

LIQUID CRYSTALS AND CHIRALITY : APPLICATION TO THE DETERMINATION
OF ABSOLUTE CONFIGURATIONS AND TO THE CONFORMATIONAL
ANALYSIS OF BIARYLS

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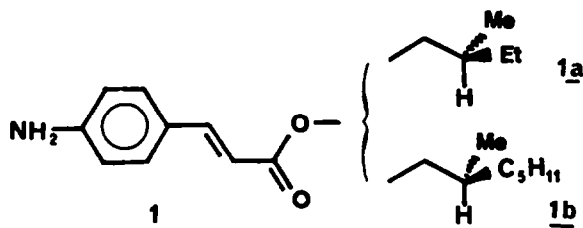
ABSTRACT - Nematic liquid crystals are extremely sensitive to optically active molecules, which at very low concentration, convert them into cholesteric liquid crystals. It will be shown that conformational factors are extremely important in determining the twisting powers of optically active trans stilbene oxide and biaryl molecules in nematic phases. The results showed that it is possible to correlate the absolute configurations of optically active bridged biaryl compounds and also the conformation (cisoid or transoid) of optically active open-chain biaryls to the sign of their twisting powers in biphenyl nematics, this liquid crystal method being in some cases complementary to CD spectroscopy.

More than 60 years ago, Friedel¹ described the close relationship between nematic and cholesteric liquid crystals : a small amount of a chiral compound, cholesteryl benzoate, dissolved in a nematic phase induces a cholesteric. The next papers on this topic appeared 40 years later by Chistiakov², Cano³ and by Buckingham⁴ who pointed out that a continuous change of a nematic phase to a cholesteric mesophase may be achieved by adding small amounts of optically active molecules, such as D-tartaric acid, which do not form by themselves a mesophase. Following the publication of Buckingham's paper, numerous articles on induced cholesterics appeared in the literature⁵.

Although it is now well established that the addition of enantiomers to nematic liquid crystals produces cholesteric phases of opposite handedness, the correlation between the absolute configuration of the solute and the handedness of the resulting helix is not obvious.

Saeva⁶ was the first to investigate this problem. He added optically active cinnamates 1, which contain one simple chiral center of known configuration, to the nematic

mesophases MBBA and BPC. The 2-methylbutyl group in (S)-1a induces a right-handed helix, both in MBBA and BPC. However, on going from (S)-2-methylbutyl 1a to (S)-2-octyl aminocinnamate 1b, cholesteric mesophases of opposite handedness are produced.



Other examples^{7,8} also showed that opposite twist can be obtained from the same enantiomer in different nematics.

However, the first empirical correlation between the configuration of a series of secondary alcohols and the handedness of the induced cholesteric mesophases was published in 1975⁹. Later, Korte¹⁰ investigated over one hundred compounds having only one chirality center in an equimolecular mixture of MBBA-EBBA and proposed the characterization of the absolute configuration of these chiral molecules by a sequence of ligand parameters in analogy to the Cahn-Ingold-Prelog nomenclature but based on "the effective volume" of the substituents of the asymmetric carbon atom. They correlated this nomenclature to the induced cholesteric handedness. Although this correlation is suitable for a large number of molecules, exceptions are known⁸ and it doesn't explain the observations of Saeva and the dependence of the twist sense on the structure of the nematic phase.

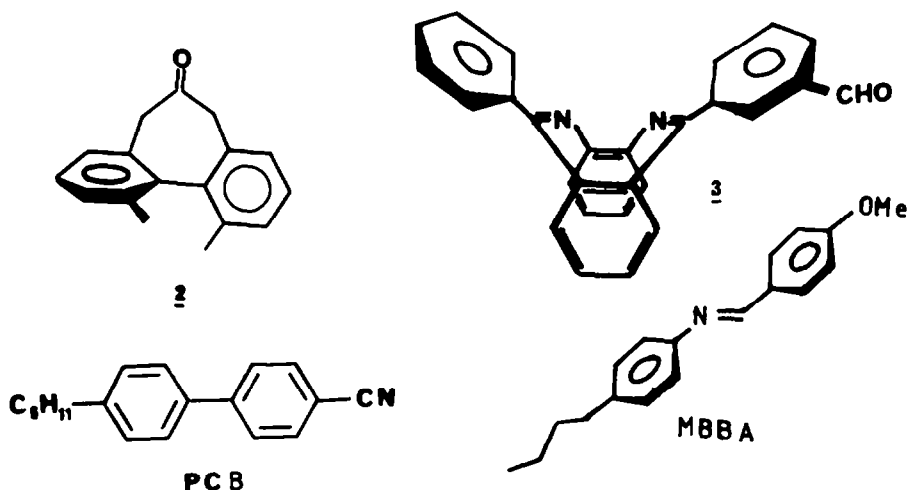
Therefore, the use of liquid crystals for the determination of the absolute configuration of optically active solute from the handedness of the resulting cholesteric helix requires far better knowledge of the mechanism of the twist of nematic by chiral molecules.

About 10 years ago, two results were obtained which are probably at the origin of this study. At that time, one of us started to study induced cholesteric phases which are characterized by the presence of a chiral guest molecule in a nematic host phase. The mole fraction of the chiral component has to be small (< 10 mole%) in order to get a linear variation of the helix pitch with the concentration. Under such conditions the helical twisting power β_M is defined as :

$$1/p = \beta_M \cdot c$$

The helix pitch p is inversely proportional to the molar concentration c of the solute.

It was observed¹¹ that the twisting power of the optically active biphenyl ketone **2** was stronger in a biphenyl-like nematic phase such as PCB than in MBBA (13.5 and 8.8 respectively) and that of optically active diazocine **3** was higher in MBBA than in PCB (44 and 23 respectively)¹².



At that time, it was concluded that twisting powers were higher when the chiral molecule had a structure similar to the nematic. But, now, in the light of the results presented in this paper, we can conclude that conformational factors are probably extremely important for the chirality transfer between a chirality guest molecule and a nematic liquid crystal.

TRANS STILBENE OXIDES : TRANSFER OF CHIRALITY THROUGH CONFORMATIONAL EFFECTS

When we studied the twisting powers of optically trans-stilbene oxides and analogous compounds¹³, we showed that trans-diaryl molecules such as **4** have much higher twisting power in MBBA than in any other liquid crystal (Table 1).

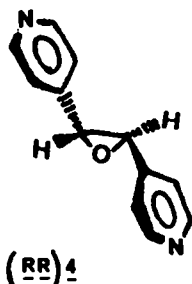


Table I : Twisting powers β_M of 4 in nematic liquid crystals.

Liquid crystals	Type	$\beta_M (\mu\text{m}^{-1}\text{mol}^{-1})$	Induced helicity
MBBA	Schiff base	- 42	M
Phase IV	Azoxybenzene	- 29	M
E ₇	biphenyl	- 11	M
1083	Phenylcyclohexane	- 10	M
ZLI 1167	Bicyclohexane	- 3	M

We obtained information about the orientation of guest molecules in the liquid crystalline matrix by linear dichroism (LD). The liquid crystalline matrix must be transparent in the UV/VIS region. Two types of information can be obtained¹⁴ :

- if the orientation of the long axis of the guest molecule is known, data concerning the electronic states involved become available.

- if the polarizations of the transitions are known, their orientation respect to the nematic director can be established.

The linear dichroism of racemic 4 and racemic styrene oxide 5 in the nematic phase ZLI 1167 shows that molecule 4 is aligned with its long axis parallel to the nematic director, while 5 behaves approximately like a disk-shaped molecule : orientation of the phenyl group with its long axis parallel to the director is only slightly favored.

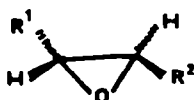


In order to explain the high twisting power of molecule 4 we had to consider conformational factors. First of all, nematics of the p-substituted benzalaniline type, such as MBBA or EBBA, are known to be non planar¹⁵ : the angle between the phenyl ring located on the nitrogen atom and the plane containing the other phenyl ring and the imino double bond is between 41 and 55°. Such a conformation is stabilized by electronic interactions between the nitrogen lone-pair and the π electrons. Therefore, in the nematic phase, mirror-image conformations are equally probable and interconvert rapidly. On the other side several reports

on phenyl oxiranes reveal a preferred conformation : x-ray analysis¹⁶ and MO calculations¹⁷ pointed out a quasi-bisected conformation with the plane of the phenyl ring group rotated towards the C-O bond of the oxirane ring. In this type of conformation the two aryl groups of (RR)-(+)-trans-stilbene oxide and analogous molecules are distorted and displays a sort of left-handed two-bladed propeller helicity (fig. 1).

It is interesting to remark (Table II) that only epoxides having two aryl groups have a high twisting power.

Table II : Twisting powers of chiral oxiranes in MBBA



R ¹	R ²	abs. conf.	β_M	Induced helicity
Ph	Ph	2R, 3R	- 35	M
4-pyridyl	4-pyridyl	2R, 3R	- 42	M
Ph	H	2R	- 1.2	M
Ph	Me	2R, 3R	- 8.5	M

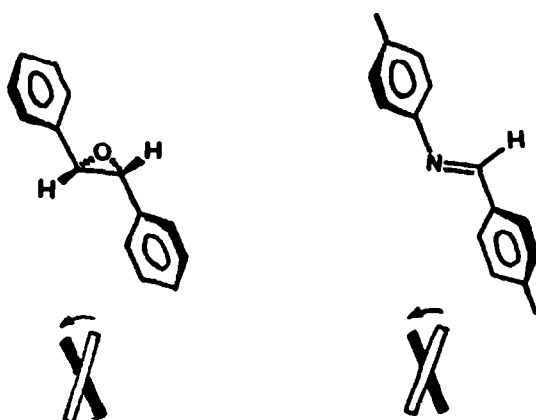


Figure 1 : The M-helicity of the conformation of trans-stilbene oxide induced the same chiral conformation to MBBA and leads to a cholesteric phase of M-helicity.

Therefore, a possible mechanism for the chirality transfer from the optically active diaryl oxirane to the solvent MBBA could be postulated : the chiral conformation of the solute induces in the solvent a chiral conformation of the same helicity and thus the formation of the cholesteric helix (fig. 1). Modification of the inducing compound such as the replacement of one aryl group by a methyl or hydrogen reduces the dynamic interaction with the solvent molecules : consequently the twisting power should decrease drastically.

The conformational similarity between MBBA and *trans*-stilbene oxides is also demonstrated in one of our paper¹⁸ which shows that substituted *trans*-stilbene oxide display liquid crystalline properties. One example is presented in figure 2 :

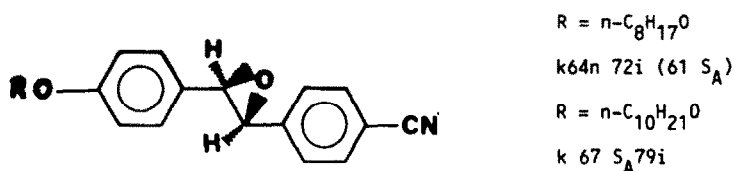


Figure 2 : *Liquid crystal properties of substituted trans stilbene oxides*

The same mechanism should explain the high twisting power of molecule 2 in PCB and that of molecule 3 in MBBA.

BRIDGED-BIARYLS : ABSOLUTE CONFIGURATION CORRELATION WITH THE NEMATIC TWIST

In order to confirm this model, the compounds 6-8 and 9-14, having a chiral cyclic binaphthyl or biphenyl structure with non-planar conformation and distinct helical configuration were investigated¹⁹. Because of their biaryl geometry, the highest twisting powers were expected to occur in biphenyl-type nematic phases, which was indeed found to be the case (Table III).

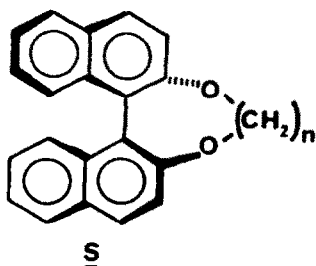


Table III : Twisting powers of chiral binaphthyl 7 and 8

Liquid crystals	Type	$\beta_M (\mu\text{m}^{-1} \text{mol}^{-1})$	
		<u>7</u>	<u>8</u>
PCB	Biphenyl	+ 79	+ 80
MBBA	Schiff base	+ 65	+ 56
1052	Aromatic ester	+ 42	+ 38
ZLI 1167	Bicyclohexyl		+ 35

On the strength of this finding, many chiral biaryls (6-8 and 9-14) were investigated in biphenyl type nematic phases (Table IV). All the absolute configurations are expressed in terms of helicity.

It is certainly gratifying to notice from Table IV, that, despite the important differences in the chemical structures of the compounds, P-helicity and M-helicity always lead respectively to positive and negative values, for the twisting powers (i.e. to right and left-handed helices).

In other words, the main factor determining the chirality of the induced mesophase is the twist sense of the biaryl moiety.

The very high values of β_M were somehow expected, since bridged biaryl compounds are conformationally rigid and having a conformation similar to the nematic molecules, should interact very well with the biphenyl-type liquid crystals.

Furthermore, it was shown¹⁹ by linear dichroism measurements that the biphenyl 8 was oriented with the axis joining the two naphthyl groups parallel to the nematic director, i.e. to the long axis of the molecule composing the nematic phase.

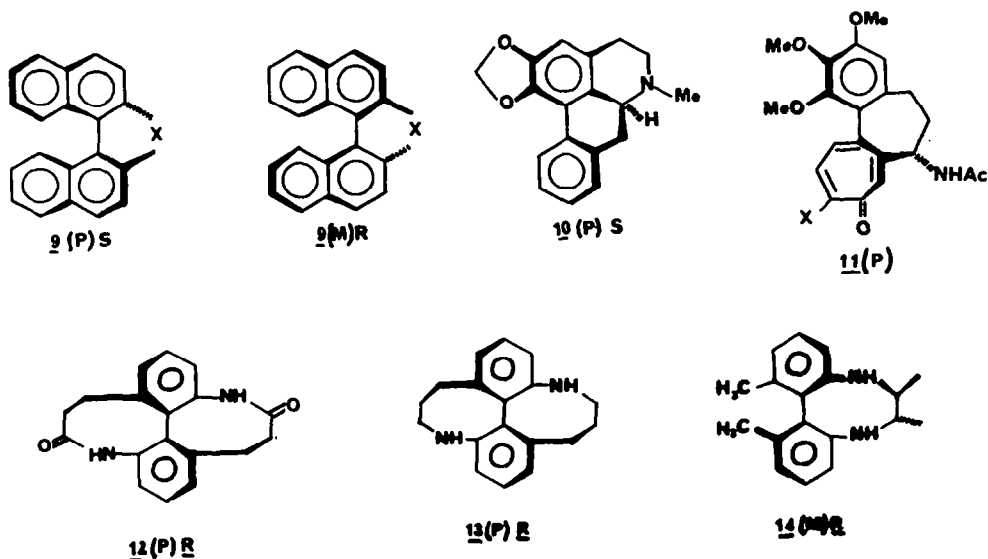


Table IV : Twisting powers of chiral biaryl compounds in liquid crystals of the biphenyl type.

Chiral Compound	Biaryl Helicity	β_M (a)	Cholesteric helicity
$\underline{S(+)} \underline{9a}$ X = $(\text{CH}_2)_2^-$	P	+69 (b)	P
$\underline{R(-)} \underline{9b}$ X = S-S-	M	-65 (b)	M
$\underline{R(-)} \underline{9c}$ X = $-\text{S}-\text{C}(\text{Me})_2-\text{S}-$	M	-71 (b)	M
$\underline{R(-)} \underline{9d}$ X = $-\text{CH}_2-\text{O}-\text{CH}_2-$	M	-55 (b)	M
$\underline{R(-)} \underline{9e}$ X = $-\text{NH}-\text{CO}-\text{NH}-$	M	-21 (b)	M
$\underline{S(+)} \underline{6}$ X = $\text{O}-\text{CH}_2-\text{O}$	P	+85 (c)	P
$\underline{S(+)} \underline{7}$ X = $-\text{O}-(\text{CH}_2)_3-\text{O}$	P	+80 (c)	P
$\underline{S(+)} \underline{8}$ X = $-\text{O}-(\text{CH}_2)_4-\text{O}-$	P	+79 (c)	P
$\underline{S(+)} \underline{10}$	P	+24 (b)	P
$\underline{S(-)} \underline{11a}$ X = OMe	P	+54 (b)	P
$\underline{S(-)} \underline{11b}$ X = SMe	P	+64 (b)	P
\underline{S} $\underline{11c}$ X = H	P	+42 (b)	P
$\underline{R(-)} \underline{9f}$ X = $-\text{SO}_2-\text{S}-$	M	- 5 (b)	M
\underline{R} $\underline{12}$	P	+58 (b)	P
\underline{R} $\underline{13}$	P	+19,8 (b)	P
\underline{R} $\underline{14}$	M	-21 (b)	M

a) $\mu\text{m}^{-1} \text{mol}^{-1}$; b) nematic phase E_7 ; c) PCB

In nematic liquid crystalline solution, 4,4'-disubstituted biphenyl compounds show non-planar conformations with torsion angles of 30° and 80° , depending on the substituents²⁰. It

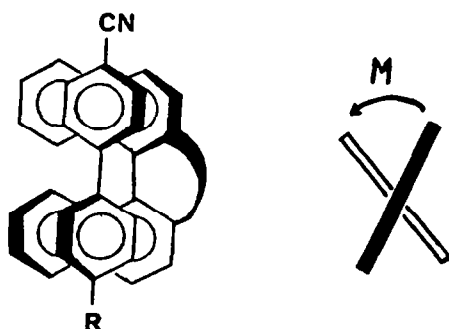


Figure 3 : Model for the interaction between chiral biaryl compounds (M-Helicity) and nematic crystals of the biphenyl-type.

is therefore reasonable to assume that such non-planar conformations exist also in biphenyl-type liquid crystals such as PCB or E₇. In the nematic phase, pairs of mirror-image conformations are equally probable but rapidly interconvert. The chiral biaryl inducer, with its biaryl axis aligned parallel to the biaryl axis of the solvent, can have close contact and interact only with molecules having the same chirality (the same chiral conformation) (fig. 3). The chirality is therefore transferred from inducer to a near molecule of the solvent and from this to the next one and so on, via chiral conformations. A biaryl compound with P-helicity leads to a cholesteric phase of the same helicity.

Biphenyl compounds 12, 13 and 14 appear to be very interesting. These molecules were recently synthesized by Hagishita and their structure determined by X-ray diffraction²¹. Molecules 13 and 14 have the R configuration but the dihedral angle between the two aromatic rings is 118° for 13 and 66° for 14. Therefore, for the same absolute configuration R they have opposite helicity (P and M respectively). This is a rare example of a cyclic structure showing a cisoid conformation for 14 and a transoid conformation for 13, a fact which will be developed for the study of non-bridged biaryls. However, their CD spectra are nearly superimposable²¹. The twisting powers of compounds 13 and 14 instead show the expected sign inversions due to the change of helicity of the biphenyl group²².

Therefore the liquid crystal method is able to characterize the helicity of the biphenyl skeleton in cases where CD spectroscopy fails.

These findings underline the importance of conformation effects on the twist mechanisms and confirm the mechanism postulated in the case of chiral stilbene oxides.

Therefore, as long as there is no ambiguity about the solute orientation in the liquid crystal matrix (linear dichroism is very informative in this domain), it is possible to correlate absolute configurations of bridged biaryls to their twist sense, the correlation being much more certain in the case of strong solute-solvent interactions, i.e. in the case of high twisting powers.

OPEN CHAIN BIARYLS : CONFORMATIONAL ANALYSIS

In sharp contrast to the bridged biaryls which exist in only one chiral conformation, chiral open-chain binaphthyls are not conformationally rigid molecules and, for a given configuration, they can exist in cisoid and transoid conformations displaying opposite helicity of the two phthalene rings (fig. 4).

Measurements of the twisting powers of open-chain binaphthyls of known absolute configurations should give direct information on the helicity of the biaryl system and hence on the preferred cisoid or transoid conformation. The data obtained for several 2,2'-disubstituted 1,1'-binaphthyls are reported in Table V¹⁹.

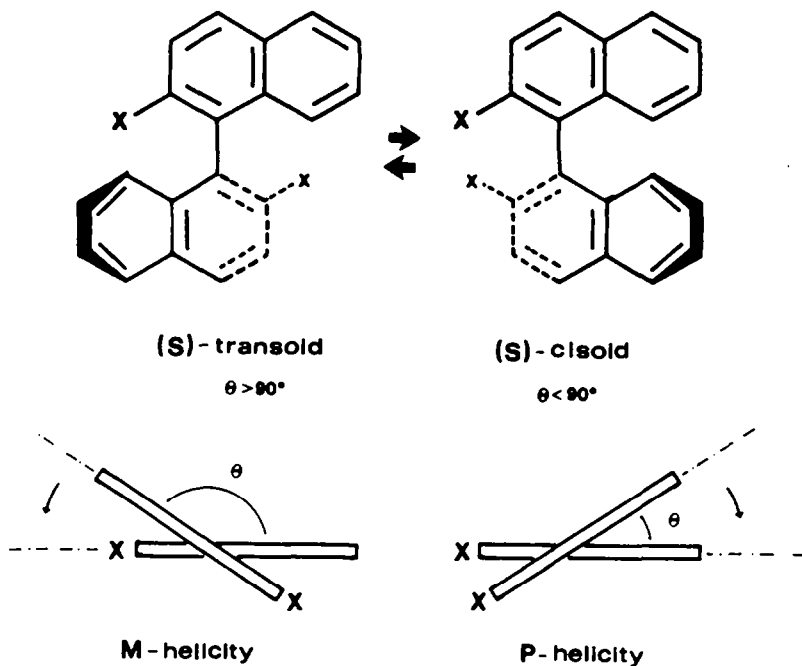


Figure 4 : Helicity of cisoid and transoid conformations of a chiral binaphthyl having S configuration.

Table V : Twisting powers of open-chain binaphthyls in biphenyl-type liquid crystals

Compound	Absolute Configuration	X	$\beta_M (\mu\text{m}^{-1}\text{mol}^{-1})$ (a)	
			PCB	E_7
<u>15a</u>	S	OH	+ 32	
<u>15b</u>	S (b)	CH ₂ OH	+ 8.5	
<u>15c</u>	S	OCH ₂ COOH	+ 4.2	
<u>15d</u>	S (c)	NH ₂		+ 2 (c)
<u>15e</u>	S	OCH ₃	+ 1.5	
<u>15f</u>	S	OCH ₂ Ph	+ 1.4	
<u>15g</u>	S	CH ₃		+ 0.5 (c)
<u>15h</u>	S	CH ₂ Br	- 4.6	
<u>15i</u>	S	CHBr ₂		- 2.4 (c)

a) A positive value of β_M corresponds to a right-handed cholesteric (P-helix).

b) the enantiomer was measured.

c) not corrected for optical purity.

The alignment of the open-chain binaphthyls is similar to that of bridged biphenyls (i.e., with the two-fold symmetry axis perpendicular to the nematic director), as shown by linear dichroism of racemic 15e in the nematic ZLI 1167, mixture of bicyclohexyl derivatives)²³. For compounds 15a to 15g the S absolute configuration is associated with positive values of the twisting power β_M while molecules 15h and 15i give a negative β_M value. Quantitative values are considerably smaller ($\beta_M = 0.5$ to $30 \mu\text{m}^{-1}$) than those observed for rigid binaphthyls ($55\text{--}80 \mu\text{m}^{-1}$).

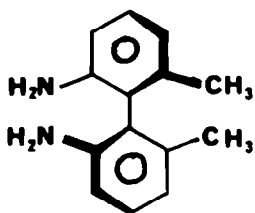
It has been shown in the literature using circular dichroism that 2,2'-disubstituted binaphthyls ($X = \text{CH}_3, \text{CH}_2\text{OH}, \text{COOH}, \text{NH}_2$) adopt a cisoid conformation²⁰. Therefore molecules 15a to 15g, being in a cisoid conformation for the S-configuration, display a P-helicity of the binaphthyl system and give as expected a right handed cholesteric. Compounds 15a, h, c, where the cisoid conformation is stabilized by hydrogen bonding, show higher values for β_M .

On the other side, circular dichroism²³ as well as X-ray diffraction²⁵ show for compounds 15h and 15i a transoid conformation for the S configuration indicating a M-helicity of the binaphthyl system which leads as expected to a left-handed cholesteric.

Therefore, the sign of β_M is determined for a given configuration by the dihedral angle between the two aromatic parts.

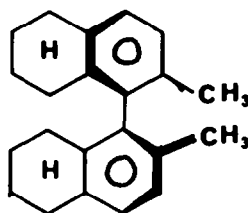
The low value of β_M could be associated either to a preferred conformation having a dihedral angle near 90° or to the existence of nearly equally populated cisoid and transoid conformations.

Similar results were obtained with molecules: 16 and 17.



(R)16

$$\beta_M = +2.0 (E_7)$$



(S)17

$$\beta_M = +1.0 (PCB)$$

(R)-16 gave a small value for β_M ²² indicating a P-helicity for the biphenyl system which for the R-configuration is associated with a transoid conformation. This result is confirmed by X-ray diffraction and circular dichroism²¹. Another result was obtained with (S)-17: a positive β_M for the S-configuration corresponding to a cisoid conformation.

Therefore, the mechanism of cholesteric induction is similar to that discussed for bridged biaryls : for the S configuration, a cisoid conformation corresponding to a P-helicity of the binaphthyl system gives a right-handed cholesteric, while a transoid conformation having M-helicity gives a left-handed cholesteric.

The sign of the twisting power of a chiral open chain biaryl of known absolute configuration in a biphenyl-type nematic can be correlated with the more populated conformation of the molecule, the correlation being more secure in the case of high twisting power, i.e., of strong solute-solvent interactions.

CONCLUSION

In recent years several modern analytical techniques have been developed in order to obtain stereochemical information. Historically, the method most commonly used for obtaining information about chirality was polarimetry. Circular dichroism and optical rotatory dispersion are now more powerful than polarimetry.

The results reported in this paper show that the extreme sensitivity of liquid crystals to optical activity makes them suitable for stereochemical studies.

We have shown that the helicity of optically active biaryl molecules is likely to be the main factor determining their twisting power in nematic liquid crystals and that the chirality of the dopant is transferred to the nematic through chiral conformations.

Such a mechanism for the chirality transfer allows the determination of absolute configurations of bridged biaryl molecules or the main conformation of open-chain biaryls from the handedness of the twist of the nematic phase.

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EXPERIMENTAL

Pitch values were determined at room temperature by means of the "droplet method"²³ using a Leitz Ortholux microscope or with the "lens" version of the Grandjean-Cano method²⁷ using a Zeiss Standard 16 microscope.

Helical handedness was determined from the sign of the rotatory power²⁸ and from the sense of the spiral-like disclination observed under circularly boundary conditions²⁹.

Liquid crystals used in this study :

MBBA	: 4-butyl-N-(4-methoxybenzylidene)aniline.
BPC	: butyl-4-(4-ethoxyphenoxycarbonyl)phenyl carbonate.
EBBA	: 4-butyl-N-(4-ethoxybenzylidene)aniline.
PBC	: 4-pentyl-4'-cyanobiphenyl.
Phase IV	: 4-butyl-4'-methoxyazoxybenzene (Licristal Merck).
E ₇	: a mixture of 4-cyano-4'-n-aryl and 4'-n-alkylbiphenyl from BDH.
ZLI 1167	: a mixture of bicyclohexane derivatives.
Phase 1083	: a mixture of phenylcyclohexane derivatives from Merck.
Phase 1052	: a mixture of aromatic esters from Merck.

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