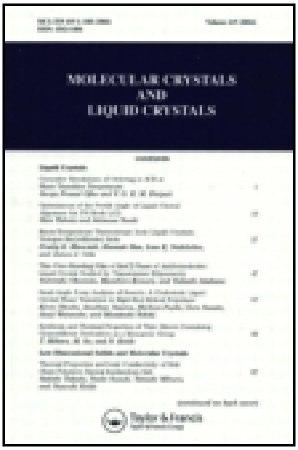

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New Chiral Esters, Diastereomeric 2-(4-Carboxybenzylidene)-p-Menthane-3-One Derivatives, as Components of LC Systems with Induced Helical Structure

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New Chiral Esters, Diastereomeric 2-(4-Carboxybenzylidene)-*p*-Menthane-3-One Derivatives, as Components of LC Systems with Induced Helical Structure

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Diastereomeric 1*R*,4*S*- and 1*R*,4*R*-2-carbomethoxybenzylidene-*p*-menthane-3-ones have been synthesized. The helical twisting power and the induced helical pitch temperature dependence have been measured for the liquid crystal mixtures based on the nematic 4-methoxybenzylidene-4'-butylaniline and 4-pentyl-4'-cyanobiphenyl containing the obtained diastereomeric chiral dopants. The distinction in the characteristics of the diastereomeric chiral dopants is discussed.

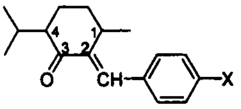
Keywords: induced cholesteric liquid crystals; chiral dopants

INTRODUCTION

Chiral α,β-unsaturated ketones containing cyclic *p*-menthane-3-one fragment are of interest as components of liquid crystals (LC) systems with induced helical structure. Various 1*R*,4*R*-2-arylidene-*p*-menthane-3-ones were studied in the details earlier [1 - 3], being available as products of the (–)-menthone reaction with benzaldehyde derivatives [1, 4, 5].

These chiral dopants (CD) have been shown [1, 2] to induce left-hand helix in the nematic mesophases and to exhibit a quite high helical twisting power (**HTP**). However, characteristics of the 1*R*,4*S*-diastereomers as CD have been not studied up to now.

In order to clarify an influence of the C-4 different configuration on a behavior of the diastereomeric 2-arylidene-*p*-menthane-3-ones in LC, we synthesized the 4-carbomethoxy substituted compounds **1a** and **2a**.



1a, **1b** – 1*R*,4*S*-*trans*-diastereomers
2a, **2b** – 1*R*,4*R*-*cis*-diastereomers
1a, **2a** X = $COOCH_3$; **1b**, **2b** X = C_6H_5

For LC mixtures based on nematic 4-methoxybenzylidene-4'-butylaniline (**MBBA**) or 4-pentyl-4'-cyanobiphenyl (**5CB**) and including the CD **1a**, **2a**, the HTP values and temperature dependences of the induced helical pitch *P* were measured. For comparison, the analogous parameters for the respective 4-phenyl substituted compounds **1b** and **2b** were obtained, too.

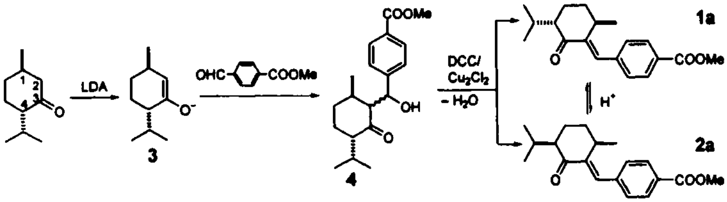
To elucidate the causes of the obtained difference in the mentioned above characteristics of the CD under study, the data about their molecular structure were used according to results of the X-ray analysis [6] and ^{1}H NMR spectra combined with the molecular simulation.

RESULTS AND DISCUSSION

Synthesis of the Target Chiral Dopants

Obtaining of chiral α,β-unsaturated ketones on the base (–)-menthone is associated with essential difficulties due to its low reactivity under interaction with benzaldehyde derivatives in base mediums [1]. A probability of the hydrolysis complicates the reaction in the case of using of the 4-carboxybenzaldehyde ester derivatives.

Therefore, the direct aldol reaction of (–)-menthone lithium 2-enolate **3** with 4-carbomethoxybenzaldehyde and followed mild dehydration of intermediate β-hydroxyketones mixture **4** has been used to obtain the desired compound **1a** with the 1*R*,4*S*-configuration (**Scheme 1**). Analogously, 1*R*,4*S*-diastereomer of the phenyl substituted compound **1b** was prepared earlier [7].



Scheme 1

In the case of the kinetic controlled direct aldol reaction (–85 °C, see Experimental) the 1*R*,4*S*-diastereomer **1a** is formed predominantly. At the higher temperature in aldol reaction (–50 °C), a mixture of both diastereomers **1a**, **2a** in the ratio 3 : 2 (HPLC) was obtained after dehydration. Probably, the epimerization of the intermediate β-hydroxyketones **4** takes place under these conditions¹⁾.

One should note that the intermediate β-hydroxyketones formed by 4-carbomethoxybenzaldehyde undergo dehydration much more slowly (up to 30 day) as compare with 4-phenylbenzaldehyde derivatives (during a week) under the same conditions [4].

The 1*R*,4*S*-*trans*-diastereomer **1a** undergoes acid catalyzed epimerisation into the more stable 1*R*,4*R*-one (Schema 1 and Experimental).

Molecular Structure of the Chiral Dopants

The molecular 1*R*,4*S*-configuration of the obtained compound **1a** follows from the X-ray data [6]. A *chair*-like conformation of the cyclohexanone ring with the *trans*-axial orientation of the methyl and isopropyl substituents is realized in the crystal of this diastereomer.

The structure of the 1*R*,4*R*-diastereomer **2a** has been proven by ^{1}H NMR spectroscopy (Figure 1). This compound spectrum is analogous fully to those for several 1*R*,4*R*-2-arylidene-*p*-menthane-3-ones studied

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1) Results of study of the β-hydroxyketones configurations and stereoselectivity of the direct aldol reaction will be published elsewhere.

before [8], but it is differentiating from the spectrum of 1*R*,4*S*-diastereomer **1a** (Figure 1, *a* and *b*). For the compound **2a**, it can be expected on analogy with the X-ray date [5, 9] for the several compounds of this series that *chair*-like conformation of the cyclohexanone ring with the axial orientation of methyl group and equatorial isopropyl one (Figure 2) is preferable. That is confirmed also by the results of molecular simulation (fraction of such conformations is 97 %). Therefore, 1*R*,4*R*-diastereomer **2a** can be considered as conformational homogeneous.

In contrast, the *chair*-like conformer with the axial alkyl groups and *twist*-form[2)] (Figure 3, *a*, *b*) co-existing in nearly equal amounts were established for the 1*R*,4*S*-diastereomer **1a** by ^{1}H NMR spectra analysis combined with the simulation results. In the Table 1, the calculated values of the torsion angles H–C–C–H for cyclohexanone ring protons of the most probable *chair*-like and *twist*-conformers as well as the respective vicinal constans of the spin-spin coupling ^3J(H,H) are listed. The ^3J(H,H) values were obtained by using of the mentioned torsion angles and Durette–Horton (1) [10] and Altona (2) [11] equations.

The carried out calculations showed that the $^3J(1,6)$, $^3J(4,5)$, $^3J(5,6)$ and $^3J(5',6')$ values are sensitive to the conformational difference. Taking into account that the experimental values $^3J_{exp}$ of these ^3J are weighted-mean magnitude:

$$^3J_{exp} = {}^3J_{chair}\, m + {}^3J_{twist}(1 - m)$$

(here, m is a fraction of *chair*-like conformer in equilibrium system; $^3J_{chair}$ and $^3J_{twist}$ are the calculated values for *chair*-like and *twist*-conformers, respectively) we estimated the fractions (m and $1-m$) of the alternative conformers. It is on average 53 % of the *chair*-like conformer if the $^3J_{chair}$ and $^3J_{twist}$ values calculated on Durette equation (1) is used. Using of the $^3J_{chair}$ and $^3J_{twist}$ values calculated on Altona equation (2) lead to 61% on average of the same conformer.

[2)] In accordance with the molecular simulation, both *chair*-like and *twist* conformers can be characterized also by a different rotameric state of the isopropyl fragment (*trans*- or *gauch*-orientation of the isopropyl C–H bond respectively 4C–H (conformers *a–c*, *d–f*, see the Table 1).

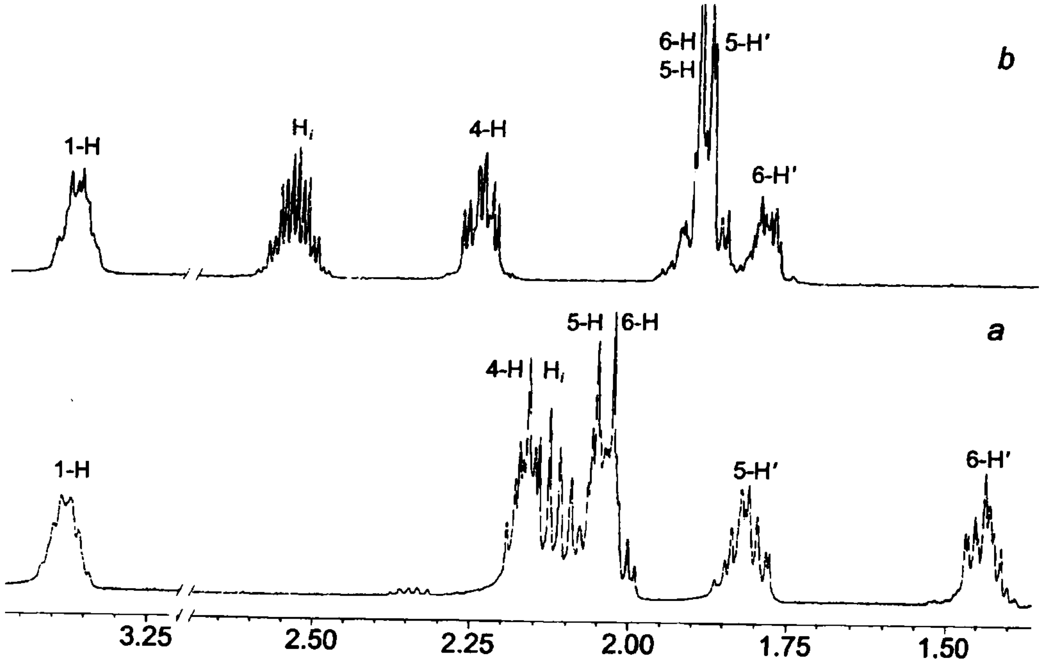

FIGURE 1 ^{1}H-NMR spectra of the compounds **1a** (*a*) and **2a** (*b*) (400 MHz, $CDCl_3$)

ABLE 1 Torsion angles H–C–C–H (φ(H,H)/degree) for the most probable conformers of the compounds **1a** nd **2a** on molecular simulation results and several vicinal constants [^3J(H,H)/Hz), calculated according to quations 1 and 2

φ(1,6)	$^3J(1,6)$		φ(1,6')	$^3J(1,6')$		φ(4,5)	$^3J(4,5)$		φ(4,5')	$^3J(4,5')$		φ(5,6)	$^3J(5,6)$		φ(5',6')	$^3J(5',6')$	
	1	2		1	2		1	2		1	2		1	2		1	2
								Compound 1a									
–64	2.5	3.4	52	4.0	4.8	–68	2.1	2.9	47	4.8	5.7	56	3.6	4.6	–174	13.5	12.8
–163	11.1	11.3	–46	5.4	5.8	–166	11.3	11.5	–47	5.3	5.7	–175	13.4	12.8	–48	5.1	5.8
–164	11.2	11.4	–47	4.3	5.7	–164	11.2	11.4	–46	5.4	5.8	–175	13.4	12.8	–48	5.1	5.9
–165	11.3	11.5	–48	5.1	5.5	–159	10.6	10.8	–41	6.2	6.6	–175	13.4	12.8	–48	5.1	5.8
	6.7			4.3			6.1			5.3			6.8			9.2	
								Compound 2a									
–62	2.7	3.6	55	3.7	4.5	57	3.8	4.2	174	11.7	12.0	59	3.2	4.2	–173	13.4	12.7
–63	2.6	3.4	53	3.9	4.8	57	3.8	4.2	174	11.7	12.0	59	3.1	4.2	–173	13.4	12.7
–62	2.7	3.5	54	3.8	4.6	58	3.6	4.0	175	11.8	12.0	59	3.2	4.2	–173	13.4	12.7
	1.5			4.2			6.1			12.1			3.6			12.8	

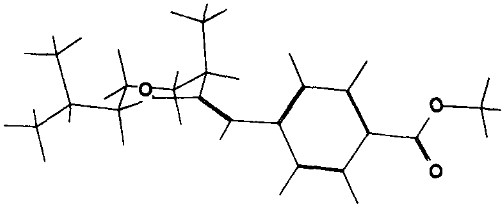

FIGURE 2 The preferable *chair*-like conformation of the compound **2a**

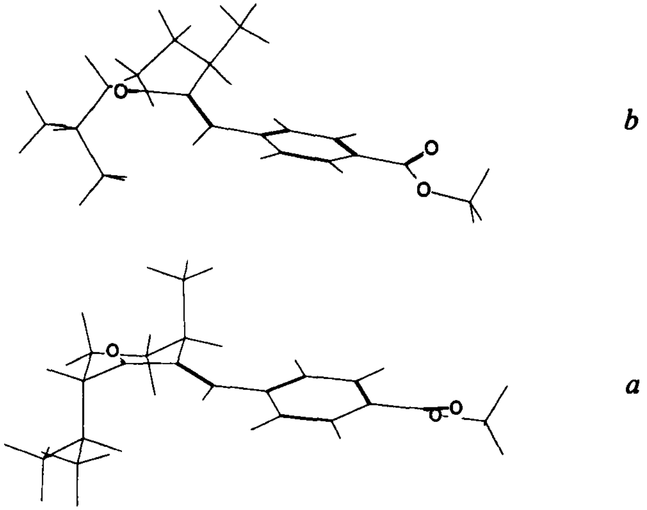

FIGURE 3. The most probable *chair*-like (*a*) and *twist* (*b*) conformations of the compound **1a**

Thus, *chair*-like conformer and *twist* one are approximately equally probable for the 1*R*,4*S*-diastereomer **1a**. The same experimental ^3J values for the carbomethoxy- and phenyl substituted compounds **1a** and **1b** give evidence that their conformational states in solutions are analogous. The reality of the co-existing of two equally probable conformer types for 1*R*,4*S*-diastereomers under study follows from that experimental fact that compound **1a** forms crystals with *chair*-like molecular conformation, but compound **1b** has in crystal *twist* one.

As one can see from a comparison of the Figures 2 and 3, the diastereomeric compounds **1a** and **2a** differ one from other in the molecular shape. The 1*R*,4*S*-isomer possesses lower anisometrical molecules than 1*R*,4*R*- one.

Behavior of the Diastereomeric Chiral Dopants in the Induced Cholesteric LC Systems

As it can be seen from the Table 2, the diastereomeric chiral dopants **1a** and **2a** as well as **1b** and **2b** induce cholesteric helix with the same sense and exhibit a close HTP (see β values). Only slight tendency to the higher $|\beta|$ values for 1*R*,4*S*-isomers can be noted. It bears evidence that the sense and magnitude of the HTP of different 2-arylidene-*p*-menthane-3-ones are defined by the configuration and environment just of the C-1 chiral center and depend slightly on those for C-4 one. Such a view is confirmed also by a significant difference in the HTP of these compounds *E*- and *Z*-isomers [12].

TABLE 2 Characteristics of the helical twisting induced by diastereomeric chiral dopants **1** and **2**

CD	Configuration	$\lvert\beta\rvert$, μm^{-1}mol.fr^{-1}		$dP/dT\times10^4$, μm/degree	
		MBBA	5CB	MBBA	5CB
1a	1*R*,4*S*	34.7 ± 1.0	33.1 ± 1.3	110 ± 10	108 ± 28
2a	1*R*,4*R*	32.8 ± 1.6	24.2 ± 2.0	61 ± 7	10 ± 30
1b	1*R*,4*S*	–	39.8 ± 1.6	–	–
2b	1*R*,4*R*	41.9 ± 1.4	36.9 ± 0.6	–	0.0 ± 30

For LC system studied, a slight increase of the induced *P* values is observed as temperature rises (parameter *dP*/*dT* is positive). Such a behavior is characteristic usually of the CD possessing a relatively low anisometric molecules [13, 14]. However, it should be pay attention to the essential difference in the *dP*/*dT* parameter for respective systems, containing diastereomeric CD **1a** and **2a**. Taking into account the results of the works [13, 14], the more value of this parameter for system containing compound **1a** agrees well with the lower molecular anisometry of this CD in comparison with its isomer **2a** (see Figures 2, 3).

Thus, the distinctions in the behavior of the 2-arylidene derivatives of the chiral diastereomeric *p*-menthane-3-ones in induced cholesteric mesophases are defined by the peculiarities of their molecular shape associated with the different conformation states.

EXPERIMENTAL

The measurement ^{1}H NMR spectra was carried out using a Jeol JNM-LA 400 FT NMR spectrometer. Infra-red spectroscopy was carried out using a Specord M 82 infra-red spectrometer. Optical rotations of chiral materials were determined using a SU-4 polarimeter. The HPLC analysis was performed on a liquid micro-column chromatograph Milichrom 5-3 using a 2 × 80 mm Silasorb normal phase column and 5% of butyl acetate in heptane as the eluent.

P values for LC systems under study were measured using conventional Grandjean – Cano technique as described in the previous report [15]. The HTP values were calculated from $\beta = (PC)^{-1}$ equation, where C is the CD mole fraction.

Conformational calculations were carried out by the molecular mechanics method with the MMX force field [16].

Synthesis of the Chiral Dopants 1a, 2a

The directed aldol condensation of (–)-menthone lithium enolate with 4-carbomethoxybenzaldehyde was carried out at –85 °C (manner 1) or at –50 °C (manner 2) as described in [4]. Crude ketol mixture was dehydrated by DCC in presence of Cu_2Cl_2 during 30 days similarly as described in [7]. Using manner 1 for aldol reaction, the isomer **1a** only was detected in reaction mixture after dehydration. In the case of the manner 2, mixture of **1a**, **2a** was formed in 3 : 2 ratio. The same isomers ratio was obtained also by acidic isomerization of **1a** (3.6 % of $HClO_4$ in methanol at 25 °C during 20 h). The mixture obtained was separated by column chromatography (silica gel, 2.5 % of ethyl acetate in hexane was used as eluent). Pure isomers **1a**, **2a** were obtained by twice crystallization from methanol. ^{1}H NMR spectra for **1a**, **2a** are shown on the Figure 1.

1a: m.p. 73-74 °C; $[\alpha]_D^{20}$ ($CHCl_3$) –205; ν_{max} (KBr) / cm^{-1} 1720, 1683, 1623, 1607; Found: C, 75.8; H, 8.0 $C_{19}H_{24}O_3$ requires C, 76.0; H, 8.1;
2a: m.p. 66-67 °C; ν_{max} (KBr) / cm^{-1} 1712, 1672, 1597, 1560; Found: C, 76.1; H, 8.1 $C_{19}H_{24}O_3$ requires C, 76.0; H, 8.1;

CONCLUSION

The diastereomeric 1*R*-2-arylidene-*p*-menthane-3-ones with *R*- and *S*-configurations of the C-4 chiral center exhibit the equal virtually helical twisting power in the induced cholesteric mesophases. At the same time, the 1*R*,4*S*-diastereomer induces the cholesteric helix which the pitch increases with the temperature to a more extent than in the case of the systems containing the 1*R*,4*R*-isomer. This difference corresponds qualitative to the distinction in the molecular anisometry caused by conformational peculiarities of the diastereomers.

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