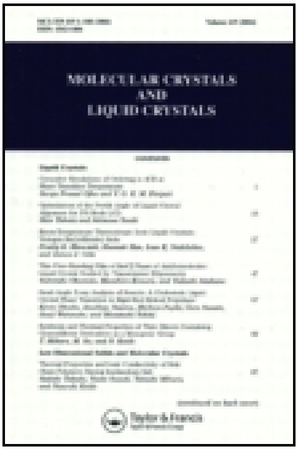

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Induced Cholesteric Mesophases: Origin and Application

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Induced Cholesteric Mesophases: Origin and Application†

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The relationship between the twisting power (β) and the molecular structure of the dopant and nematic solvent are discussed. High values of β are observed whenever two (or more) planar or quasi-planar moieties, chirally distorted one with respect to the other, are present in the dopant. For high twisting powers, the mechanism of induction seems to be connected to the transfer of chirality from the solute to the solvent via chiral conformations of the latter. Sterochemical and analytical applications are briefly discussed.

INTRODUCTION

Traces of chiral compounds are able to transform nematic mesophases into cholesteric phases.[1] The ability of the chiral solute to twist the nematic phase (β, twisting power) is currently defined as[2a,b,3,]

$$\beta = (p \cdot c \cdot r)^{-1} \tag{1}$$

where p is the pitch, c the concentration (expressed in mole. of the solute per mole. of the solvent) and r the enantiomeric purity of the dopant. We found it convenient to express the pitch in μm as in this way one obtains values of β which in most cases range from the unity up to 100. The values of β for non-mesogenic chiral solutes are usually constant with concentration in the range of dilution utilized with the "lens method."[4]

The study of the variations of the twisting power with the structure

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of the chiral dopant, nematic solvent and temperature affords valuable information about the cholesteric phase.[3,5,6,7,8] It is also possible to utilize the phenomenon of the cholesteric phase induction for several analytical[9,10,11,2b] and sterochemical[3,2a,b,12,13,14,15,16,17,18,19] applications which often offer favourable alternatives to classical chiropitical techniques.

ORIGIN

I) Influence of the molecular structure of the dopant

The values of β are obviously strongly dependent on the molecular structure of the dopant and are related to the structure of the liquid crystal used as a solvent, as will be discussed in the next paragraph.

A few theoretical treatments of the molecular twisting power have been published.[5,6,20,21] However, the relationship between the twisting power and the molecular structure of the dopant is still not defined. Experimental work in this field is largely incomplete and in most cases has been carried out on conformationally poorly defined open-chain derivatives.

From selected values reported in the literature and a few new examples studied in this work we have compiled Figure 1.

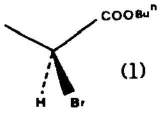
An inspection of the examples reported allows the following points to be made:

a) The number of chiral centres and the type of chirality (axial dissymmetry of asymmetric atoms) are not relevant factors.

b) The presence of two-fold or three-fold symmetry axes is compatible with high values of the twisting power (derivative *10* has a *C3* axis and shows the highest value of β, while the theoretical work in ref. 6 predicts, for derivatives having this symmetry element, β = 0). However, the presence of these elements is not necessarily associated with high values of β (see derivatives 2,3,5 and 9).

c) Although the presence of large planar fragments often enhances the values of β (see 4, Ar = 1 − napht. and 6), a molecule does not have to be nearly planar or contain a large planar fragment in order to show high twisting power.

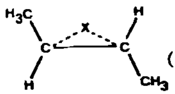
d) Conformational rigidity is an important but not sufficient condition. Derivatives 2, 3, and 5 are rigid molecules, but their twisting powers are small or very small. On the other hand, the class of derivatives 8 shows high values of β while that of the analogous non-bridged derivative 9 is very small.



(1)

β = + 0.5 (MBBA/EBBA)

(Ref. 2b)

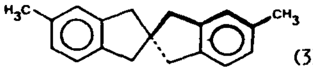


(2)

X = O, S

β = + 0.5 (MBBA)

(Ref. 13)

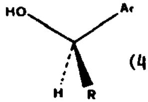


(3)

β = − 0.95 (MBBA/EBBA)

β = − 1.03 (PHASE IV)

(Ref. 2b)

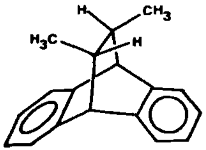


(4)

Ar = Ph, R = CH$_3$
β = − 1 (MBBA)

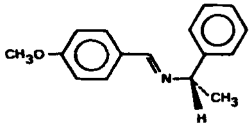
Ar = 1-Napht., R = CH$_3$
β = − 7.7 (MBBA)

(Ref. 12b)



(5)

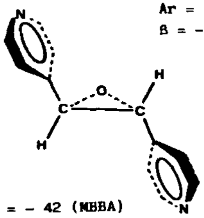
β = −7.5 (E7)



(6)

β = − 17.1 (MBBA)

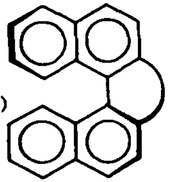
(Ref. 16)



(7)

β = − 42 (MBBA)

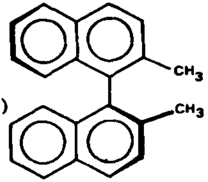
(Ref. 13)



(8)

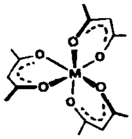
β = + 55 to + 85 (E7 or K15)

(Ref. 8)



(9)

β = + 0.5 (E7)

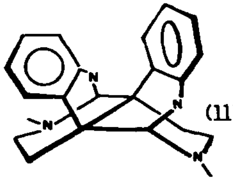


(10)

M = Cr

β = − 15 (E7)

β = − 102 (MBBA)



(11)

β = − 0.8 (MBBA)

FIGURE 1

e) The presence of highly polarizable aromatic groups is not a necessary condition.

f) The presence of two (or more) planar or quasi-planar molecular moieties chirally distorted, one with respect to the other, and in a fixed conformation is generally associated with high values of β.

g) In some cases, even if condition f is fulfilled, the presence of severe steric hindrance, which probably prevents the approach of the solvent to the twisted structure, lowers the value of β considerably.

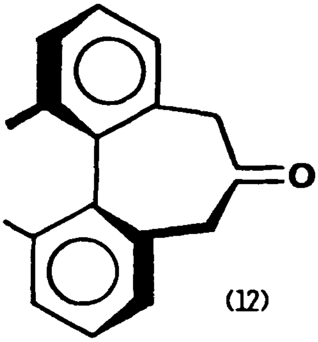
The points reported above allow a rough estimate of the relative magnitudes of the twisting powers and should be considered in connection with the solvent effects described in the following paragraph. They do not allow any *a priori* prediction of the handedness of the induced cholesterics and in particular of the alternation of the screw sense of the helix with the number of bonds between the chiral centre and the ring system observed for mesogenic[22] and non-mesogenic[23] open-chain derivatives.

ii) Influence of the nematic solvent

The values of β are very sensitive to variations of the nematic solvent. With regard to this, β, as defined in eq. 1, is not truly a solute-solvent interaction since it contains the twist elastic constant of the nematic K_{22}.[20,21,24] Strickly speaking, whenever comparisons are made between twisting powers in different nematics, one should use the relation

$$\beta_{\text{corr.}} = \beta \cdot K_{22}, \qquad (2)$$

in which the resistance of a given nematic to the twist is somehow compensated; however, the available values[25-29] of K_{22} do not show differences as important as some of the observed variations of β. Furthermore, the measurements should be performed at the same reduced temperature,[2b,7] even if the temperature effects on β are particularly strong only near transitions to the smectic phases.[7] Solladie et al. first observed the variations of β for derivative 12 (Figure 2) and deduced that the twisting powers are high when the nematic solvent has a structure similar to that of the inducing molecule.[18,3] Assuming that the measurements were performed at ca.22°C, correction of β with the twist elastic constants (eq. 2) makes the difference even larger, confirming the importance of the structural similarity (Figure 2).



(12)

L.C.	β	T	$K_{22}/10^{-7}$ (*)
MBBA	+10.2	22°C	4.4
K15	+15.2	22°C	6.4

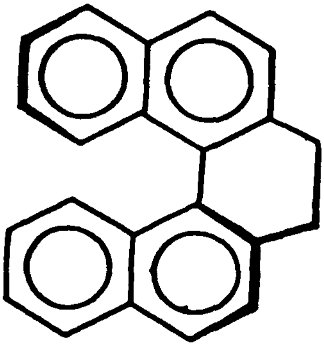
(REF. 18)

(*) in c.g.s. units; ref. 25–27,29

FIGURE 2

A similar trend was observed in the case of the epoxide 7 which shows[13] values of β ranging from −42 (*MBBA*, room temperature) to −3 (*ZLI 1167*, 59°C). To visualize the similarity between *MBBA* and derivative 7, one must remember that *MBBA* is neither a linear nor a planar molecule but exists in the liquid, liquid crystalline and solid state in non-planar twisted conformations.[13] Similarly, bridged binaphthyls of type 8 show maximum twisting powers in the biphenyl-type liquid crystals.[8]

To give more substance to the observations reported above, we have measured the twisting powers of a bridged binaphthyl at various concentrations in *MBBA* and *K15*, at the same reduced temperature, at which the values of K_{22} are known. The data reported in Figure 3 confirm that the highest values of β are found in solvents having structural similarity to the inducer. These considerations are not valid



L.C.	β	T/Tc	$K_{22}/10^{-7}$ (*)
MBBA	+37	0.96	3.2
K15	+70	0.96	6.4

(*) in c.g.s. units; ref. 25–27,29

FIGURE 3

when specific solute-solvent interactions occur, as in the case of carbinols which in *MBBA* are selectively hydrogen-bonded to the imino nitrogen of the Schiff base.[30] In the case of 1-phenylethanol, even an inversion of the helix handedness was observed in passing from *MBBA* to the nematic phase *1008* (mixture of benzoate esters).[12b] Also the tendency of the solvent and solute to give intermolecular charge-transfer interactions can considerably influence the values of β.

iii) Mechanism of transmission of chirality

In the case of low values of the twisting power (0.5 to 5), there is little hope of reaching some conclusion on the possible mechanism by which the chirality is transferred from the inducer to the solvent, particularly for open-chain derivatives which are conformationally mobile. The situation is less ambiguous for molecules showing high values of β, where a very small number of chiral inducers are able to transfer their chirality to a large number of nematic hosts.

As a starting point it is very important to know the orientation of the dopant with respect to the local nematic director and this can be found using linear dichroism techniques in the *UV*[8,13] or *IR*[2b,30] spectral regions. Deuterium NMR offers a valuable alternative when selectively deuterated compounds are available.[31a,b]

Bridged binaphthyls (8) are probably the case in which the mechanism of chirality transmission is best understood.[8] The twisting powers of a series of similar derivatives are high (between 55 and 85 in biphenyl-type liquid crystals), therefore even molecules of the solvent lying in layers quite distant from the inducer become twisted. The orientation of the solute, as determined by linear dichroism in the *UV* region, is with the axis joining the two naphthyl groups parallel to the nematic director (Figure 4) and the values of β, are maximum in the biphenyl-type nematic solvents. 4,4'-Substituted biphenyls in nematic liquid crystalline solutions show non-planar conformations with torsion angles from ca.30° to ca. 80° according to the substituents. It is therefore reasonable to assume that such non-planar conformations exist also in biphenyl-type liquid crystals such as *K15* or *E7*. Obviously in the nematic phase pairs of mirror-image conformations are equally probable and interconvert rapidly.

The chiral biaryl inducer, aligned with its biaryl axis parallel to the biphenyl axis of the solvent, can have close contact and interact only with molecules having the same chirality (Figure 4). The chirality is therefore transferred from the inducer to a near molecule of the solvent and from this to the next-near and so on, via chiral conformations until the chirally ordered aggregate attains a metastable size

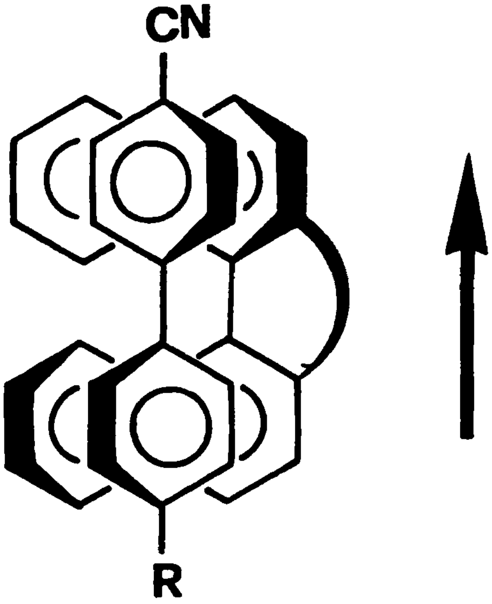


FIGURE 4

and thermally disintegrates as it aggregates further. It remains to be understood why a pile of *P*-distorted biaryls couple to give a right-handed cholesteric phase. In the literature there is no theoretical work on models of this type. The only analogous problem is the generation of a skew structure due to the coupling of two models of chiral molecules. The models are cylindrical surfaces containing lines of polarizability chirally twisted.[20,21] Adopting a Meier-Saupe interaction potential between the polarizabilities of the two "molecules," if the individual models are right-handed, leads to a preferred right-handed skew structure.[20,21]

As the main factor determining the handedness of the induced cholesteric, for the binaphthyls, is the *P* or *M* helicity of the dopant, it is not surprising that the open chain derivative 9 shows a very small twisting power. For a given absolute configuration this molecule can in fact exist in several conformations some of which have *P* and some *M* helicity. The observed twisting power is in this case an average value which is influenced by the conformer population. The mechanism seems to be similar also in the case of the epoxide 7, although conformational uncertainties further complicate the situation. From LD measurements, the epoxide is aligned with the axis connecting the two aryl groups parallel to the nematic director; maximum twisting power is observed in *MBBA*. As depicted in Figure 5, the maximum interaction between solute and solvent is attained when the latter, which exists in chiral conformations,[13] adopts the same chirality as the inducer. Again the transmission of chirality to the bulk of the solvent is achieved by means of chiral conformations. Assuming that in the epoxide the conformation of the pyridyl groups is "quasi-bisected," the *R* configuration corresponds to *M*-helicity of the pyridyl groups and the observed left-handed cholesteric could be congruent with what has been reported for bridged biaryls.

The case of the metal complex 10, which shows unexpected high values of β seems again connected to the previous examples. The molecule has a nearly globular shape and even if the liquid crystalline matrix could exert some distortion on it,[32] its orientation is not likely to be relevant.

The high values of β again indicate transmission of the chiral information to layers of the solvent which are far from the inducer. Whatever the orientation of the complex is, the liquid crystal solvent can interact with and be distorted by only two of the three blades of the propeller-like complex. For Λ configuration the stereochemical relation of two pairs of "blades" is similar to *P* chiral biaryls. Indeed a *P* cholesteric is observed indicating again a situation similar to those reported above.

APPLICATIONS

Correlation of configurations

Chiral compounds are usually characterized by their Optical Rotatory power and by Circular Dichroism spectroscopy, the latter technique being extensively utilized for correlative and non-empirical deter-

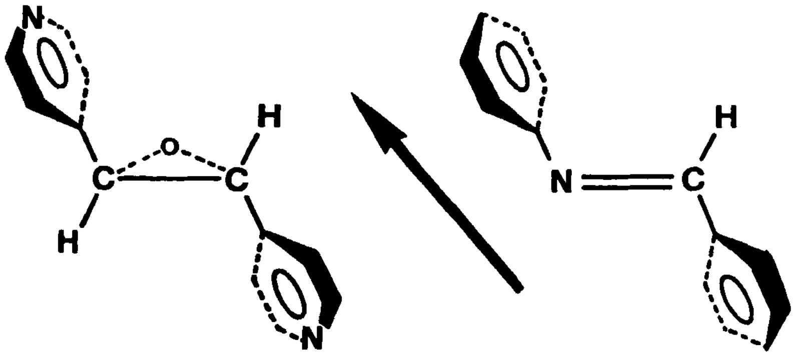


FIGURE 5

minations of the absolute configuration. The amount of active compounds required for these measurements varies from few to several milligrams. The origin of the optical rotation is in the interaction between light and molecules, while the twisting power originates from interaction between solute and solvent molecules. Therefore one can reasonably expect to get different answers using the two techniques. In particular the liquid crystal method should be more sensitive to the molecular shape and less to the nature of the chromophoric groups. This should allow configurational intercorrelations which are not possible with Circular Dichroism.

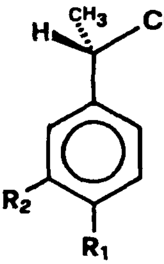
The first successful stereochemical application of this idea was the correlation of configurations of a series of secondary alcohols of the type 4 (Figure 1) using a qualitative comparison of the handedness of cholesteric phases induced in *MBBA*.[12a] The investigation was subsequently extended to quantitative measurements which showed a smooth variation of the twisting power with the molecular structure of the alcohols.[12b] As a new example of empirical correlation, we report here the twisting powers of a series of anti-inflammatory molecules (Figure 6). The configurations of all derivatives correlate to the handedness of the induced cholesterics: *S*-configurations correspond to *P*-helices.

Other structures for which a correlation was found were epoxides,[13] biaryl derivatives including several alkaloids,[8] complexes of type 10 containing different metals,[33] substituted benzylamines,[16] and amino alcohols.[17]

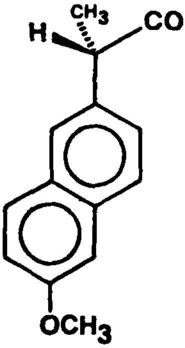
In a more general empirical approach, proposed by Korte et al.,[2] the prediction of the configuration is based on the sequence of priority of the ligands attached to a tetrahedral centre. Generally speaking the configurational information is complementary to that obtained by the chiroptical techniques and more general than that deduced from the quasi-racemate method, with the further advantage of requiring very small amounts of active materials.

Amplification of chirality

The passage from molecular to macrostructural chirality somehow amplifies the molecular asymmetry. This can be used to characterize molecules showing very low optical rotations such as compounds chiral solely by isotopic substitution which can be characterized at the mg. level,[14] while chiroptical techniques even at higher concentrations are often not sensitive enough. The enantiomeric purity[2b] and the racemisation rates[3,18] can be evaluated on very small samples. Traces of chiral compounds can easily be detected. Jacques and coworkers first utilized liquid crystals to detect spontaneous resolution



(I)



(II)

		B (PHASE IV)
(+)-S-KETOPROFEN	(I), R_1= H, R_2= Benzoyl	+ 0.5
(+)-S-INDOPROFEN	(I), R_1=  , R_2= H	+
(+)-S-IBUPROFEN	(I), R_1= i-Pr, R_2= H	+ 0.04
(+)-S-SUPROFEN	(I), R_1= 2-Thienoyl, R_2= H	+ 0.5
(+)-S-NAPROXEN	(II)	+ 2.3

FIGURE 6 Twisting powers of anti-inflammatory derivatives in Phase IV. For Indoprofen only the handedness is given because of the very low solubility in all liquid crystals tested.

of racemates when individual crystals were not sufficiently large to allow measurement of the optical rotation.[9] The liquid crystal technique seems particularly useful for the determination of chiral metabolites which can be characterized in quantities about 100 times smaller than those needed for measurements of optical rotation.[10] Quantitative determination of thin layer chromatographic fractions of heroin using *MBBA* as a solvent allows the dosage of amounts down to 0.4 μgs. and the + sign of the cholesteric helix represents a further identification factor.[11]

Experimental

Measurement of the pitches were carried out with the "lens method"[4] with a standard Zeiss microscope equipped with a heating platform, with temperature stability of ± 0.3°C. The handedness of the cholesterics was deduced from the sign of the rotatory power[34] and cross-checked with the double spiral method.[35] The anti-inflammatory derivatives were provided by Dr. A. Gazzaniga (Pavia).[36] Derivative 5 was provided by Prof. J. Jacques (Paris).[38] Metal complex 10 was from Prof. S. F. Mason (London).[37] Commercial Calycanthine 11 was used without further purification. Liquid crystals *MBBA*, *EBBA*, *K15* and *E7* were commercial products and were used without further purification.

Acknowledgments

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