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The stable conformations of 4,4'-dichloro-*trans*-stilbene in solution by liquid crystal NMR spectroscopy

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HIGHLIGHTS

- ▶ 4,4'-Dichloro-*trans*-stilbene is the prototype of biologically important stilbenes.
- ► Conformations of 4,4'-dichloro-trans-stilbene in solution were studied by LXNMR.
- ▶ Stable structures: C_2 (rings disrotated of ~19°) and C_i (rings conrotated of ~19°).

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ABSTRACT

The mechanisms conferring to the *trans*-stilbene derivatives their well known important biological properties are not yet completely clear; then, it is reasonable to suppose that their conformational equilibrium could play some kind of role (as found for many other molecules of pharmacological interest). In this scenario, the 4.4'-dichloro-*trans*-stilbene (DCS) can be considered as the prototype of a series of stilbenes substituted in 4.4'-dichloro-*trans*-stilbene (DCS) can be considered as the prototype of a series of stilbenes substituted in 4.4'-dichloro-*trans*-stilbene (DCS) can be considered as the prototype of a series of stilbenes substituted in 4.4'-dichloro-*trans*-stilbene (DCS) is solution by Liquid Crystal NMR Spectroscopy (LXNMR), one of the best techniques to obtain this kind of information in the liquid state of matter. Our results show that the molecule is basically not planar: the most populated conformations we found are (a) the couple of symmetry-related, propeller-like structures, belonging to the C_2 point group and characterized by the phenyl rings *disrotated* of about 18.7° with respect to the vinyl plane and (b) the couple of symmetry-related C_i structures (where the rings are parallel, like the pedals of a cycle) having this time the two rings *conrotated* of an angle of ~18.7° with respect to the vinyl fragment.

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1. Introduction

Stilbene derivatives are a class of very interesting molecules, including natural compounds (first of all, the well known 3,5,4'-trihydroxy-trans-stilbene, called resveratrol) exhibiting a plethora of beneficial effects (an ample survey of which is given, for example, in [1] and in the references cited therein). In particular, a resveratrol analog, the 4,4'-dihydroxy-*trans*-stilbene (DHS), showed recently to have important antioxidant and antiestrogenic activities as well as other very interesting biological properties ([1–3] and references therein). Despite their recognized healthy properties, the mechanisms by which these compounds are effective are not yet completely clear [1]. A rigorous investigation aiming at collecting all the useful elements to shed more light on the nature of these effects cannot leave out of consideration the role of the conformational equilibrium of these derivatives. In order to address the general problem of stable conformations of 4,4'-disubstituted analogs of trans-stilbene in liquid phase, we decided to undertake the study of the prototype molecule 4,4'-dichloro-trans-stilbene (DCS) by resorting to the very powerful techniques of Liquid Crystal NMR Spectroscopy (LXNMR), recently used to investigate the conformational distribution of trans-stilbene [4] (for a general survey of LXNMR fundamentals and examples of application, the reader is referred to Refs. [5-13]. The DCS molecule is shown in Fig. 1, where also three possible stable structures, with their point groups, are represented: C_{2h} (full planar molecule), C_2 (disrotatory, propeller-like conformation, where the rings are tilted at the same angle with respect to the vinyl plane, i.e. $\phi_1 = \phi_2$, and C_i (conrotatory conformation, where the rings are parallel to each other, i.e. tilted at angles equal in magnitude but opposite in sign: $\phi_1 = -\phi_2$). The DCS has been on purpose synthesized, as described in the following Section 3, then dissolved in the nematic solvent ZLI1132 [4], where its anisotropic ¹H NMR spectrum has been recorded at room temperature. The successful analysis of the NMR spectrum led us to the knowledge of the direct dipolar coupling constants D_{ij} between the i-j pairs of hydrogen nuclei present in

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Fig. 1. Structure, torsional angles and hydrogen numbering of 4,4'-dichloro-trans-stilbene. Below, the possible stable rotamers (with the corresponding point groups) are also shown.

the molecule; then the obtained D_{ij} values were interpreted by means of the AP-DPD model ([4] and references therein) in order to obtain the sought conformational distribution.

In the following, all these phases of the work will be described in detail, till the conclusions and considerations on the treated case.

2. Theory

As said in Section 1, a successful LXNMR spectral analysis allows to obtain the invaluable experimental data represented by the observed D_{ii}^{obs} dipolar (or direct) couplings between the *i*th and *j*th magnetically active nuclei of the studied molecule (in this case, the protons of DCS). The observed dipolar couplings result from partial averages over all the relevant motions of the molecule (internal vibrations and rotations as well as the whole molecular tumbling) with respect to the external magnetic field B_0 , conventionally aligned along the Z direction of the Laboratory reference system. When interproton dipolar couplings only are considered (as in the presently studied case) the approximation of neglecting the effects of high-frequency, small-amplitude molecular vibrations is quite safe [4,6]. Moreover, small flexible molecules undergoing large-amplitude internal rotations (characterized, for DCS, by the ϕ_1 and ϕ_2 torsional degrees of freedom) can be described by explicitly taking into account the torsional probability distribution $p(\phi_1, \phi_2)$. Following what said above, the observed dipolar couplings can be given, with a good approximation, by the following formula ([4] and references therein):

$$D_{ij}^{obs} \approx \left(\frac{3\cos^2 \alpha - 1}{2}\right) \\ \cdot \left[\frac{2Z_{iso}}{3Z} \int_{\phi_2} \int_{\phi_1} p_{iso}(\phi_1, \phi_2) W(\phi_1, \phi_2) \sum_{\rho\sigma} S_{\rho\sigma}(\phi_1, \phi_2) D_{ij}^{\rho\sigma}(\phi_1, \phi_2) d\phi_1 d\phi_2\right]$$
(1)

It is the presence, in this expression, of the function $p_{iso}(\phi_1, \phi_2)$ (i.e., the conformational probability distribution of the solute in a "virtual" isotropic solution at the experiment temperature; see below for more details) that makes the content of information of the observed dipolar couplings so appealing for conformational studies. Anyway, in order to fully understand the meaning of Eq. (1),

it needs to describe all its ingredients. The angle α is that between B_0 , along the *Z* LAB direction, and $\hat{\mathbf{n}}$, the director of the mesophase located by the Euler angles { β , γ } in the molecule-fixed frame; the terms $S_{\rho\sigma}(\phi_1, \phi_2)$ (named "order parameters" and constituting the so-called Saupe matrix [5]) describe the degree of statistical alignment of the solute molecular axes to the director, and can be written as follows:

$$S_{\rho\sigma}(\phi_1,\phi_2) = \frac{\int \left((3[\cos\omega_{\rho}]_{(\beta,\gamma)} [\cos\omega_{\sigma}]_{(\beta,\gamma)} - \delta_{\rho\sigma})/2 \right) p_{\Omega}(\beta,\gamma,\phi_1,\phi_2) \sin\beta \, d\beta \, d\gamma}{\int p_{\Omega}(\beta,\gamma,\phi_1,\phi_2) d\beta \, d\gamma}$$
(2)

where ω_{ρ} (a function of β and γ) is the instantaneous angle between $\hat{\mathbf{n}}$ and the ρ axis of the solute reference system, and $\delta_{\rho\sigma}$ is the Kronecker delta function. The probability function $p_{\Omega}(\beta, \gamma, \phi_1, \phi_2)$ of Eq. (2) is given by:

$$p_{\Omega}(\beta,\gamma,\phi_1,\phi_2) = \frac{\exp[-U_{ext}(\beta,\gamma,\phi_1,\phi_2)/k_BT]}{Q}$$
(3)

with

$$Q = \int \exp[-U_{ext}(\beta,\gamma,\phi_1,\phi_2)/k_B T] \sin\beta \, d\beta \, d\gamma \, d\phi_1 \, d\phi_2 \tag{4}$$

where k_B is the Boltzmann constant and $U_{ext}(\beta, \gamma, \phi_1, \phi_2)$ is a solutesolvent purely anisotropic external orientational potential. It is essential to emphasize that $p_{\Omega}(\beta, \gamma, \phi_1, \phi_2)$ is related to $p_{LC}(\beta, \gamma, \phi_1, \phi_2)$ (the probability of finding the mesophase director (β, γ) -oriented in the solute-fixed frame, when the probe-molecule is in its { ϕ_1, ϕ_2 } conformation in the liquid crystalline solution) and to $p_{iso}(\phi_1, \phi_2)$ by the following formula:

$$p_{LC}(\beta,\gamma,\phi_1,\phi_2) = \frac{p_{\Omega}(\beta,\gamma,\phi_1,\phi_2)p_{iso}(\phi_1,\phi_2)W(\phi_1,\phi_2)Z_{iso}}{Z}$$
(5)

where the partition functions Z_{iso} and Z and W of Eqs. (1) and (5) are the following:

$$Z_{iso} = \int p_{iso}(\phi_1, \phi_2) d\phi_1 d\phi_2 \tag{6}$$

$$Z = \int W(\phi_1, \phi_2) \cdot p_{iso}(\phi_1, \phi_2) d\phi_1 d\phi_2$$
⁽⁷⁾

$$W(\phi_1, \phi_2) = \int \exp[-U_{\text{ext}}(\beta, \gamma, \phi_1, \phi_2)/k_B T] \sin\beta \, d\beta \, d\gamma \tag{8}$$

Finally, in Eq. (1), $D_{ij}^{\rho\sigma}(\phi_1, \phi_2)$ are the cartesian components, given in the molecular frame, of the D_{ij} tensor of the dipolar coupling between the *i*th and *j*th nucleus:

$$D_{ij}^{\rho\sigma}(\phi_1,\phi_2) = -\frac{\kappa_{ij}}{r_{ij}^3(\phi_1,\phi_2)} \\ \cdot \left[3\cos\vartheta_{ij}^{\rho}(\phi_1,\phi_2)\cos\vartheta_{ij}^{\sigma}(\phi_1,\phi_2) - \delta_{\rho\sigma}\right]$$
(9)

with

$$K_{ij} = \frac{\mu_0 \hbar \gamma_i \gamma_j}{16\pi^2} \tag{10}$$

 γ_i and μ_0 being respectively the *i*th nuclear magnetogyric ratio and the vacuum magnetic permeability, and ϑ_{ij}^{ρ} the angle between the distance vector r_{ij} and the ρ molecular axis. In order to calculate the above mentioned order parameters $S_{\rho\sigma}(\phi_1, \phi_2)$, it is necessary to adopt a theoretical model describing the interdependent conformational–orientational problem. Here, we used the approximation called AP-DPD approach (Additive Potential [14,15] for the treatment of the ordering interactions, combined with the Direct Probability Description of the torsional distribution $p_{iso}(\phi_1, \phi_2)$) [16–24]. According to the DPD method, the $p_{iso}(\phi_1, \phi_2)$ of DCS was modeled directly as a sum of bidimensional Gaussian functions [4], by using the following general form:

$$p_{iso}(\phi_1, \phi_2) \propto \sum_{\text{(over the different } C_X - symmetry structures)} \frac{w_{(C_X)}}{n_{(C_X)}} \\ \cdot \sum_{k=1}^{n_{(C_X)}} e^{-\left(\frac{\sin^2\left(\phi_1 - \left(\phi_1^M\right)_{C_X}^k\right)}{2h_1^2} + \frac{\sin^2\left(\phi_2 - \left(\phi_2^M\right)_{C_X}^k\right)}{2h_2^2}\right)}\right)}$$
(11)

...

where $n_{(C_X)}$ is the number of rotamers belonging to the C_X point group; $w_{(C_X)}$ is the global relative weight of the C_X structures (so that $\sum_{(\text{over all the } C_X)} w_{(C_X)} = 1$); $(\phi_i^M)_{C_X}^k$ represents, for the *i*th torsion, the twist angle corresponding to the *k*th of the $n_{(C_X)}$ most probable conformations with C_X symmetry; and, finally, h_1 and h_2 give the width at half maximum height along each dimension of the bidimensional Gaussians (the recently introduced [4] use of sinusoidal functions in the exponent of the Gaussians assures the right periodicity of the p_{iso} probability distribution, simplifying its analytical expression with respect to those used in the past papers [16–24]). The term $U_{ext}(\beta, \gamma, \phi_1, \phi_2)$ of Eqs. (3), (4), and (8) represents, as said above, the purely anisotropic external orientational potential that, within the AP model approach [14,15], is approximated as follows:

$$U_{ext}(\beta, \gamma, \phi_1, \phi_2) = -\varepsilon_{2,0}(\phi_1, \phi_2)C_{2,0}(\beta) - 2\text{Re}(\varepsilon_{2,2}(\phi_1, \phi_2))\text{Re}(C_{2,2}(\beta, \gamma))$$
(12)

where the $C_{2,m}(\beta, \gamma)$ are modified spherical harmonics [25], and the $\varepsilon_{2,m}(\phi_1, \phi_2)$ are the elements of suitable conformation-dependent solute–solvent interaction tensors. Following the AP philosophy, the $\varepsilon_{2,m}(\{\varphi\})$ elements (where $\{\varphi\}$ represents the proper *n*-uple of torsional variables) are constructed as sums of conformational-ly-independent terms $\varepsilon_{2,p}(l)$ representing the single contributions of each rigid fragment *l* in the molecule to the whole interaction tensors:

$$\varepsilon_{2,m}(\{\varphi\}) = \sum_{l} \sum_{p} \varepsilon_{2,p}(l) D_{p,m}^2(\Lambda_{\varphi}^l)$$
(13)

(the second-rank Wigner rotation matrix $D_{p,m}^2(\Lambda_{\phi}^l)$ [25] relates the conformation-dependent Λ_{ϕ}^l orientation of the *l*th molecular subunit to the molecule-fixed reference frame). The unknown $\varepsilon_{2,p}(l)$ values are adjusted to reproduce at best the experimental data. Once they are known, following the equations given above, it is possible to predict the behavior of the order parameters as a function of the molecular conformation. This theoretical background will be operatively described in Section 4.

3. Experimental

3.1. Synthesis of 4,4'-dichloro-trans-stilbene

The DCS has been prepared following the procedure described in [26]. The 4-chlorobenzyl-phosphonate (1.19 g, 4.53 mmol) and sodium methoxide (270 mg, 4.99 mmol, 10% excess) were dissolved in dry dimethylformamide (25 ml) in a 250 ml RB flask fitted with a thermometer, calcium chloride guard tube, dropping funnel and magnetic stirrer. A solution of 4-chlorobenzaldehyde (640 mg, 4.57 mmol) in dry dimethylformamide (10 ml) was added dropwise, with stirring and cooling in an ice-bath (the temperature of the reaction was maintained between 30 °C and 40 °C). The reaction mixture was left stirring at room temperature for \sim 20 h, then hydrolyzed with water (25 ml). The precipitated product was collected on a filter, washed with water and freed of the solvent at reduced pressure. Then, the 4,4'-dichloro-trans-stilbene obtained was further purified by column chromatography with Merk 60 silica gel (70-230 mesh) and with hexane as eluent. Finally, the solid DCS weighed 0.81 g (3.25 mmol, 42%).

3.2. Preparation of the sample, NMR experiment and analysis of ${}^{1}\text{H}$ LXNMR spectrum

A dilute solution (approximately 5 wt.%) was prepared by dissolving the DCS (previously synthesized as described above) in the commercial nematic solvent ZLI1132 (from Merk). The sample was heated a few times up to its nematic-isotropic transition temperature $T_{\rm NI}$ and strongly shaken to homogenize the solution; then, it has been left to cool slowly in the magnetic field of the NMR spectrometer. The experimental ¹H LXNMR spectrum, shown in Fig. 2. was recorded at room temperature (298 K) on a Bruker Avance 500 MHz (11.74 T) instrument. The first step of the analysis of such a complex spectrum requires a quite good estimation of the spectral parameters, which must be close enough to the correct set so that the trial parameters can be used in a successful iterative analysis. The starting values of chemical shifts δ_{ii} were taken from the routine analysis of the proton NMR spectrum of an isotropic solution of DCS dissolved in $CDCl_{3}$; the scalar couplings J_{ii} were assumed to have the usual values [4], while two different sets of dipolar couplings were produced by tentatively fixing the geometry of the molecule in both planar, C_{2h} symmetry, and slightly non-planar, C₂ symmetry, conformation. As already observed for the case of *trans*-stilbene [4], the sets of D_{ij} obtained by fixing DCS in its planar conformation gave simulated trial spectra (corresponding to different sets of D_{ij}^{trial} obtained as functions of the S_{ij} variables) invariably showing a distribution of lines completely incompatible with the experimental one; so they were necessarily rejected, together with the hypothesis of the full planarity of the molecule.

On the contrary, the spectrum simulated with the set of dipolar couplings obtained by assuming a C_2 conformation with a torsion angle $\phi_1 = \phi_2$ of about 17° (similar to what previously found for *trans*-stilbene [4]) and the longitudinal and biaxiality order parameters having, respectively, the trial values of $S_{long} = 0.6$ and $S_{biax} = 0.12$ showed a certain similarity, in terms of total width and line distribution, with the experimental one. Starting from this set of dipolar couplings, the analysis of the spectrum was successfully carried out by using a home-made iterative computer program called ARCANA [27]: the resulting observed dipolar



Fig. 2. The 500 MHz ¹H LXNMR experimental spectrum (bottom, in blue) of 4,4'-dichloro-*trans*-stilbene dissolved in the liquid crystalline nematic mesophase ZLI132 at 298 K. For comparison, the spectrum calculated by using the D_{ij}^{obs} spectral parameters (obtained from the analysis and reported in Table 1) is also shown, in black, at the top of the figure.

couplings are reported in Table 1 (third column, where the errors affecting the D_{ij}^{obs} report on the accuracy with which ARCANA extracts the dipolar coupling values from the peak positions of the experimental spectrum), whereas the calculated spectrum is shown in Fig. 2 (top).

4. Conformational analysis: results and discussion

We think at this point it can be useful, for sake of clarity, to spend few words once more emphasizing the distinctive feature of Eq. (1), making the LXNMR technique so useful for studying the conformations of flexible molecules in solution. As said above, the p_{iso} function in the formula allows for the determination of the conformational probability from the experimental dipolar couplings. This distribution should be considered, in principle, as the "real" conformational distribution of our solute in a "conventional" isotropic liquid, sharing with the used liquid crystalline solvent (at the work temperature, of course) the same physical properties determining the thermodynamics of the solution (as, for example,

Table 1

Chemical shifts $\delta_{ij} = v_i - v_j$, scalar couplings J_{ij} (assumed as in [4]) and observed dipolar couplings D_{ij}^{abs} (*i* and *j* labels as in Fig. 1) from the analysis of ¹H LXNMR spectrum of 4,4'-dichloro-trans-stilbene dissolved in ZLI1132. In the last column, the D_{ij}^{AP-DPD} obtained by AP-DPD method (see Section 2), are reported for comparison. Finally, the whole agreement is given by the RMS (the root mean square target function) between AP-DPD-calculated and observed dipolar couplings.

i, j	J_{ij} (Hz)	D ^{obs} _{ij} (Hz)	$D_{ij}^{\text{AP-DPD}}$ (Hz)
1, 2	8.00	-4860.10 ± 0.02	-4860.20
1, 3		31.86 ± 0.03	31.90
1, 4	2.00	371.32 ± 0.06	370.09
1, 5		-458.92 ± 0.03	-459.33
1, 6		-165.66 ± 0.02	-164.26
1, 9		-1881.08 ± 0.04	-1881.07
1, 10		-2965.13 ± 0.05	-2965.13
2, 3	2.00	373.17 ± 0.05	374.87
2,6		-76.77 ± 0.04	-75.50
2, 9		-440.17 ± 0.05	-439.78
2, 10		-442.16 ± 0.05	-442.32
9, 10	17.50	1020.72 ± 0.07	1020.22
		δ_{ij} (Hz)	
1, 2		-115.23 ± 0.04	
9, 2		-206.54 ± 0.04	

polarity, density, etc.), with the exception of its ordering power (in other words, unlike the $p_{IC}(\phi_1, \phi_2)$ of Eq. (5), $p_{iso}(\phi_1, \phi_2)$ is in principle free from possible conformational effects induced by the orientational ordering of the mesophase). In the light of the previous sections, the basic steps leading to the LXNMR determination of the rotameric distribution of the molecule, as well as of its conformational-dependent ordering (very useful to investigate orientational mechanisms [28-32], to which we are however not interested in this work) can be quickly recalled: the dipolar coupling tensor $D_{ii}^{\rho\sigma}(\phi_1,\phi_2)$ (for each (ϕ_1,ϕ_2) conformation and for each *i*–*j* pair of hydrogens) is obtainable on the basis of a chosen molecular geometry, whereas the interdependent Saupe matrices $S_{\rho\sigma}(\phi_1,\phi_2)$ and torsional distribution $p_{iso}(\phi_1,\phi_2)$ are derived from a fit of the experimental data set (represented by the observed direct couplings D_{ij}^{obs} obtained from the analysis of the ¹H LXNMR spectrum) by assuming a model (in our case, the above mentioned AP-DPD) for their dependence upon the (ϕ_1, ϕ_2) angles. For DCS, as usually done in literature [4,7,17], the phenyl rings and the vinyl "rigid" fragments were assumed to keep a fixed structure as they rotate relative to each other. Moreover, each ring was assumed to have a $C_{2\nu}$ symmetry, so requiring a couple of interaction parameters $\varepsilon_{2,0}^{R}$ and $\varepsilon_{2,2}^{R}$; on the contrary, the *ene* group, assumed as effectively described by an axially-symmetric interaction tensor, needs a single independent element $\varepsilon_{2,0}^{(H_6-C=C-H_7)}$, the component along the C=C bond direction. Then, we tried to reproduce the whole set of D_{ii}^{obs} (Table 1), assuming the same geometries of the fragments adopted for trans-stilbene and given in [4] and adjusting (in a iterative way, by a non-linear fitting program based on the gradients method [33]), the following parameters: the $\mathcal{E}_{2,0}^{R}$, $\mathcal{E}_{2,2}^{R}$ and $\mathcal{E}_{2,0}^{(H_{0}-C=C-H_{7})}$ interaction tensor parameters of Eq. (13); the $\phi_{1}^{M} = \pm \phi_{2}^{M}$ angle, the $h_{1} = h_{2}$ value and the $w_{(C_{2})} = 1 - w_{(C_{1})}$ weight of Eq. (11). This has been made in order to minimize the RMS (root mean square) target function:

$$\text{RMS} = \left\{ M^{-1} \sum_{i < j} \left[D_{ij}^{obs} - D_{ij}^{(\text{calc_by_AP-DPD})} \right]^2 \right\}^{\frac{1}{2}}$$
(14)

being M = 12 the number of independent couplings. It is worth emphasizing that ϕ_1^M , h_1 and $w_{(C2)}$ can be varied independently, but with the constraint that $p_{iso}(\phi_1, \phi_2)$, sampled in this case every 3° torsional steps, is normalized (in particular, because of the molecular symmetry, we normalized the distribution function for $-45^\circ \le \phi_1 \le 45^\circ$ and $-45^\circ \le \phi_2 \le 45^\circ$). By the optimized values of iteration parameters, reported in Table 2 (more details are given

 Table 2

 Adjusted values of the iteration parameters

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required	by the A	AP-D	PD	approach.	

	DCS in ZLI1132
$\phi_1^M = \pm \phi_2^M (\circ)$	18.69 ± 0.17
$h_1 = h_2 (\circ)$	4.66 ± 2.64
$W_{(C_2)}$	0.63 ± 0.01
$\varepsilon_{2,0}^{R}$ (RT)	1.702 ± 0.002
$\varepsilon_{2,2}^R$ (RT)	0.720 ± 0.004
$e^{(H_6 - C = C - H_7)}$ (RT)	0.291 ± 0.015



Fig. 3. Experimental probability distribution $p_{iso}(\phi_1, \phi_2)$ for DCS dissolved in the nematic solvent ZLI1132 at 298 K, obtained by the LXNMR conformational analysis.

in [34]) we were finally successful in reproducing the observed direct couplings with a very low, highly satisfactory RMS of just 0.85 Hz (the single dipolar couplings $D_{ij}^{\text{AP-DPD}}$ calculated by this approach are reported, for comparison, in the last column of Table 1).

The surface $p_{iso}(\phi_1, \phi_2)$, resulting from the procedure described above, is shown in Fig. 3. The main feature of the obtained $p_{iso}(\phi_1, \phi_2)$ function is certainly represented by the existence of four symmetry related maxima of the probability function, corresponding to the C_2 (absolute maxima) and C_i (relative maxima) structures characterized by having, respectively, $\phi_1^M = \phi_2^M$ and $\phi_1^M = -\phi_2^M$, with $\phi_1^M = 18.69^\circ$ (see Table 2).

The result obtained about the locations of the stable rotamers of DCS is very close to that of *trans*-stilbene [4], the magnitude of torsional angles being $\sim 18.7^{\circ}$ for DCS vs $\sim 17^{\circ}$ for trans-stilbene. This basically indicates very limited effects of the 4,4' Cl-substitutions on the positions of the conformational minima, as reasonably expected. Also the relative weights $w_{(C_X)}$ of the two structures C_2 and C_i in DCS (related to the heights of the peaks of Fig. 3 and amounting to $w_{(C_2)} = 63\%$ and $w_{(C_i)} = 37\%$) are not far from what found for *trans*-stilbene (where the ratio $w_{(C_2)}$: $w_{(C_i)}$ was 59:41 in percentage [4]). Continuing with the comparison, the $p_{iso}(\phi_1, \phi_2)$ distribution we obtained for DCS is characterized by sharper peaks with respect to that of trans-stilbene (as shown by comparing Fig. 3 of this work with Fig. 4 of [4]). From a physical point of view, this would seem to suggest that DCS is more confined in the vicinity of its conformational minima with respect to the trans-stilbene molecule; anyway, in our opinion, this simple deduction should be more carefully and critically evaluated. As a matter of fact, the sharpness of the peaks is related to the magnitude of the h_i parameters of Eq. (11), determining the width at half-maximum height along each dimension of the bidimensional Gaussian. The value $h_1 = h_2 = 10^\circ$ for *trans*-stilbene (Table 2 of [4]) has been obtained by a parametrical ("trial and error") adjustment process; then, it is difficult to estimate the possible error affecting it. On the contrary, the smaller value $h_1 = h_2 = 4.7^\circ$ for DCS (Table 2) resulted from a fitting of the experimental data where the h parameter has been used as a variable by a computer iteration process; so we can assess it is affected by a quite high error of ±2.64°, leading to a window of possible *h* values ranging from $\sim 2^{\circ}$ to $\sim 7.5^{\circ}$. This indeterminacy on the "real" value of h makes the results for DCS and *trans*-stilbene more similar than it seems apparently. Finally, for sake of completeness, the $p_{LC}(\phi_1, \phi_2)$ too has been determined and compared to the $p_{iso}(\phi_1, \phi_2)$. The two distributions resulted to be basically very similar; being anyway the peaks of the $p_{\rm LC}(\phi_1, \phi_2)$ slightly sharper than those of $p_{\rm iso}(\phi_1, \phi_2)$. From the comparison, one could be induced to think that this is probably due to the "orienting power" exerted by the liquid crystal on the solute molecule (and absent in the $p_{iso}(\phi_1, \phi_2)$ distribution). Anyway this is just a possible intuitive explanation, not necessarily "the right one"; in particular, it cannot be generalized (in our experience, for other solutes and other solvents this kind of effect is not always observed; see, for example, [22]).

5. Conclusions

Four stable conformations, two by two symmetry related (represented by a couple of global minima, where the molecule exhibits a propeller-like C_2 symmetry, and a couple of C_i local minima, where the rings are "conrotated" of the same angle) have been found for the DCS molecule in a nematic solution, by the well tested experimental method of LXNMR conformational analysis. Given that DCS can be reasonably considered as the prototype molecule of many different compounds with innumerable properties (see Section 1), we think that the results of this work could contribute to a better understanding of useful structure–property relationships.

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