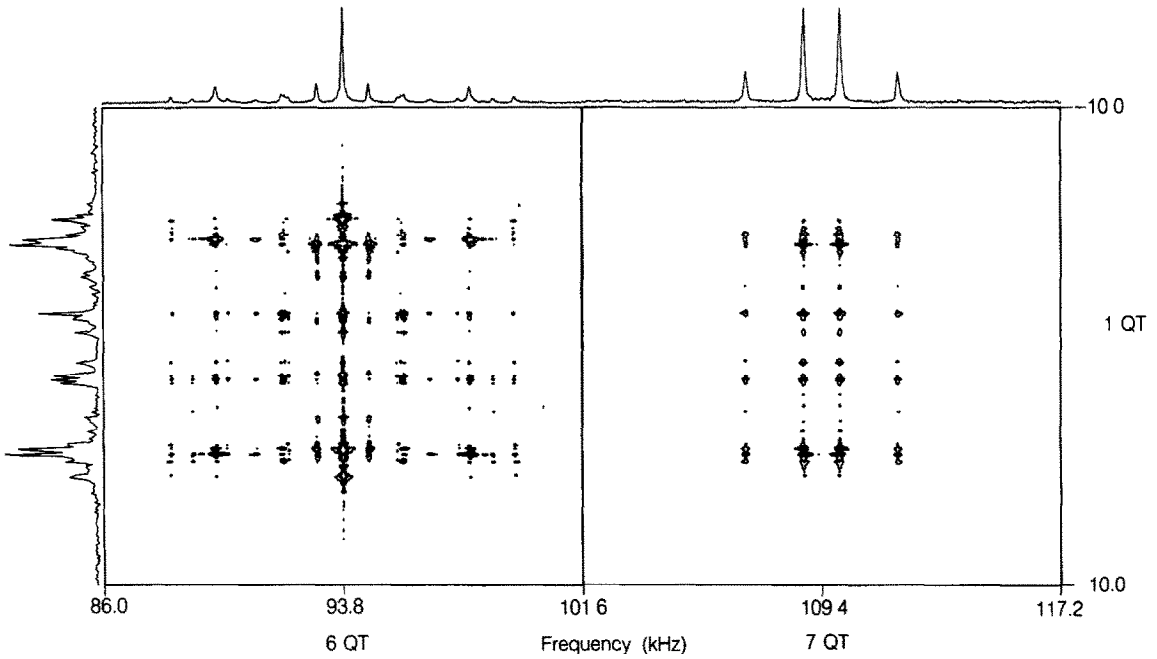

Fig. 1. Experimental six- (6QT) and seven- (7QT) quantum transitions of hexane-d_6 deuterated at the methyl positions, correlated with the single-quantum (1QT) transitions in a two-dimensional multiple-quantum spectrum, using TPPI. The plot has been symmetrized in ω_1 about the centre of each order.

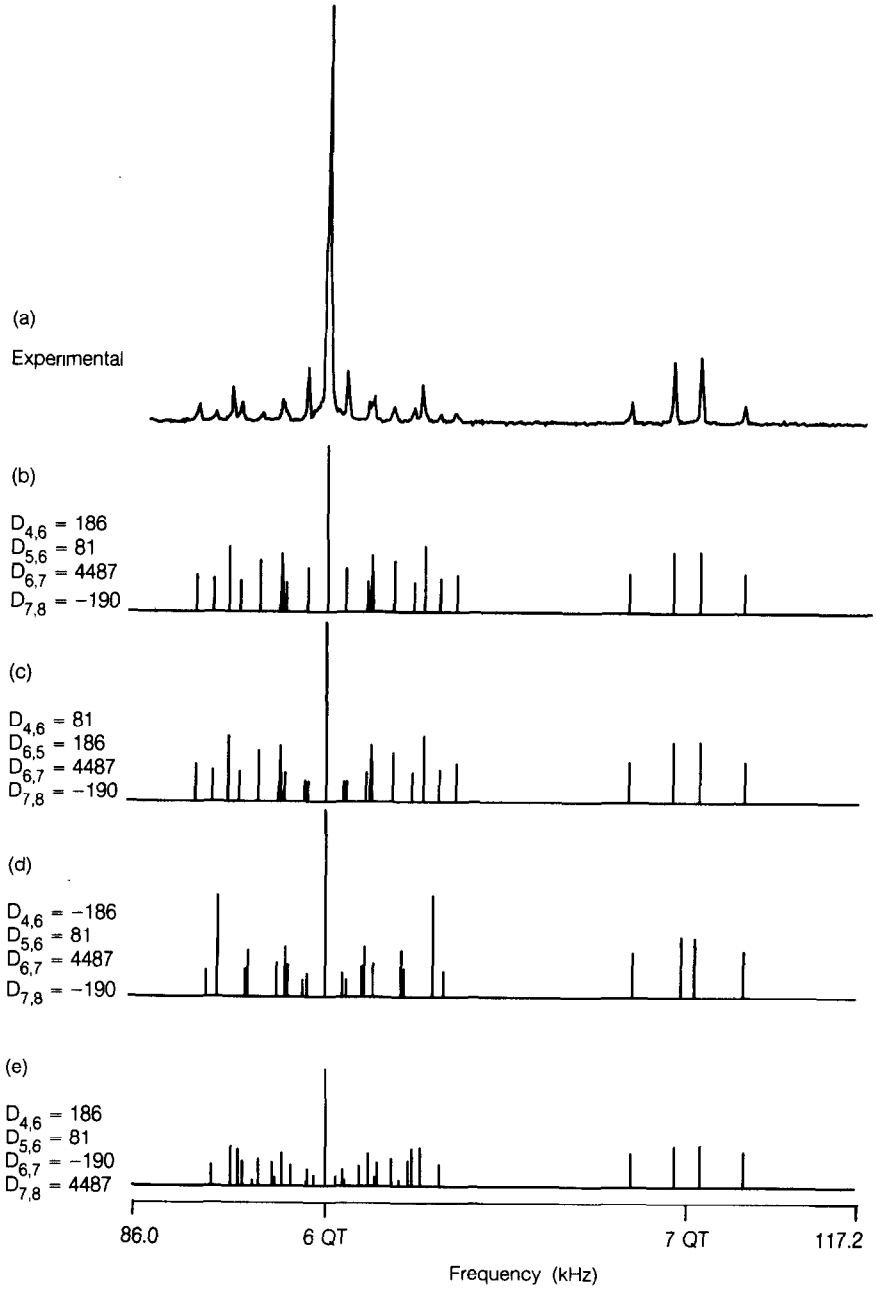

Fig. 2. Comparison of the experimental six- and seven-quantum spectra and spectra calculated for various possible assignments and signs of the dipole coupling constants. All spectra have a digital resolution of 30.5 Hz per point. (a) Projection along ω_1 (the multiple-quantum order) of the spectra in fig. 1. (b–e) Ultimate τ-averaged spectra [5] calculated according to the assignments in table 1 with the exceptions specified on the left-hand side of the figure. The calculated spectra are scaled by a factor 1.09. The assignment of (b) corresponds to model I and that of (c) to model II.

six-quantum spectrum may be fit with the correct set of dipole coupling constants only, convergence from an arbitrary starting point has proved to be extremely difficult [6].

One of the best ways to check the experimental assignment or to derive a starting set for calculating multiple-quantum spectra, is to calculate the dipole coupling constants from a model. We have done so for the *n*-hexane, using a model which conforms to the equation

$$\langle D_{ij} \rangle = \sum_{\alpha,\beta} S_{\alpha\beta} \sum_{n} P_n D^n_{ij\alpha\beta} \ , \qquad (2)$$

where $S_{\alpha\beta}$ is the $\alpha\beta$ component of the average order parameter of the molecule, $D^n_{ij\alpha\beta}$ is the $\alpha\beta$ component of the ijth dipole tensor along the molecular axes of conformer n. The averaging over conformations is performed by a summation over the seven conformers ttt, ttg, tgt, tgg, g^+tg^+, g^+tg^- and ggg weighted with their probabilities P_n. The molecular axes chosen were the axes of the principle moment of inertia tensor. The assumption made with this model is that there is one average order parameter for all conformations. It is equivalent to the assumption that the orientational energy is independent of the internal coordinates [7,10].

A least-squares fit to the experimental $\langle D_{ij} \rangle$ was performed using eq. (2). The results are given in the last column of table 1. The fit is reasonable, given the present error limits on the data and the fact that the model of a single-order tensor is crude. The average deviation between a calculated and experimental coupling constant is ≈ 30 Hz, which is approximately the range of experimental error.

The dipole coupling constants arrived at with this model are consistent with the experimentally determined assignments. In addition, the intuitive assignment of the $\langle D_{ij} \rangle$ to or within methyl groups was checked. This was not possible using the multiple-quantum spectrum. We note here that a very similar fit and average deviation resulted from the alternative assignment of model II, in which $D_{4,6}$ and $D_{5,6}$ were interchanged.

4. Conformational probabilities

Molecule (A) is the ttt conformer of *n*-hexane. The model calculation of section 2.2 allows an estimation of the order tensor and the conformational probabilities for all seven conformers of hexane. These are given in table 2 for models I and II. Our present data favour model I, but model II is also possible. There is an estimated 15% error in the results. It is interesting to note the relatively high probability of the all-trans conformer. It implies a trans to gauche energy of conversion of ≈ 0.96 kcal/mol (≈ 0.91 for model II), employing the RIS model of Flory [11]. This is considerably higher than the generally accepted value of 0.5 kcal/mole for liquid *n*-hexane [12]. However, there has been considerable discrepancy in the literature on the interpretation of Raman data, with some authors reporting a 0.9 kcal/mole energy difference [13]. In addition, computer model calculations of alkanes dissolved in liquid crystals have indicated much greater success at fitting quadrupole coupling constants using energies higher than the accepted value of 0.5 kcal/mole [14].

Table 2
Conformational probabilities and order parameters

	Population						
	ttt	ttg	tgt	tgg	g^+tg^+	g^+tg^-	ggg
model I	0.37	0.29	0.17	0.08	0.01	0.08	0.00
model II	0.35	0.29	0.17	0.06	0.11	0.02	0.00

	S_{zz}	S_{xx-yy}	S_{xy}	S_{xz}	S_{yz}
model I	0.207	0.056	−0.003	−0.015	0.009
model II	0.212	0.046	−0.020	−0.030	0.012

The order tensor axes deviate only slightly from the inertia tensor axes (model I). The order tensor of table 2 can be diagonalized by the Euler angle rotation $\alpha = -24°$, $\beta = 3.6°$ and $\gamma = 27°$. The experimental quadrupole splittings also agree with those calculated using the set of $\{P_n\}$ and S. The experimental values of ν_Q for M, E_1 and E_2 are 9.8, 29.8 and 33.6 kHz, in agreement with ref. [13]. The values extracted from the model normalized to E_2 are 9.3, 29.5 and 33.6, using an asymmetry parameter $\eta = 0.038$ [15].

5. Conclusion

In this paper and a previous communication, we have described an application of two-dimensional and multiple-quantum NMR together with model calculations in liquid crystal solvents to the determination and assignment of the dipole coupling constants of a flexible molecule. An estimate of dynamic molecular structure in the form of conformational probabilities was obtained. Such an approach should be useful as a probe of liquid state structure and as a starting point for molecular dynamics calculations of partially oriented molecules.

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