

Scope and Limitations of Accurate Structure Determination of Solutes Dissolved in Liquid Crystals

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The determination of accurate structures of relatively small molecules dissolved in liquid-crystal solvents is no trivial matter. Extensive vibrational corrections to the observed dipolar couplings are required. Vibrational force fields are often available, but the usual harmonic corrections are strictly limited to small-amplitude internal motions. Moreover, the need to also apply anharmonic corrections and to include the elusive vibration–reorientation interaction is problematic and can only be fulfilled for a very limited set of small molecules. In this paper we discuss the implications for the accuracy of the structure of larger molecules for which this information is not available. We discuss the examples of azulene and biphenylene, and set realistic limits on their proton structures, derived from ¹H dipolar couplings extracted from NMR spectra obtained in different liquid-crystal solvents and analyzed with sophisticated evolutionary algorithms.

1. Introduction

The concept of molecular structure, or stereochemistry as it is now known, dates back to the late nineteenth century when the Frenchman Joseph-Achille le Bel¹ and the Dutchman Jacobus Henricus van 't Hoff² were the first to consider the three-dimensional structure of organic compounds. The importance of molecular geometry and its relevance for chemistry is now fully realized, and many methods, both experimental and theoretical, have been developed to study and determine molecular structure in great detail. These methods comprise scattering and diffraction techniques that involve particles (electrons, neutrons) or photons, a large variety of spectroscopic applications over a wide range of wavelengths, and increasingly *ab initio* computational techniques.

X-ray diffraction methods in solids are widely used to obtain structural information. This technique has the drawback that the scattering cross section of hydrogens in a molecule is small. Hence, their positions are usually not well determined. Neutron diffraction is sensitive to proton positions and is usually carried out in the liquid state. However, for accurate structure determination, electron diffraction and spectroscopic techniques in the gas phase are commonly employed. These methods give the best results for relatively small molecules.

In an approximate sense, all these methods lead to molecular structures that are similar, but on a more detailed level there are significant differences that usually all arise from the same basic source. This has to do with the fact that the concept of a molecule as a “rigid” entity is rather far from the truth. Instead, a molecule possesses a dynamic structure due to the ubiquitous presence of internal vibrational motions. These vibrational

motions can have surprisingly large amplitudes depending on the masses of the atoms involved. Amplitudes of bond bending motions can be larger than 10°, and bond stretching can cause instantaneous changes in bond lengths of ~0.1 Å. Another complication is that the various experimental methods for structure determination are applied to molecules in different states of aggregation. It is not *a priori* obvious that a molecule that experiences interactions with others in the solid or liquid state would have the same structure as measured in the isolation of the gas phase. Much will depend on the strength of intermolecular interactions in the condensed phases. What then do we mean when we speak about an “accurate” molecular structure?

To avoid many of the complications, the concept of a “vibrationless molecule” is of course appealing. In the case of *ab initio* calculations, optimized molecular structures with “equilibrium” bond lengths corresponding to the minima of the relevant potential energy wells can be obtained. Although these quantities can now be computed rather routinely, obviously this does not provide a straightforward link to the observables obtained from experimental methods, which always involve some sort of averaging over all internal vibrational motions. To make matters worse, the vibrational averaging that is implicit in all experimental techniques depends strongly on the observable in question. Hence, to extract an experimental geometry that is “corrected” for the effects of vibrational motion requires different approaches for different experimental methods. These problems may make a comparison among results obtained with different techniques rather risky. The situation is further aggravated by the fact that in the literature there is an abundance of “structures” that all involve different ways of applying vibrational corrections, even when the same experimental method is used.³

In dealing with vibrational motion, approximations cannot be avoided. Commonly harmonic potentials are assumed for the nuclear motion, with every normal vibrational mode

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behaving as a harmonic oscillator with the familiar expressions for vibrational energies and wave functions. The observables obtained from the different experimental methods are calculated as expectation values of the relevant operators, each of which in its own way depends on internuclear distance r . For instance, in the case of electron diffraction the nuclear probability distribution function $P_{ij}(r)$ for each pair of atoms i and j in the molecule is central to the description of the scattering results. Experimentally, the range of momentum transfer scattering parameters s is restricted by the finite range of available detectors, yielding a distribution which is proportional to $P(r)/r$. A model for $P(r)$ is required to correct this experimental quantity for vibrational motion. For microwave spectroscopy the observable that must be corrected for vibrational motion is the rotational constant $B(r) \sim 1/r^2$. In the case of nuclear magnetic resonance (NMR) of solutes dissolved in ordered liquids, vibrational corrections to dipolar couplings that are proportional to $1/r^3$ are required. For an accurate description of the internal motion, the harmonic approximation is usually not adequate. More realistic potential energy curves possess a degree of anharmonicity that significantly affects the averaging process of the observables associated with the various experimental techniques employed for structure determination. In practice, however, experimental information about anharmonicities in the internuclear potential is only available for a small collection of simple molecules.

In this paper we wish to focus on the determination of molecular structure by means of NMR of solutes dissolved in ordered solvents such as nematic liquid crystals. The method is applicable to molecules that contain atoms whose nuclei possess spin, preferably with $I = 1/2$ such as protons, and is limited to relatively small molecules. Experimental dipolar couplings can be determined with a high degree of accuracy, and the challenge of the method is to “translate” this experimental accuracy into a similarly accurate molecular structure. A few issues are obvious from the very start. First, contrary to most methods for accurate structure determination that are performed in the gas phase, NMR experiments are carried out in an ordered liquid phase that may affect solute structures in an unknown manner. Second, the NMR method only allows for the determination of *relative* structures, never *absolute* ones. In addition, in order to extract reliable structural information from experimental dipolar couplings, the predominant problem of how to account for the intricacies of internal and reorientational motion must be dealt with.

Over the years a large body of NMR data on solutes in nematic phases has been accumulated, and a great deal of information about molecular structures has been published.^{4–13} However, the majority of these structures is based on an incomplete theory in which a “rigid” structure is taken as the starting point and effects of vibrational motion (usually in the harmonic approximation) have been added later on an ad hoc basis. Unfortunately, this approach neglects the interplay that exists between vibrational and reorientational motions. In this paper we shall argue that the corrections that should be applied to the dipolar couplings to account for the vibration–reorientation interaction are not insignificant.

The existence of vibration–reorientation coupling is evident from the fact that the tetrahedral molecule methane shows unexpected dipolar splittings when dissolved in anisotropic solvents. The mechanism underlying this observation has been elucidated and indicates that the initial point of view that the molecule should be “distorted” in the liquid-crystal environment is incorrect. An ab initio study of molecular hydrogen and its

isotopologues in a nematic phase has shown that the solute–solvent interaction only affects to some extent the rotational part of the wave function, while leaving the vibrational and electronic parts essentially untouched.¹⁴

A complete structure determination on the basis of dipolar couplings corrected for all the necessary vibrational (harmonic and anharmonic) and vibration–reorientation coupling effects can only be performed for a very limited set of small, well-characterized solute molecules. For such solutes, accurate structures derived from observed dipolar couplings, which are subsequently corrected for all the above effects, invariably show that deviations from the gas-phase geometry are slight at best. This is in excellent agreement with the fact that the solute–solvent interaction is relatively weak and has a minor influence on the solute structures in nematic phases, completely in line with the ab initio results on molecular hydrogen.

The question remains of how accurate are structures derived for larger solutes partially oriented in liquid-crystalline phases. In particular, it would be useful to have some idea about the significance of neglecting the vibration–reorientation interaction in such cases. Recently the analysis of increasingly complicated NMR spectra has received an important impetus through the application of evolutionary algorithms (EAs).^{15,16} In principle, the experimental dipolar couplings of larger spin systems can now be obtained with much greater ease than before, making a discussion about accuracies of derived structures all the more important.

In the present paper we shall give an overview of the limitations still inherent in the most complete theory available to date and of all the corrections to the dipolar couplings required in this theoretical treatment. We shall briefly review the studies known to us on small solutes in which all these corrections were incorporated. Clearly, for larger solutes for which complete force field information is not available, an analysis at the same level of detail is impossible. As an illustration we shall discuss recent NMR studies on azulene and biphenylene dissolved in various nematic phases, and analyzed with advanced EA techniques. Incorporation of very approximate vibration–reorientation coupling contributions will give some indication about the accuracies of the derived structures.

2. Experimental Section

Biphenylene and 1,3,5-trichlorobenzene (tcb) were codissolved in the isotropic phases of the liquid crystals Merck ZLI 1132 (1132) and N-(*p*-ethoxybenzylidene)-*p'*-*n*-butylaniline (EBBA) to a concentration of about 2 and 1 mol %. Similarly, azulene and tcb were codissolved in 1132 and a “magic mixture” of 55 wt % 1132 and 45 wt % EBBA to 5 and 1 mol % solute concentrations. Each of these liquid-crystal/solute mixtures were placed into a 5 mm O.D. standard NMR tube and mixed thoroughly in the isotropic phase. Finally, a capillary tube filled with deuterated acetone was placed axially symmetric inside the tube with the aid of Teflon spacers to provide a lock signal. Spectra were acquired on a Bruker Avance 400 MHz NMR spectrometer with the temperature kept at 298.5 K by the Bruker air-flow system.

The ¹H NMR spectra of azulene and biphenylene (both with C_{2v} symmetry and hence requiring two independent order parameters each) are complicated, and their analysis by conventional means is very time-consuming. Recently we implemented EAs in order to solve highly complex spectra of solutes dissolved in liquid-crystal solvents.^{15,16} The spectral analysis requires reasonable starting values and realistic ranges for the dipolar couplings. These are obtained by assuming an ap-

TABLE 1: Fitting Parameters (Hz) from EA Fits to 400 MHz Azulene Spectra

parameter	EBBA ^a	1132	MM
D ₁₂ = D ₂₃	-328.77 ± 0.17	-763.91 ± 0.29	-585.08 ± 0.26
D ₁₃	78.90 ± 0.15	-36.45 ± 0.25	2.32 ± 0.20
D ₁₄ = D ₃₈	-11.05 ± 0.13	-65.73 ± 0.22	-45.02 ± 0.17
D ₁₅ = D ₃₇	-55.42 ± 0.09	-85.01 ± 0.16	-71.14 ± 0.12
D ₁₆ = D ₃₆	-113.29 ± 0.19	-141.77 ± 0.17	-124.64 ± 0.16
D ₁₇ = D ₃₅	-281.5 ± 0.9	-337.82 ± 0.75	-300.72 ± 0.90
D ₁₈ = D ₃₄	-1724.9 ± 1.4	-2088.38 ± 1.64	-1854.22 ± 1.64
D ₂₄ = D ₂₈	-174.81 ± 0.11	-237.52 ± 0.20	-204.26 ± 0.18
D ₂₅ = D ₂₇	-92.53 ± 0.20	-114.90 ± 0.27	-101.45 ± 0.21
D ₂₆	-79.66 ± 0.08	-95.95 ± 0.16	-85.28 ± 0.12
D ₄₅ = D ₇₈	-2268.4 ± 1.1	-2764.14 ± 1.16	-2448.31 ± 1.22
D ₄₆ = D ₆₈	-218.10 ± 0.16	-320.58 ± 0.22	-270.11 ± 0.16
D ₄₇ = D ₅₈	-3.55 ± 0.12	-64.81 ± 0.19	-42.02 ± 0.15
D ₄₈	43.57 ± 0.14	-20.24 ± 0.23	0.67 ± 0.18
D ₅₆ = D ₆₇	-16.86 ± 0.25	-711.83 ± 0.50	-455.82 ± 0.39
D ₅₇	88.11 ± 0.18	-38.85 ± 0.32	2.05 ± 0.25
δ ₁ - δ ₂ ^b	-0.9990	-1.0297 ± 0.0008	-0.9920 ± 0.0005
δ ₁ - δ ₄ ^b	-0.2830	-0.1260 ± 0.0008	-0.2219 ± 0.0006
δ ₁ - δ ₅ ^b	0.3910	0.4824 ± 0.0009	0.4357 ± 0.0007
δ ₁ - δ ₆ ^b	-0.5010	-0.4538 ± 0.0008	-0.4574 ± 0.0005
J ₁₂ = J ₂₃	3.9 ± 0.3	3.8 ± 0.4	3.7 ± 0.3
J ₁₃	1.5 ± 0.3	1.3 ± 0.4	0.8 ± 0.4
J ₁₄ = J ₃₈	0.7 ± 0.2	0.7 ± 0.4	1.0 ± 0.3
J ₁₅ = J ₃₇	0.6 ± 0.2	0.6 ± 0.3	0.5 ± 0.2
J ₁₆ = J ₃₆	0.2 ± 0.3	-0.2 ± 0.3	0.1 ± 0.3
J ₁₇ = J ₃₅	0.2 ± 0.5	0.5 ± 0.6	0.6 ± 0.6
J ₁₈ = J ₃₄	-0.9 ± 1.3	-0.4 ± 1.1	-0.1 ± 1.3
J ₂₄ = J ₂₈	0.3 ± 0.2	0.4 ± 0.6	0.6 ± 0.5
J ₂₅ = J ₂₇	-0.3 ± 0.3	-0.1 ± 0.5	-0.2 ± 0.4
J ₂₆	0.5 ± 0.1	0.5 ± 0.3	0.7 ± 0.2
J ₄₅ = J ₇₈	9.9 ± 0.8	9.5 ± 0.9	9.4 ± 0.9
J ₄₆ = J ₆₈	0.7 ± 0.3	1.0 ± 0.6	1.0 ± 0.4
J ₄₇ = J ₅₈	0.5 ± 0.2	0.4 ± 0.3	0.3 ± 0.3
J ₄₈	-0.2 ± 0.3	-0.1 ± 0.5	-0.2 ± 0.4
J ₅₆ = J ₆₇	9.5 ± 0.4	9.9 ± 0.5	9.9 ± 0.5
J ₅₇	0.6 ± 0.3	1.1 ± 0.6	1.8 ± 0.4

^a Data reported from line-assignment fit in ref 48. ^b δ is the downfield shift in ppm.

proximate solute geometry and by using a simple phenomenological model^{13,17} to estimate the order parameters, from which approximate dipolar couplings are calculated. Indirect couplings are taken from isotropic spectra or from the literature. With the EA method rapid convergence was achieved and accurate dipolar couplings were obtained (see Tables 1 and 2 for spectral parameters obtained for azulene and biphenylene). These couplings were then used to derive accurate structural information about the solute.

3. Theoretical Background

In this section the theory underlying the analysis of experimental NMR results for solutes in uniaxial nematic solvents will be discussed. We shall develop the theory starting from a *nonrigid* rotating and vibrating molecule embedded in an anisotropic environment, in contrast to the historical approach where the starting point was a fictitious rigid solute.^{18–20} The need for vibrational corrections was only fully realized later, and they were added almost as an afterthought.^{21–23} Unfortunately, this approach overlooked a coupling term between reorientation and vibration that in our treatment arises quite naturally and will be shown to be important when it comes to accurate structure determination.

The orientational order of a solute dissolved in a nematic liquid crystal arises from the interaction of the solute with the anisotropy $\Delta G = G_{\parallel} - G_{\perp}$ in the mean liquid-crystal field which often has cylindrical symmetry around the direction of the space-fixed magnetic field direction *Z*. The potential *U* that describes

the interaction leading to solute orientational order in this anisotropic mean field is given by:^{24–26}

$$U = -\frac{1}{3}\Delta G\beta_{kl}(Q_m)\mathbf{S}_{kl}(\Omega) \quad (1)$$

with the orientation operator

$$\mathbf{S}_{kl}(\Omega) = \frac{3}{2}\cos\theta_{kz}\cos\theta_{lz} - \frac{1}{2}\delta_{kl} \quad (2)$$

where *k* and *l* are molecule-fixed axes *x*, *y*, *z* for the solute, and $\cos\theta_{kz}$ is the direction cosine between the molecule-fixed *k*-axis and the space-fixed *Z*-axis. The Einstein convention that implies summation over repeated indices that indicate Cartesian coordinates is used throughout this paper. The potential is a function of both the vibrational normal modes *Q_m* of the solute and of the Euler angles Ω that describe its orientation. In principle, this potential couples vibrational and reorientational motions.

In the potential defined in eq 1 it is assumed that the interaction between solvent and solute can be written in a simple bilinear form, in which solvent and solute properties are introduced in a factorized manner. This simple model gives a picture of the liquid-crystal environment as providing an average second-rank mean field tensor, *G_{ij}*, that interacts with some second-rank tensorial property, β_{ij} , of the solute molecule. The tensor β_{ij} is supposed to be determined by the electronic structure and hence the geometry of the solute molecule, and therefore depends on its vibrational (normal) coordinates. Because this potential will be used to predict second-rank tensorial properties such as dipolar and quadrupolar couplings, it is reasonable to neglect possible higher-order terms. It should be stressed that the form of the potential defined in eq 1 does not require specific knowledge of the orientation mechanism(s). The interaction is written as $\Delta G\beta_{kl}(Q_m)$, but the values of these quantities are unknown without specific assumptions about the actual nature of the orienting interaction. Moreover, there is no a priori reason why a single mechanism should dominate the orienting process; indeed, there is excellent evidence that solute orientational order involves more than one mechanism.^{13,27} Hence, the quantities $\Delta G\beta_{kl}(Q_m)$ should in general be viewed as a sum of contributions $\Delta G^i\beta_{kl}^i(Q_m)$ for every interaction *i*.

The observables that we wish to calculate are the dipolar and quadrupolar couplings that are measured, usually with high accuracy, by means of NMR. These observables have the following general form:

$$A(Q_m, \Omega) = a_{kl}(Q_m)\mathbf{S}_{kl}(\Omega) \quad (3)$$

that is, they depend on both the rotational and vibrational coordinates and have a multiplicative structure. In order to proceed, approximations must be made.

First, the potential *U* of eq 1 will be treated as a perturbation on the zeroth-order problem, for which we take the harmonic approximation for the vibrational problem and the rigid rotor for the rotational degree of freedom. The zero-order wave function will then be a simple product of harmonic oscillator wave functions for each normal mode and a rigid rotor wave function. Second, assuming that the normal coordinates describe small displacements from the equilibrium structure of the molecule, the quantities $\beta_{kl}(Q_m)$ and $a_{kl}(Q_m)$ that depend on molecular geometry will be expanded in a truncated Taylor

TABLE 2: Fitting Parameters (Hz) from EA Fits to Biphenylene Spectra

parameter	EBBA	1132	MM ^a	isotropic ^b
D ₁₂ = D ₃₄ = D ₅₆ = D ₇₈	-1765.14 ± 0.05	-1966.51 ± 0.05	-1627.418 ± 0.012	
D ₁₃ = D ₂₄ = D ₅₇ = D ₆₈	-20.16 ± 0.07	-123.42 ± 0.07	-80.698 ± 0.016	
D ₁₄ = D ₅₈	89.87 ± 0.14	6.04 ± 0.23	24.986 ± 0.047	
D ₁₅ = D ₄₈	-32.85 ± 0.12	-60.30 ± 0.24	-44.997 ± 0.047	
D ₁₆ = D ₂₅ = D ₃₈ = D ₄₇	-78.89 ± 0.07	-88.55 ± 0.07	-73.101 ± 0.016	
D ₁₇ = D ₂₈ = D ₃₅ = D ₄₆	-177.03 ± 0.06	-180.79 ± 0.06	-153.094 ± 0.014	
D ₁₈ = D ₄₅	-753.89 ± 0.13	-759.67 ± 0.19	-645.505 ± 0.040	
D ₂₃ = D ₆₇	809.12 ± 0.15	73.62 ± 0.24	235.308 ± 0.051	
D ₂₆ = D ₃₇	-63.57 ± 0.12	-66.08 ± 0.24	-55.523 ± 0.047	
D ₂₇ = D ₃₆	-81.17 ± 0.15	-81.68 ± 0.19	-69.478 ± 0.047	
δ ₁ - δ ₂ ^c	-0.4200 ± 0.0004	-0.3622 ± 0.0006	-0.4223 ± 0.0001	-0.10
J ₁₂ = J ₃₄ = J ₅₆ = J ₇₈	7.1 ± 0.1	7.5 ± 0.8	6.77 ± 0.07	6.8
J ₁₃ = J ₂₄ = J ₅₇ = J ₆₈	0.7 ± 0.1	1.2 ± 0.1	0.75 ± 0.04	0.74
J ₁₄ = J ₅₈	1.0 ± 0.3	0.8 ± 0.4	1.07 ± 0.09	1.08
J ₁₅ = J ₄₈	-0.2 ± 0.2	0.5 ± 0.4	-0.10 ± 0.09	0.0
J ₁₆ = J ₂₅ = J ₃₈ = J ₄₇	0.3 ± 0.1	0.1 ± 0.1	0.15 ± 0.03	0.0
J ₁₇ = J ₂₈ = J ₃₅ = J ₄₆	0.0 ± 0.1	-0.2 ± 0.2	0.08 ± 0.06	0.0
J ₁₈ = J ₄₅	0.3 ± 0.3	0.3 ± 0.8	-0.08 ± 0.14	0.0
J ₂₃ = J ₆₇	8.1 ± 0.3	8.4 ± 0.4	8.28 ± 0.09	8.24
J ₂₆ = J ₃₇	-0.0 ± 0.2	-0.7 ± 0.4	-0.17 ± 0.09	0.0
J ₂₇ = J ₃₆	0.0 ± 0.3	0.3 ± 0.7	0.47 ± 0.12	0.0

^a From ref 50. ^b From ref 53. ^c δ is the downfield shift in ppm.

series around the equilibrium structure of the solute. This choice is extremely convenient, because the equilibrium geometry represents the location of the minima of the potential energy surface, is unaffected by molecular vibrations, and is isotope-independent. In this approach the choice of normal coordinates is not crucial; the Taylor expansions could also be formulated in terms of other coordinates such as Cartesian displacement coordinates, symmetry displacement coordinates, or internal displacement coordinates.

It is essential to emphasize that the use of truncated Taylor expansions can only be expected to be realistic for small-amplitude vibrational modes. Large-amplitude vibrational motions and associated low-frequency normal modes such as internal rotations, ring-puckering motions, the vibrations of hydrogen in a hydrogen bond, etc., cannot be dealt with in the same fashion.²⁶

For structure determination the focus should be on the dipolar couplings. The theoretical treatment outlined above leads to various contributions to these couplings. Since the rotational degree of freedom can be treated classically for all molecules except molecular hydrogen, and rotational energy differences are usually much smaller than vibrational level spacings, considerable simplification is obtained:

$$D_{\mu\nu} = \langle d_{kl,\mu\nu} \rangle_{\text{vibrations}} \langle \mathbf{S}_{kl} \rangle_{\text{rotations}} + \langle d_{kl,\mu\nu} \mathbf{S}_{kl} \rangle_{\text{vibrations, rotations}} = D_{\mu\nu}^e + D_{\mu\nu}^a + D_{\mu\nu}^h + D_{\mu\nu}^{\text{nonrigid}} \quad (4)$$

with

$$d_{kl,\mu\nu} = -\frac{h\gamma_{\mu}\gamma_{\nu}}{4\pi^2} (\cos \theta_{\mu\nu,k} \cos \theta_{\mu\nu,l} / r_{\mu\nu}^3) \quad (5)$$

Here $\cos \theta_{\mu\nu,k}$ signifies the direction cosine between the internuclear $\mu\nu$ -direction and the molecule-fixed k -direction, $r_{\mu\nu}$ is the instantaneous internuclear distance, and the superscripts “e”, “a”, and “h” label the equilibrium, anharmonic, and harmonic terms, respectively. Note that in eq 4 the vibrational and reorientational motions in the term

$\langle d_{kl,\mu\nu} \rangle_{\text{vibrations}} \langle \mathbf{S}_{kl} \rangle_{\text{rotations}}$ are strictly decoupled. In contrast, the term $\langle d_{kl,\mu\nu} \mathbf{S}_{kl} \rangle_{\text{vibrations, rotations}}$ accounts for correlated vibrational–reorientational motion.

For any solute in any liquid-crystal solvent the following contributions to the dipolar couplings in eq 4 must be considered:

$$D_{\mu\nu}^e = d_{kl,\mu\nu}^e \langle \mathbf{S}_{kl} \rangle_{\text{rotations}} \quad (6)$$

$$D_{\mu\nu}^a = \sum_m \left(\frac{\partial d_{kl,\mu\nu}}{\partial Q_m} \right)^e \langle Q_m \rangle \langle \mathbf{S}_{kl} \rangle_{\text{rotations}} \quad (7)$$

$$D_{\mu\nu}^h = \frac{1}{2} \sum_{m,n} \left(\frac{\partial^2 d_{kl,\mu\nu}}{\partial Q_m \partial Q_n} \right)^e \langle Q_m Q_n \rangle \langle \mathbf{S}_{kl} \rangle_{\text{rotations}} \quad (8)$$

$$D_{\mu\nu}^{\text{nonrigid}} = \frac{1}{3} \Delta G \sum_m \left(\frac{\partial d_{kl,\mu\nu}}{\partial Q_m} \right)^e \left(\frac{\partial \beta_{ij}}{\partial Q_m} \right)^e \frac{1}{\omega_m^2} \langle \mathbf{S}_{kl} \mathbf{S}_{ij} \rangle_{\text{rotations}} \quad (9)$$

Expressions for the derivatives $(\partial d_{kl,\mu\nu} / \partial Q_m)^e$ and $(\partial^2 d_{kl,\mu\nu} / \partial Q_m \partial Q_n)^e$ have been given in various places.^{21,28–30}

At this point we note that the quantity $(\partial \beta_{ij} / \partial Q_m)^e$ in the *nonrigid* contribution in eq 9 is unknown as long as the orienting mechanism is unknown, and it is usually considered as an adjustable parameter. The magnitude of the term $(\partial d_{kl,\mu\nu} / \partial Q_m)^e$ is expected to decrease with increasing distance between the nuclei, and the $1/\omega_m^2$ dependence emphasizes the relative importance of normal modes at lower frequencies. More on the special role of this contribution will follow later.

For a harmonic vibrational potential the relevant results can be summarized as follows:

$$\langle Q_m Q_n \rangle = \delta_{mn} \left\langle v_m \left| Q_m^2 \right| v_m \right\rangle \quad (10)$$

$$\left\langle v_m \left| Q_m^2 \right| v_m \right\rangle = \frac{h}{2\pi\omega_m} \left(v_m + \frac{1}{2} \right) \quad (11)$$

where v_m is the vibrational quantum number and ω_m is the vibrational frequency of normal mode m . By taking a quantum average over all vibrational states^{31–33} we obtain:

$$\left(v_m + \frac{1}{2} \right)_T = \frac{1}{2} \coth \left(\left(\frac{h}{2\pi} \right) \frac{\omega_m}{2kT} \right) \quad (12)$$

from which the required thermal average of $\langle Q_m Q_n \rangle$ is readily evaluated. Note that the harmonic approximation is often poor, especially in the case of low-frequency modes where eq 12 is likely to fail.

For a harmonic potential the vibrational quantum average of each normal coordinate $\langle Q_m \rangle$ is zero. Moreover, $\langle Q_m^p Q_n^q \rangle = 0$ whenever one of the exponents p or q is odd. However, for an anharmonic potential the quantum averages over totally symmetric normal modes need not vanish. These quantum averages depend on the higher-order anharmonic cubic and possibly quartic force fields. When the semidiagonal cubic anharmonic force constants Φ_{mil} of the potential expressed in normal coordinates are known, we have:^{31,33,34}

$$\langle Q_m \rangle = -\frac{1}{2\omega_m^2} \sum_l \Phi_{mil} \left\langle v_l \left| Q_l^2 \right| v_l \right\rangle \quad (13)$$

Boltzmann thermal averages are then obtained as in the case of the harmonic contributions (see eqs 11 and 12). Unfortunately, the anharmonic force field is only available for a very limited number of small very well characterized molecules. The fact that for larger molecules the anharmonic force field is often neglected is one of the serious impediments in obtaining structures commensurate with the highly accurate experimental dipolar couplings.

The relevant classical thermal averages of eqs 6–9 can be calculated using Boltzmann statistics:

$$S_{kl} = \langle \mathbf{S}_{kl} \rangle_{\text{rotations}} = \frac{\int \mathbf{S}_{kl} \exp(-U(\Omega)/kT) d\Omega}{\int \exp(-U(\Omega)/kT) d\Omega} \quad (14)$$

$$\langle \mathbf{S}_{ij} \mathbf{S}_{kl} \rangle_{\text{rotations}} = \frac{\int \mathbf{S}_{ij} \mathbf{S}_{kl} \exp(-U(\Omega)/kT) d\Omega}{\int \exp(-U(\Omega)/kT) d\Omega} \quad (15)$$

The $\langle \mathbf{S}_{kl} \rangle_{\text{rotations}}$ are the familiar S_{kl} Saupe order parameters that describe the orientational order of the solute in the liquid-crystal solvent. The quantities $\langle \mathbf{S}_{ij} \mathbf{S}_{kl} \rangle_{\text{rotations}}$ are required to obtain the *nonrigid* contribution to the dipolar couplings.

It should be noted that for small orientational order (when only terms proportional to ΔG are carried in the expansion of the exponentials that contain the orienting potential in eqs 14 and 15) the equilibrium, anharmonic, and harmonic contributions to the dipolar couplings are proportional to the solute orientation parameters S_{kl} , whereas the *nonrigid* contribution shows a different dependence. The S_{kl} scale with ΔG (the anisotropy in the liquid-crystal field) if terms of order $(\Delta G)^2$ are neglected. Under those conditions, all four contributions to the dipolar couplings in eqs 6–9 scale with ΔG . For the quadrupolar

couplings very similar expressions as for the dipolar ones can be obtained. Anisotropies in indirect couplings are usually neglected, but might be important when heavier nuclei are present.

Clearly, in eq 4 the first three contributions to the dipolar couplings can be calculated from the equilibrium geometry and from the harmonic and anharmonic force fields. This does not require any knowledge about the mechanism(s) that determine the solute partial orientation in the nematic solvent. The situation is entirely different for the *nonrigid* contribution to the dipolar coupling. Its calculation from first principles requires knowledge about the orientation mechanism(s) that is usually lacking. Moreover, for small degrees of orientational order the relative importance of the *nonrigid* term compared to the other contributions tends to increase. This situation spells ill for accurate solute structure determinations, especially when NMR spectra are obtained at low orientational order.

The theory discussed so far implicitly assumes solutes that occur in a *single* rigid conformation. The situation with solutes that undergo conformational change on the time scale of the NMR experiment is appreciably more complicated. First, it should be realized that the concept of an “average” solute that can be described with one set of Saupe orientation parameters is invalid. In principle, every conformer requires its own independent set of order parameters, and the observed dipolar couplings are described by:

$$D_{\mu\nu} = \sum_m P_m d_{kl,\mu\nu}^m S_{kl}^m \quad (16)$$

where P_m stands for the population of conformer m .³⁵ When the solute interconverts among several symmetry-related conformers, the number of orientation parameters may be reduced. In general, however, five independent order parameters are required for every conformer. Second, in eq 16 only products of populations and order parameters occur. To separate the two, independent information about either populations or order parameters is required. These complications make the accurate determination of structural parameters of solutes that undergo conformational change a challenging undertaking.

4. Discussion

In the theoretical section the various contributions to the dipolar couplings are summarized. From eqs 6–9 it is clear that in order to obtain the corrected experimental dipolar couplings that are required to extract accurate equilibrium geometries, detailed information about the harmonic and anharmonic force fields, and about the rather elusive vibration–reorientation coupling contribution, is essential. In Sections 4.1–4.6 we shall consider all the data that are to the best of our knowledge available in the literature, and for which a full analysis was performed.

For larger solutes, dipolar couplings corrected for all the relevant effects cannot be obtained. Usually anharmonic vibrational force fields are not available, and only harmonic corrections can be applied. Clearly, under those circumstances equilibrium structures cannot be extracted. When comparing such structural information to that derived from other experimental methods, in which anharmonic corrections were also neglected, great care must be taken.³ For solutes other than those discussed in Sections 4.1–4.6 the vibration–reorientation interaction was never incorporated, and its inclusion is a priori impossible without detailed knowledge about the orienting

mechanism(s). In Section 4.7 we shall focus on azulene and biphenylene and shall discuss the consequences that ignorance of the *nonrigid* contributions has for their accurate structure determination.

4.1. Methane (CH₄). Methane (CH₄) is a well-characterized molecule that possesses an equilibrium structure with tetrahedral symmetry and therefore should show no anisotropic splittings in a liquid-crystal solvent. The fact that it does was puzzling for a long time, but the explanation lies in the fact that the correlated vibrational–reorientational motion leads to NMR spectra that appear anisotropic. In this case the “*nonrigid*” term that appears in the description of the dipolar couplings is the *only* contribution that causes this behavior. Hence, the importance of this term can be studied independent of other complications. Although the mechanism(s) that are at the root of the interaction between solute and solvent “field” are not known, the relevant ($\partial\beta_{ij}/\partial Q_m$)^e parameters can be fitted to the experimentally observed dipolar couplings. In a series of papers on methane and its deuterated and tritiated isotopologues^{24,28,36,37} it has been shown that the perturbation approach as described in the theoretical section is fully adequate, that the perturbations are small, and that the anisotropic couplings are not due to any actual distortion of the methane molecule in the liquid crystal. Instead, the importance of the *nonrigid* contribution was established beyond a doubt.

4.2. Acetylene (HCCH). Acetylene (HCCH) possesses a linear, well-characterized equilibrium structure. Its harmonic and cubic force fields are well-known experimentally. The molecule and its various isotopologues were studied initially in a number of liquid-crystal solvents, and curious results were obtained that were tentatively explained on the basis of an ad hoc two-site model.³⁸ It was assumed that acetylene in a liquid-crystal solvent occupied two different sites with different geometries and degrees of orientation. Later, a detailed study on a series of isotopologues was carried out and 13 different dipolar couplings were measured.²⁹ Harmonic terms up to order 6, as well as the anharmonic force field, were included in the vibrational analysis. In addition, the vibration–reorientation coupling was taken into account, which involves three independent derivatives of the solute β tensor with respect to the symmetric normal coordinates. Especially the observed CH dipolar couplings required large harmonic corrections (up to 10%), but also the anharmonic and *nonrigid* corrections were sizable (~1 and 6%, respectively). The HH dipolar couplings also required corrections of order 3% due to the *nonrigid* contribution. With the inclusion of all these effects, the observed dipolar couplings could be fitted, essentially to within experimental error. Moreover, the complete analysis led to a structure that corresponds very well to the gas-phase geometry, while the need to invoke a two-state model or other elusive explanations was no longer present.

4.3. Methyl Fluoride (CH₃F). Initial experiments on methyl fluoride dissolved in a number of nematic liquid crystals led to very unusual results. Depending on experimental conditions the HCH bond angle was found to vary by several degrees. The degree of solute orientational order was observed to be small, and under conditions where S_{zz} was close to zero, not all the dipolar couplings were found to vanish at the same time.³⁹ Inclusion of the vibration–reorientation interaction proved to be the key to understanding the problems. In a first paper two important assumptions in estimating the vibration–reorientation coupling were made: (i) bond additivity was assumed, thus requiring two independent parameters for all different bonds in the molecule; and (ii) the torques acting on the CH bonds in the solutes methane, methyl fluoride, and methyl iodide were

assumed to be proportional to each other.⁴⁰ These assumptions led to a satisfactory description for all the observed dipolar couplings, and a solute structure very similar to the gas-phase geometry. In a later paper, methyl fluoride and several of its isotopologues were studied in detail.²⁵ In this analysis the vibration–reorientation coupling was incorporated, assuming only bond additivity, and excellent correspondence between observed and calculated dipolar couplings was obtained. As in ref 40, the structure obtained could again not be distinguished from the known gas-phase geometry, and elusive ad hoc explanations were no longer necessary.

4.4. Methyl Iodide (CH₃I). Initial experiments on methyl iodide also led to HCH bond angles that varied by several degrees, depending on the precise experimental conditions of temperature and concentration in the nematic phases.⁴¹ When, as in the case of methyl fluoride, vibration–reorientation coupling was incorporated, the same two assumptions as in ref 40 led to a satisfactory understanding of the different experiments, and again the solute structure was found to be indistinguishable from the gas-phase geometry. In a later paper, the role of vibration–reorientation interaction in CH₃I was completely neglected and large apparent variations in the HCH angle were obtained.⁴² A detailed study on ethane²⁶ indicated that the effects due to the vibration–reorientation coupling for a methyl group could be transferred reasonably well from one solute molecule to the next. Moreover, it was pointed out that transferring the vibration–reorientation contributions from methyl fluoride to methyl iodide removed the apparent discrepancies in the HCH angle to a large extent.

4.5. Ethane (CH₃CH₃). Ethane is the simplest molecule that shows large-amplitude vibrational motion in the form of internal rotation. This large-amplitude motion cannot be dealt with in a routine manner. Because of the high symmetry of the ethane molecule, the internal rotation belongs to a unique irreducible representation of the D_{3d} symmetry group and cannot couple to the remaining small-amplitude normal modes. Hence, the internal rotation can be dealt with separately and classically. An extensive study on ethane and 5 isotopologues was performed, and the observed dipolar couplings were analyzed including the contributions from harmonic and anharmonic force fields and the vibration–rotation interaction.²⁶ To estimate the latter contribution, the transferability of these corrections from the methyl group in methyl fluoride²⁵ was employed. All the observed dipolar couplings could be interpreted quite accurately on the basis of this complete analysis. The liquid-phase structure obtained was indistinguishable from the known accurate gas-phase geometry.

4.6. Benzene (C₆H₆). An extensive study on benzene in several liquid-crystal solvents showed that, even if harmonic vibrational corrections were included, the proton framework in the solute often deviated significantly from the expected hexagonal symmetry.⁴³ These deviations could be rationalized by assuming a number of ad hoc models in which an orientation-dependent deformation of the solute was assumed. In a later study the complete theory of vibration–reorientation coupling, as developed for methane with tetrahedral symmetry,^{24,28,36} was applied to less symmetrical solutes.^{44,45} With this complete description the apparent deviations from hexagonal symmetry could be explained in a natural manner. The structure obtained for benzene dissolved in various liquid-crystal solvents showed detailed agreement with the gas-phase geometry.

4.7. Azulene (C₁₀H₈) and Biphenylene (C₁₂H₈). In general, analysis of the ¹H NMR spectra of solutes in nematic solvents gives very accurate values of the dipolar couplings between pairs of protons – in principle these couplings can be used to

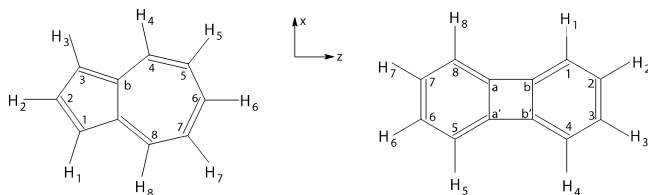


Figure 1. Azulene (left) and biphenylene (right).

determine the *relative* proton geometries (i.e., the overall shape of the solutes).

Absolute structures cannot be derived because the expressions for the dipolar couplings contain the product of structural and orientational order parameters, and one assumption is required to separate these products. Since there is no good way of knowing the order parameters, one internuclear distance has to be assumed as a scaling quantity. If vibration–reorientation interaction can be neglected, the relative structure is determinable from ratios of dipolar couplings, because the orientational parameters divide out of this ratio. However, in the presence of vibration–reorientation interaction this is no longer true. While only proton coordinates are reported in some of the literature, it is more common to “determine” the molecular geometry by either fitting the carbon skeleton inside the proton “cage”, or by measuring extra couplings between ^1H and ^{13}C .

Here we use the eight-proton spin solutes azulene and biphenylene to investigate the importance of *nonrigid* effects in structure determination of solutes that are more complicated than those discussed above, and for which adequate information to make a direct estimate of the vibration–reorientation interaction is not available. We shall compare structures obtained from the NMR spectra of these solutes in three different nematic solvents. Instead of comparing the six (azulene) or three (biphenylene) independent relative proton coordinates, we shall set the carbon geometry to that determined from electron diffraction studies for azulene⁴⁶ and biphenylene,⁴⁷ and shall fit the protons around this by varying six (azulene) or three (biphenylene) independent coordinates. The fits are performed in various ways, and values of the fitted coordinates so obtained are presented in Figures.

Azulene and biphenylene are interesting molecules whose structures have been the subject of various investigations, both in the gas phase^{46,47} and as solutes in liquid-crystal solvents.^{48–50} The NMR spectra of orientationally ordered azulene and biphenylene as solutes in nematic solvents are quite complicated. We reinvestigate both molecules partly because they are good candidates for testing the application of evolutionary algorithms to the analysis of the complicated spectra obtained from solutes (containing many protons) that are orientationally ordered in nematic solvents.^{15,16} These evolutionary algorithms lead to spectral assignments, and the dipolar couplings for azulene in 1132 and in a magic mixture of 55 wt % 1132 with EBBA (Table 1), and for biphenylene in 1132 and EBBA (Table 2) are readily obtained.

4.7.1. Azulene. The dipolar couplings so obtained for azulene, in conjunction with those published for azulene in EBBA,⁴⁸ are used for the present investigation. The 16 independent dipolar couplings obtained from each spectrum can be used to determine the relative proton structure of azulene (assumed to be planar), which is defined by six independent geometric coordinates—here we choose to vary distances $R(\text{CH}_1)$, $R(\text{CH}_4)$, and $R(\text{CH}_5)$ and angles $\angle\text{C}_2\text{C}_3\text{H}_3$, $\angle\text{bC}_4\text{H}_4$, and $\angle\text{C}_4\text{C}_3\text{H}_5$ (see Figure 1). The other structural parameters used for the calculations are given in Figure 1 of ref 48 and in ref 46. The distance

scale is fixed by the carbon skeleton and by setting $R(\text{CH}_2) = R(\text{CH}_6) = 1.09 \text{ \AA}$. There are, in addition, two orientational order parameters necessary to describe the orientational order of this C_{2v} symmetry molecule. Thus, the problem is overdetermined by eight couplings, and it is to be anticipated that a very accurate molecular structure should be obtainable.

First, we fit the experimental dipolar couplings from each nematic solvent to a rigid structure—the results for the three liquid-crystal solvents used are presented in columns 1–3 of Figure 2. As is easily seen (especially for the C–H distances) the structure differs significantly with solvent. One possible interpretation is that the structure *does* depend on solvent. However, this interpretation is not warranted because we have neglected vibrational and other *nonrigid* terms in the analysis.

Our original study (in EBBA) took effects of harmonic vibrations into account in the usual manner. Applying these same corrections for harmonic vibrations to all three spectra we obtain the results presented in columns 4–6 of Figure 2. Again, the structure appears to differ significantly with solvent.

For molecules as large as azulene, no experimental information about anharmonicities in the internuclear potentials is available. Of course one could envisage calculating the required anharmonicities employing sophisticated quantum-chemical calculations. For the 48 normal modes in azulene this would be a major undertaking without guarantees for success. The unavoidable differences between calculated and real anharmonicities would only lead to rather uncertain additional corrections to the experimental dipolar couplings. These corrections would come on top of corrections owing to the presence of the vibration–reorientation interaction discussed below. Larger total errors on the dipolar couplings would only serve to strengthen the conclusions of this paper. Therefore, in the case of azulene we limit ourselves to the r_α structure, rather than to the equilibrium structure r_e that can be obtained for molecules where experimental anharmonicities are available.³

The error limits reported in columns 1–6 of Figure 2 are those propagated from the measured errors in the dipolar couplings. For the EBBA spectrum, these are the standard deviations calculated by LEQUOR.⁵¹ For the other two spectra that were analyzed using EA, errors were estimated from the covariance matrix with the assumption that the line positions in the spectra are measurable to an accuracy of 1.0 Hz. The method is described in Meerts and Schmitt⁵² as “assigned fit”. We note that the experimental dipolar couplings are fitted to a model that involves structural parameters. It often happens that the dipolar couplings recalculated from the parameters obtained in the fit differ from the experimental ones by an amount larger than the experimental errors in the dipolar couplings. This indicates that the structural model is probably not perfect, and that the errors calculated from propagation of the experimental errors in the dipolar couplings are not realistic. To elucidate this point, in columns 7–9 of Figure 2 we repeat the vibrational fitting of columns 4–6, but now we take the rms of the fit of structural parameters to dipolar couplings into account by assigning an error of $\sqrt{(\text{rms}^2 + \text{spectrum fit error}^2)}$ to each dipolar coupling. Clearly, the error limits have increased as expected, but the differences between solvents are still outside these larger error limits.

The calculations so far make no attempt to account for possible effects of vibration–reorientation interaction. In the case of azulene (and biphenylene) these interactions are difficult to estimate since the detailed orientation mechanisms are unknown. Thus, it seems appropriate to estimate the neglect of *nonrigid* effects by adding a realistic error to the experimental

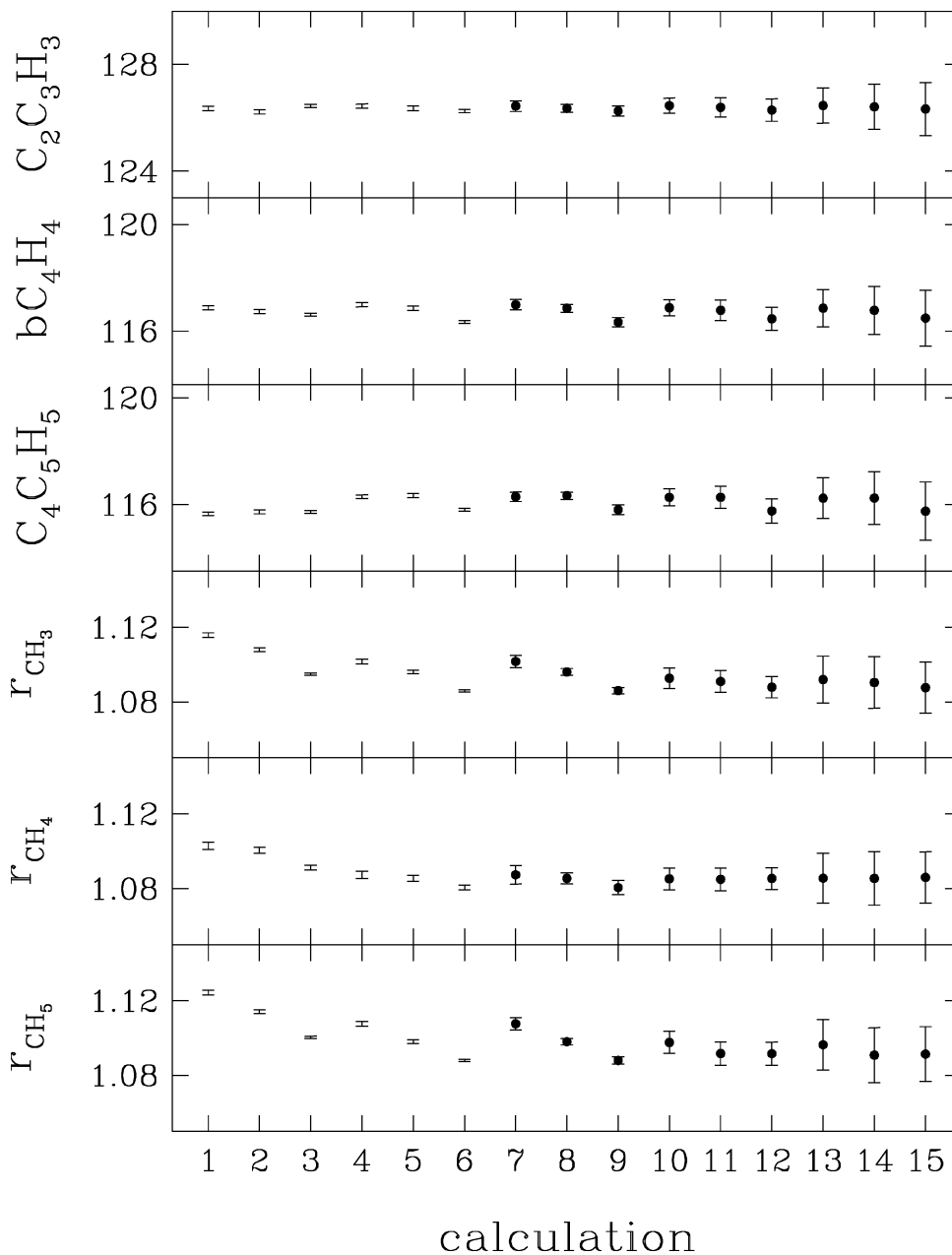


Figure 2. Azulene: fitting structural parameters to dipolar couplings. For each case, results are presented in solvent order 1132, MM, and EBBA. The error limits displayed for the structural parameters are those propagated from the errors assumed for the experimental dipolar couplings. Columns 1–3 are fits to a rigid structure. The errors used for the dipolar couplings are those obtained directly from the spectral analysis, err. All other columns (4–15) include corrections for harmonic vibrations to the dipolar couplings. Columns 4–6 use the spectrum errors err. For columns 7–9 the errors assigned to the dipolar couplings are $\sqrt{(\text{rms of fit of geometric parameters to dipolar couplings}^2 + \text{err}^2)}$. Errors used for columns 10–12 and 13–15 include a component that is scaled by $1/r^3$ using as basis the discrepancy found for benzene and acetylene. The errors in the dipolar couplings are then taken as $\sqrt{(1/r^3 \text{ scaled error}^2 + \text{err}^2)}$. The order parameters obtained from the fits of columns 13–15 are: $S_{zz} = 0.3230 \pm 0.0018$, $S_{xx} = 0.0255 \pm 0.0013$ for 1132; $S_{zz} = 0.2871 \pm 0.0018$, $S_{xx} = -0.0011 \pm 0.0011$ for MM; and $S_{zz} = 0.2677 \pm 0.0017$, $S_{xx} = -0.0550 \pm 0.0009$ for EBBA.

dipolar couplings that are utilized in the weighted least-squares fitting of structural parameters. To estimate values for these errors, we rely on the magnitudes of the *nonrigid* effects in other solutes, especially those discussed above. We conclude from eq 9 that the *nonrigid* contribution scales as $\partial d_{kl,\mu\nu}/\partial Q_m$ (from eq 5 we note that $d \propto r^{-3}$), hence to a first approximation we assume that $\partial d_{kl,\mu\nu}/\partial Q_m$ has negligible r dependence and we scale $D_{\mu\nu}^{\text{nonrigid}}$ values by $r_{\mu\nu}^{-3}$. Such an assumption would be reasonable for normal modes that do not appreciably affect the internuclear distance involved. For normal modes that change the relevant internuclear distance in linear fashion, a $r_{\mu\nu}^{-4}$ dependence would be more realistic. In the following we shall

present calculations based on an $r_{\mu\nu}^{-3}$ dependence, but we have checked exhaustively that our conclusions are not significantly affected if an $r_{\mu\nu}^{-4}$ dependence were assumed. In the context of the present paper the precise dependence on internuclear distance is therefore not a key element.

Benzene, which was studied in eight different liquid-crystalline solvents,⁴³ provides a test for this assumption. *Nonrigid* contributions for benzene in several nematic liquid crystals can be calculated from data reported in ref 45. The values found for phase IV are -6.714 , -0.540 , and -0.106 Hz for the ortho, meta and para couplings. If we take $D_{\text{ortho}}^{\text{nonrigid}} = -6.714$ Hz and use hexagonal symmetry (with r^{-3} scaling),

TABLE 3: The r_{α} Geometric Parameters for Biphenylene From Reference 47

parameter	value
C_1-C_b	$1.365 \pm 0.012 \text{ \AA}$
C_1-C_2	$1.415 \pm 0.012 \text{ \AA}$
C_2-C_3	$1.359 \pm 0.015 \text{ \AA}$
$C_a-C'_a$	$1.427 \pm 0.018 \text{ \AA}$
C_a-C_b	$1.518 \pm 0.006 \text{ \AA}$
$\angle C_b-C_b-C_1$	$122.5 \pm 0.6^\circ$
$\angle C_b-C_1-C_2$	$115.0 \pm 1.2^\circ$
$\angle C_1-C_2-C_3$	$122.5 \pm 1.2^\circ$

we estimate $D_{\text{meta}}^{\text{nonrigid}} = -1.3 \text{ Hz}$ and $D_{\text{para}}^{\text{nonrigid}} = -0.8 \text{ Hz}$, which are numbers that are somewhat larger than those reported in ref 45. To provide a “reasonable” estimate of the *nonrigid* effect, we choose the larger ortho coupling as a basis. Using the value of -6.714 Hz for $D_{\mu\nu}^{\text{nonrigid}}$ for benzene ortho protons (i.e., 102.1 Hz \AA^3), and applying $r_{\mu\nu}^{-3}$ scaling to provide other values, as before we add as errors to the experimental dipolar couplings the values $\sqrt{(1/r^3 \text{ scaling}^2 + \text{spectrum fit error}^2)}$. In general, the first term dominates, especially for near protons. The result of this fit is presented in columns 10–12 of Figure 2. The resulting fit is excellent, and the agreement among solvents is markedly improved over that in the earlier fits (columns 1–9): the variation of parameters is now within the parameter error limits. Calculations based on an $r_{\mu\nu}^{-4}$ dependence do not change this picture.

The rationale for using the larger benzene discrepancy is realized when we examine acetylene data. If we used results for acetylene (discussed above) to provide an estimate of the error that we should add to account for the *nonrigid* effect, then the added error would be 251.6 Hz \AA^3 for 1132 and 219.4 Hz \AA^3 for EBBA. We show in columns 13–15 of Figure 2 results obtained using the larger number for the scaling. It is of course difficult to define a precise number to use in general. However, the numbers of 100 and 250 Hz \AA^3 mentioned above are probably indicative of what we can realistically expect.

4.7.2. Biphenylene. The dipolar couplings obtained for biphenylene in 1132 and EBBA, in conjunction with those published for biphenylene in the magic mixture,⁵⁰ are also used for the present investigation. The 10 independent dipolar couplings obtained from each spectrum can be used to determine the relative proton structure of biphenylene (assumed to be planar), which is defined by three independent geometric coordinates—here we choose to vary the $R(\text{CH})$ bond distance (keeping it equal for the two independent C–H bonds, this being a sufficient criterion, in conjunction with the carbon skeleton, to enable separation of geometrical from orientational parameters) and the CCH angles $\angle C_b C_1 H_1$ and $\angle C_1 C_2 H_2$ (see Figure 1). The other structural parameters used for the calculations are given in Table 3. There are, in addition, two orientational order parameters necessary to describe the orientational order of this D_{2h} symmetry molecule. Thus, the problem is overdetermined by five couplings, and again it is to be anticipated that a very accurate molecular structure should be obtainable.

Fits (similar to those for azulene) were performed: to a rigid molecule (columns 1–3 of Figure 3); applying corrections from ref 50 for harmonic vibrations (columns 4–6 of Figure 3), but (as in the case of azulene) neglecting the effects of anharmonicity; including the rms of the fit of structure to dipolar couplings (columns 7–9 of Figure 3); using r^{-3} scaling with basis 102.1 Hz \AA^3 from data for the ortho coupling in benzene (columns 10–12 of Figure 3); and using r^{-3} scaling with the basis set from acetylene data to 251.6 Hz \AA^3 (columns 13–15 of Figure 3). As was the case for azulene, the results differ with

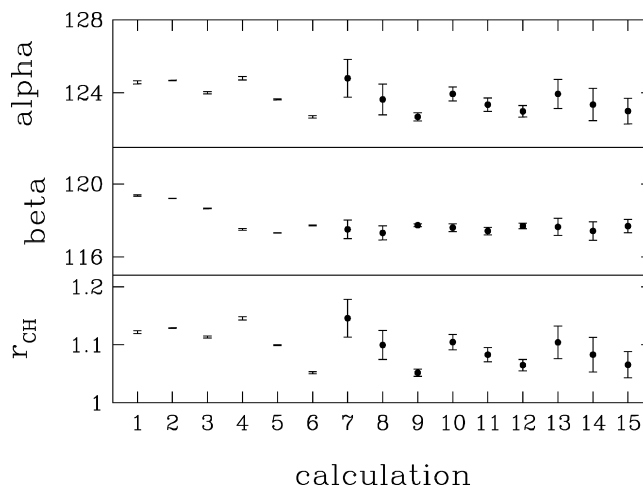


Figure 3. Biphenylene: fitting structural parameters to dipolar couplings. The columns represent the same fits as described in the caption to Figure 2. The order parameters obtained from the fits of columns 13–15 are: $S_{zz} = 0.369 \pm 0.008$, $S_{xx} = -0.0020 \pm 0.0014$ for 1132; $S_{zz} = 0.308 \pm 0.007$, $S_{xx} = -0.0244 \pm 0.0013$ for MM; and $S_{zz} = 0.355 \pm 0.007$, $S_{xx} = -0.0957 \pm 0.0020$ for EBBA.

solvent for the first three fits. Unlike azulene, in this case scaling the *nonrigid* effect to the benzene value gives parameters that do not agree within the error limits, although the level of disagreement is not as bad as for the first three fits. When we use the larger acetylene value for scaling we do obtain agreement among solvents. As with azulene, these conclusions are not affected significantly if an $r_{\mu\nu}^{-4}$ dependence is assumed.

5. Conclusions

When solute molecules are dissolved in uniaxial nematic liquid crystals, in general dipolar couplings can be obtained with a high degree of accuracy. Moreover, the use of sophisticated EAs has significantly extended the range of spectral fitting methods to larger spin systems. In practice, however, it is a formidable challenge to “translate” these dipolar couplings into a similarly accurate molecular structure. The reason is that important corrections for harmonic and anharmonic vibrational motion and vibration–reorientation interaction must be incorporated. A complete analysis can only be performed for a very limited collection of small, well-characterized molecules. For larger solutes anharmonic force fields are commonly not available, and one is usually limited to the application of harmonic corrections. Hence, equilibrium structures cannot be obtained, and comparisons with structures obtained with other experimental methods that equally suffer from the lack of anharmonic force fields require great care. In addition, possible effects of the neglect of vibration–reorientation interactions on structures of larger solutes have not been considered so far.

From the studies of small solute molecules in which all the corrections to the dipolar couplings that are required from theory have been applied, a number of important conclusions can be drawn. First, the solute structures derived from such a complete analysis in which all the (often sizable) corrections have been incorporated in as much detail as possible, correspond extremely well to the experimental gas-phase structures known from well-tested methods such as microwave spectroscopy and electron diffraction. Also, the good agreement with gas-phase structures derived from modern, routinely available *ab initio* methods such as Gaussian is pleasing. Second, these observations support the notion that solute–solvent interactions are relatively weak and do not affect the electronic structure of the solute to a significant

degree. The vibration-reorientation interaction does not lead to any significant "distortion" of the solute molecule.

For larger molecules for which detailed information on molecular force fields is mostly lacking, the situation is much less promising. Notwithstanding the fact that with modern spectral fitting methods dipolar couplings can be extracted from very complicated NMR spectra with high accuracy (~ 0.1 Hz), the neglect of the various corrections cannot lead to a correspondingly accurate experimental solute structure, especially when the degree of orientational order is small. Depending on the precise circumstances, uncertainties in bond lengths of $\sim 10^{-1}$ to 10^{-2} Å and in bond angles of ~ 1 to 2 degrees are not uncommon. The interpretation of such difference in terms of ad hoc explanations is a very dangerous and usually unwarranted undertaking.

The present studies on azulene and biphenylene are a case in point. These molecules that occur in a single conformation have been studied in various nematic phases. Since information on anharmonic force fields is not available, an equilibrium structure cannot be derived. Moreover, the fact that only rather crude estimates can be used for inclusion of the vibration-reorientation interaction adds significantly to the uncertainties in the final structures. However, the results for azulene and biphenylene do emphasize the importance of accounting for the *nonrigid* contributions to the dipolar couplings if one wishes to extract accurate molecular structures from the NMR spectra of orientationally ordered molecules. These corrections are difficult and tedious, and require knowledge about the orientation mechanisms. Hence, it is important to take account of *nonrigid* effects in some other manner—here we suggest to add an error that is proportional to $1/r_{\mu\nu}^3$. A reasonable suggestion would seem to use the benzene or acetylene *nonrigid* contributions as a basis, and to add errors in the range of $100\text{--}250$ Hz $\text{Å}^3 \times 1/r_{\mu\nu}^3$. When such errors are incorporated into the fitting procedure, structures of solutes in different liquid-crystal solvents are essentially identical within realistic error limits, thus refuting the notion of solvent-dependent structures. Moreover, the structures obtained correspond very well to gas-phase geometries. Neither assuming an $r_{\mu\nu}^{-4}$ dependence for the *nonrigid* effect, nor the inclusion of calculated values for possible anharmonicities would change these conclusions.

In summary, the magnitudes of the contributions to the dipolar couplings arising from the vibration-reorientation interaction obtained in small, well-characterized molecules can be taken as approximate guidance for the uncertainties associated with the observed dipolar couplings in larger molecules. As the interaction between vibrational and reorientational motions does not scale with the degree of order, better estimates of molecular structure should result from NMR spectra taken with a high degree of solute orientational order. In the case of larger molecules that undergo conformational change, the situation is more complicated. Even in the normal harmonic approximation the description of low-frequency, large-amplitude vibrational modes breaks down. Hence, that type of internal motion should be dealt with separately.

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