Chiral β-hydroxycarbonyl compounds based on (−)-menthone: structure and behavior in liquid crystalline systems

L. A. Kutulya,[a] L. D. Patsenker,[a] V. V. Vashchenko,[a] V. P. Kuznetsov,[a] V. I. Kulishov,[b] Yu. N. Surov,[c] and V. V. Kravets[a]*

[a]*Institute for Single Crystals, National Academy of Sciences of Ukraine, 60 Prospekt Lenina, 310001 Khar'kov, Ukraine. Fax: +7 (057 2) 32 0273*

[b]*Institute of Physics, National Academy of Sciences of Ukraine, 46 Prospekt Nauki, 252650 Kiev, Ukraine. Fax: +7 (044) 265 1589*

[c]*Khar'kov State University, 4 Pl. Svobody, 310077 Khar'kov, Ukraine. Fax: +7 (057 2) 47 1272*

It has been established by X-ray structural analysis that 2-(1'-biphenyl-4-yl-1'-hydroxy)methyl-*p*-menthan-3-one, one of the products of the reaction of (−)-menthone triisopropyloxytitanium enolate with 4-phenylbenzaldehyde, has a 1*R*,2*S*,4*S*,1'*S* configuration. In crystals, this β-hydroxyketone adopts a chair conformation with equatorial methyl and isopropyl groups and an axial 2-(1'-biphenyl-4-yl-1'-hydroxy)methyl substituent. Unlike the stereoisomeric compound with the 1*R*,2*R*,4*S*,1'*S* configuration, the exocyclic fragment of which has an intramolecular >C=O...H—O— hydrogen bond in crystals and solutions, in the crystals of the 1*R*,2*S*,4*S*,1'*S* ketol under study, molecules are linked by a network of cooperative —O—H...O—H...O—H... hydrogen bonds. Based on the results of molecular mechanics calculations and experimental data of ^{1}H NMR and IR spectroscopy, conformations of molecules of this compound, which are in equilibrium in solution, have been characterized. Based on data on spatial structures of stereoisomeric β-hydroxyketones and the character of H-bonds formed by these compounds, the characteristic features of the effect of these chiral alloying additives on the supramolecular structure and macroscopic properties of liquid crystalline systems have been interpreted.

Key words: stereoisomeric 2-(1'-biphenyl-4-yl-1'-hydroxy)methyl-*p*-menthan-3-ones, molecular structure, X-ray structural analysis, crystal structure, conformational analysis, molecular mechanics, hydrogen bond, induced cholesteric liquid crystals, twisting power.

One of the most important problems in modern physical chemistry of liquid crystalline systems is the establishment of regularities of the effect of spatial structures of chiral alloying additives on macroscopic properties of mesophases: efficiency of induction of helical supramolecular structures, temperatures of phase transitions, moduli of elasticity, *etc.*[1] This spurs growing interest in the preparation of new chiral compounds, including compounds based on (−)-menthone,[2,3] and study of their spatial structures and stereochemical aspects of the corresponding reactions (see, for example, Refs. 4—7).

The molecular structure of the chiral β-hydroxyketone (ketol), one of the products of the reaction of (−)-menthone bromomagnesium enolate with 4-phenylbenzaldehyde, has been studied in crystals and solutions by X-ray structural analysis, ^{1}H NMR spectroscopy, and conformational calculations.[8,9] It has been established that this ketol has the 1*R*,2*R*,4*S*,1'*S* stereochemical configuration and exists in crystals and solutions in a conformation with an intramolecular —OH...O=C< hydrogen bond. The use of (−)-menthone triisopropyloxytitanium enolate rather than its bromomagnesium analog made it possible to isolate β-hydroxyketone **1a**, which is not identical to 1*R*,2*R*,4*S*,1'*S* stereoisomer **1b** obtained previously.

The main aim of this study is to establish the stereochemical configuration of 2-(1'-biphenyl-4-yl-1'-hydroxy)methyl-*p*-menthan-3-one (**1a**), one of the products of the reaction of (−)-menthone triisopropyloxytitanium enolate with 4-phenylbenzaldehyde,* by X-ray structural analysis and to compare molecular and crystal structures of two stereoisomeric β-hydroxyketones **1a**

* The results of a study of stereoselectivity of the reactions of different (−)-menthone enolates with aromatic aldehydes will be published later.

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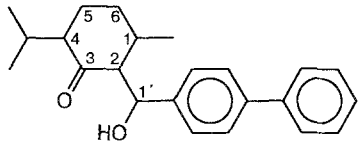
and **1b** and their conformations in solutions based on the data of ^{1}H NMR and IR spectroscopy and the results of theoretical conformational analysis.

It was also important to elucidate the character of hydrogen bonds formed by the OH group of compounds **1a** and **1b** under study in crystals and solutions including solutions in mesomorphic solvents.



1a: 1*R*,2*S*,4*S*,1'*S*

1b: 1*R*,2*R*,4*S*,1'*S*

The obtained comprehensive information on the structural features of stereoisomeric ketols **1a,b** would be useful for analysis of the effect of these chiral additives on macroscopic properties of liquid crystals of different chemical nature, primarily, on the efficiency of inducing of helical ordering in mesophases, which is characterized by the value of the twisting power β. In particular, in this work, the task was set of studying the regularities of the changes in the twisting power of chiral compounds **1a,b** in induced cholesteric systems based on nematic mesogenic compounds, 4-methoxybenzylidene-4'-(*n*-butyl)aniline and 4-(*n*-pentyl)-4'-cyanobiphenyl, which exhibit different basicity and interact with proton-donating chiral additives under study in potentially different ways.

Results and Discussion

The molecular structure of β-hydroxyketone **1a**, which was established by X-ray structural analysis, is shown in Fig. 1; the atomic numbering scheme is also shown in Fig. 1. The bond lengths and bond angles are given in Tables 1 and 2, respectively; data on compound **1b** are given for comparison. In structure **1a**, the cyclohexanone ring has, like stereoisomeric compound **1b**,[8] an almost undistorted chair conformation, as indicated by the alternating signs of torsion angles in the cycle and their absolute values (54.8—62.5°), which differ little from the typical value (60°) for an ideal chair conformation. A chair-type conformation of the cycle and its very slight deformation in the structure under study is characterized by deviations of pairs of atoms, C(1) and C(4) or C(2) and C(5) or C(3) and C(6), in opposite directions from the calculated mean planes passing through the corresponding opposite bonds of the cycle. The methyl and isopropyl groups of compound **1a**, like compound **1b**, are in *trans*-equatorial orientation with respect to the cyclohexanone ring. This is evident from the values of the C(7)C(1)C(2)C(3), C(7)C(1)C(6)C(5), C(8)C(4)C(3)C(2), and C(8)C(4)C(5)C(6) torsion angles, which are close to 180°, and from the slight deviations of the C(7) and C(8) atoms in opposite directions from the above-mentioned calculated planes. Therefore, when the approach to the synthesis of β-hydroxyketones based on (−)-menthone (generation of intermediate enolate carbanions with strong sterically hindered organometallic bases), which is substantiated in Ref. 7, is used, a 1*R*,4*S* configuration of the initial ketone is retained independently of the nature of the

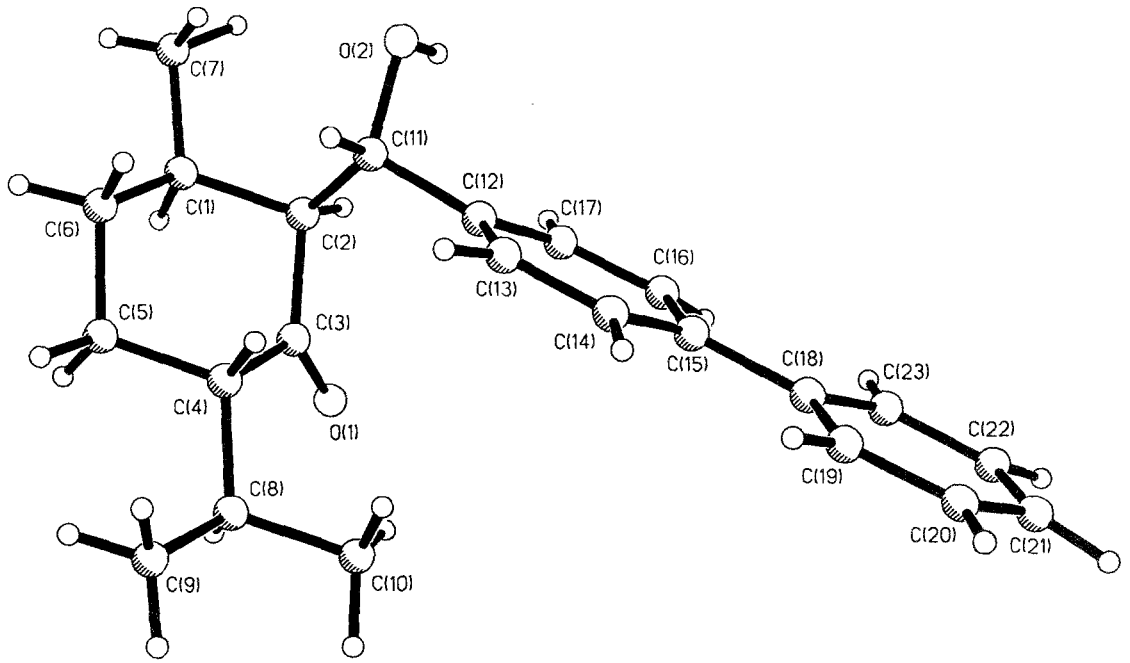


Fig. 1. Molecular structure of compound **1a**.

Table 1. Bond lengths (d/Å) in the structures of stereoisomeric ketols **1a** and **1b**

Bond	**1a**	**1b**	Bond	**1a**	**1b**
C(1)—C(2)	1.563(7)	1.538(3)	C(11)—C(12)	1.525(7)	1.516(3)
C(1)—C(6)	1.506(9)	1.509(4)	C(12)—C(13)	1.354(8)	1.390(3)
C(1)—C(7)	1.526(8)	1.545(4)	C(12)—C(17)	1.371(8)	1.372(3)
C(2)—C(3)	1.526(7)	1.517(3)	C(13)—C(14)	1.381(8)	1.375(3)
C(2)—C(11)	1.528(8)	1.530(3)	C(14)—C(15)	1.361(9)	1.384(3)
C(3)—C(4)	1.508(8)	1.497(3)	C(15)—C(16)	1.367(8)	1.384(3)
C(3)—O(1)	1.207(7)	1.220(3)	C(15)—C(18)	1.495(7)	1.480(3)
C(4)—C(5)	1.529(8)	1.547(3)	C(16)—C(17)	1.373(9)	1.384(3)
C(4)—C(8)	1.534(8)	1.529(3)	C(18)—C(19)	1.397(9)	1.383(3)
C(5)—C(6)	1.533(8)	1.516(4)	C(18)—C(23)	1.364(9)	1.394(4)
O(2)—C(11)	1.448(6)	1.421(3)	C(19)—C(20)	1.370(8)	1.377(4)
O(2)—H(O)	0.939(4)	0.860(15)	C(20)—C(21)	1.382(10)	1.371(4)
C(8)—C(9)	1.508(11)	1.519(4)	C(21)—C(22)	1.361(9)	1.370(4)
C(8)—C(10)	1.522(9)	1.516(4)	C(22)—C(23)	1.382(9)	1.373(4)

Table 2. Bond angles in the structures of stereoisomeric ketols **1a** and **1b**

Angle	ω/deg		Angle	ω/deg	
	1a	**1b**		**1a**	**1b**
C(2)—C(1)—C(6)	110.6(4)	110.9(2)	C(11)—C(12)—C(13)	121.9(5)	121.4(2)
C(1)—C(2)—C(3)	105.5(4)	107.0(2)	C(11)—C(12)—C(17)	122.7(5)	121.9(2)
C(2)—C(3)—C(4)	115.7(4)	116.2(2)	C(13)—C(12)—C(17)	115.5(5)	116.6(2)
C(3)—C(4)—C(5)	105.7(5)	104.0(2)	C(12)—C(13)—C(14)	122.2(6)	121.4(2)
C(4)—C(5)—C(6)	111.4(4)	111.4(2)	C(13)—C(14)—C(15)	122.0(6)	122.2(2)
C(1)—C(6)—C(5)	113.4(6)	113.5(2)	C(14)—C(15)—C(16)	116.4(5)	116.0(2)
C(2)—C(1)—C(7)	114.0(4)	111.8(2)	C(14)—C(15)—C(18)	122.4(5)	122.4(2)
C(6)—C(1)—C(7)	112.3(4)	110.9(2)	C(16)—C(15)—C(18)	121.2(6)	121.5(2)
C(3)—C(4)—C(8)	114.5(5)	113.3(2)	C(15)—C(16)—C(17)	120.9(6)	121.8(2)
C(5)—C(4)—C(8)	113.7(4)	115.2(2)	C(12)—C(17)—C(16)	123.1(6)	121.9(2)
O(1)—C(3)—C(2)	120.7(5)	120.8(2)	C(15)—C(18)—C(19)	120.6(6)	121.8(2)
O(1)—C(3)—C(4)	123.5(5)	122.6(2)	C(15)—C(18)—C(23)	123.4(5)	121.2(2)
C(1)—C(2)—C(11)	115.5(5)	114.0(2)	C(19)—C(18)—C(23)	116.0(5)	117.0(2)
C(3)—C(2)—C(11)	112.3(4)	112.4(2)	C(18)—C(19)—C(20)	122.2(6)	121.2(2)
C(4)—C(8)—C(9)	112.3(5)	110.0(2)	C(19)—C(20)—C(21)	119.9(6)	120.8(2)
C(4)—C(8)—C(10)	112.8(5)	113.7(2)	C(20)—C(21)—C(22)	119.1(5)	118.9(3)
C(9)—C(8)—C(10)	108.1(5)	110.6(2)	C(21)—C(22)—C(23)	120.1(6)	120.5(3)
C(2)—C(11)—O(2)	109.9(4)	110.5(2)	C(18)—C(23)—-C(22)	122.7(6)	121.5(3)
O(2)—C(11)—C(12)	109.0(4)	112.1(2)	C(11)—O(2)—H(O)	107.0(10)	98.9(10)
C(2)—C(11)—C(12)	113.6(5)	114.9(2)			

cation in the intermediate enolate. However, the new chiral C(2) center, which appears in the reaction of aromatic aldehyde with different (−)-menthone enolates, adopts different configurations in the structures of **1a** and **1b**. In compound **1a**, an *S* configuration of the above-mentioned center (unlike an *R* configuration of this center in ketol **1b**) is unambiguously evidenced by the spatial orientation of the 2-(1'-biphenyl-4-yl-1'-hydroxy)methyl substituent in the axial position (the C(11)C(2)C(1)C(6) and C(11)C(2)C(3)C(4) torsion angles are −69.6 and 64.2° for **1a** and 177.0 and 172.4° for **1b**, respectively). Clearly, this substituent in compound **1a** is in the *cis* position with respect to the methyl group and, correspondingly, in the *trans* position with respect to the 4-isopropyl group.

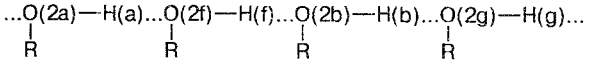
Therefore, β-hydroxyketone **1a** under study, which is a derivative of (−)-menthone, is 1,2-*cis* substituted and 2,4-*trans* substituted cyclohexanone. The chiral C(11) center, which appears when ketol **1a** is formed, adopts an *S* configuration (Fig. 1). A conformation of the exocyclic fragment of molecule **1a** determined by hindered rotation around the C(2)—C(11) bond is characterized, as in the case of the structure of **1b** studied previously,[8] by the transoid orientation of the aryl substituent with respect to the C(1)—C(2) bond: the C(1)C(2)C(11)C(12) torsion angle for compounds **1a** and **1b** is 164.0 and 174.4°, respectively. In this conformation, the aryl substituent is remote substantially from the $>C(1)HCH_3$ fragment, owing to which unfavorable nonbonded interactions of these fragments are eliminated. The hydroxyl group at the C(11) atom in the structure of **1a** is remote from the carbonyl oxygen atom (the O(1)—H(O) distance is 4.45 Å) so that the formation of an intramolecular hydrogen bond is impossible.

This is the difference between β-hydroxyketone **1a** and its stereoisomer **1b** studied previously.[8]

In crystals, the biphenylyl fragment of ketol **1a** under study is planar unlike stereoisomeric compound **1b**, in which the torsion angle between benzene rings is 26°. This difference is, apparently, a consequence of different packings of molecules in crystals of these compounds. Some steric strain, which occurs in crystals of the molecular structure of **1a**, is evidenced by the observed shortened intramolecular contacts between hydrogen and carbon atoms in *ortho* positions of different cycles of the biphenylyl group: H(14)...H(19), H(16)...H(23) (2.06 and 2.11 Å, the sum of van der Waals radii according to the data in Ref. 10 is 2.32 Å), H(14)...C(19), H(16)...C(23), H(19)...C(14), H(23)...C(16) (2.61, 2.64, 2.66, and 2.70 Å, the sum of van der Waals radii is 2.87 Å), C(14)...C(19), and C(16)...C(23) (2.94 and 2.95 Å, the sum of van der Waals radii is 3.42 Å). The twists of the aryl substituent with respect to the C(11)—C(12) bond in studied stereoisomers **1a** and **1b** are substantially different (the corresponding torsion angle is −121.6 and −53.1°, respectively).

As in the case of the structure of **1b** studied previously, the isopropyl fragment in compound **1a** adopts a conformation with a *trans* orientation of the C(8)—H(8) bond with respect to the C(4)—H(4) bond. The characteristic feature of the conformation of compound **1a** observed in crystals is the substantial spatial proximity of the benzene ring at the C(11) atom and the isopropyl fragment (see Fig. 1).

In crystals of ketol **1a**, two systems of shortened intermolecular contacts are observed. Molecules related by a translation along the X axis $(1+x, y, z)$ form contacts of the C(4b)—H(4b)...O(1a) type shown in Fig. 2. Geometric characteristics of the intermolecular contacts are given in Table 3. The hydroxyl groups of molecules related by a screw axis $(0.5+x, 0.5-y, 1-z)$ form a cooperative hydrogen bond in the form of a chain with crystallographic 2_1 symmetry:



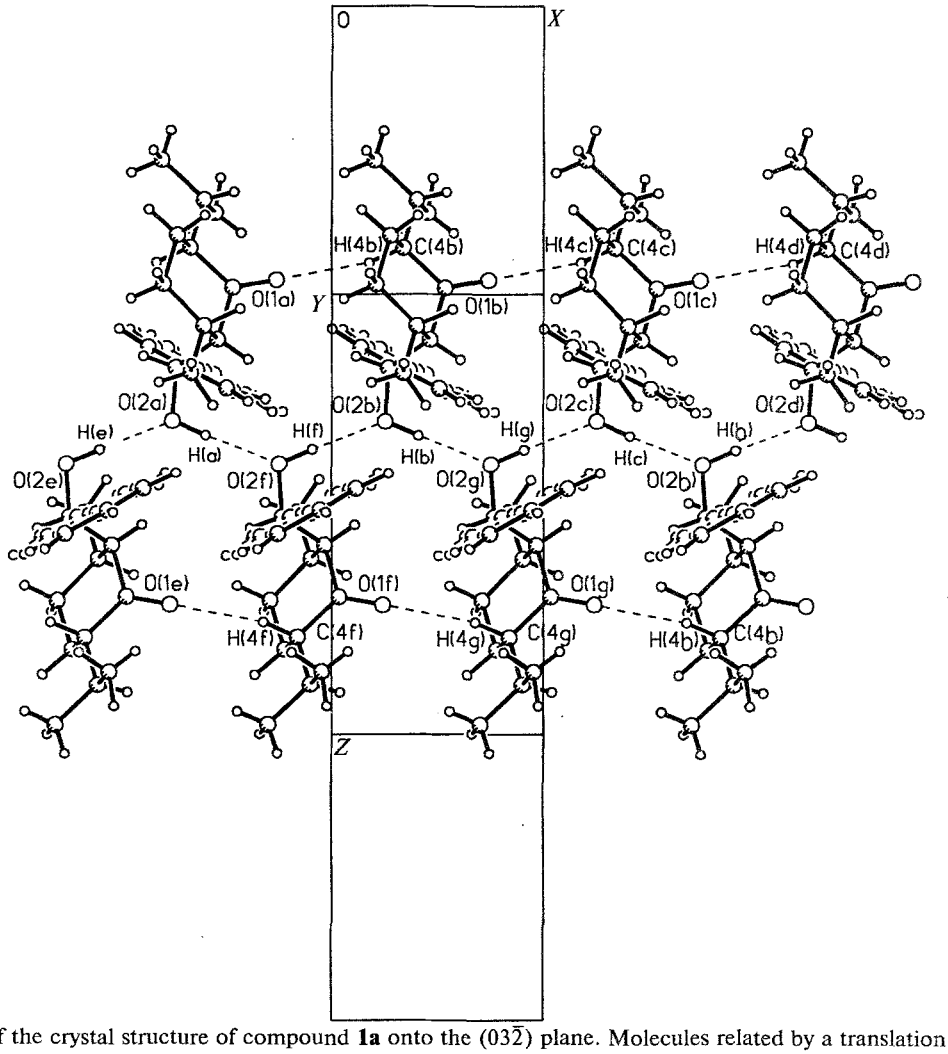


Fig. 2. Projection of the crystal structure of compound **1a** onto the $(03\bar{2})$ plane. Molecules related by a translation along the X axis $(1+x, y, z)_4$ and a screw axis $(0.5+x, 0.5-y, 1-z)$ are shown.

Table 3. Geometric characteristics of intermolecular contacts in the structure of **1a**

D—H...A	D...A/Å	D—H/Å	H...A/Å	∠DHA /deg
O(2)—H...O(2') (0.5+*x*, 0.5−*y*, 1−*z*)	2.978	0.94	2.05	170
C(4)—H(4a)...O(1') (1+*x*, *y*, *z*)	3.417	1.06	2.46	149

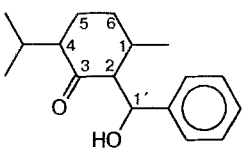
Each molecule has four shortened contacts; molecules linked by these contacts form a ribbon extended along the *X* axis.

Therefore, from the X-ray structural data it follows that in the crystal phase, β-hydroxyketone **1a** forms an intermolecular O—H...O—H hydrogen bond rather than a O—H...O=C< bond as was established for the crystal structure of 2-(1'-hydroxy-1'-phenyl)methyl-2-methylcyclohexanone.[11]

According to the X-ray structural data,[8] stereoisomeric ketol **1b** unlike **1a** is characterized by the presence of intramolecular hydrogen bonds in crystals. This type of an H-bond manifests itself in the IR spectra (KBr) as the narrow ν(OH) band at 3497 cm^{-1} and the reduced value of ν(C=O) = 1691 cm^{-1}. A rather strong intramolecular hydrogen bond is retained also in CCl_4 solutions at least in the concentration range 10^{-4}—$2 \cdot 10^{-2}$ mol L^{-1}: ν(OH) = 3522 cm^{-1} and ν(C=O) = 1697 cm^{-1}. It was possible to observe cleavage of an intramolecular hydrogen bond and formation of intermolecular H complexes only when a strong base like DMSO was added. In this case, the ν(OH) band of intermolecular associates at 3372 cm^{-1} (Δν(OH) = 150 cm^{-1}) is observed only with a tenfold excess of a base. The association constant, which was determined from the change in the peak intensity of the ν(OH) band as the concentration of the base changes,[12] is rather low (0.86). In systems containing mesogenic 4-methoxybenzylidene-4'-(*n*-butyl)aniline and 4-(*n*-pentyl)-4'-cyanobiphenyl as bases, no H complex formation was observed.

In the case of ketol **1a**, the formation of intermolecular hydrogen bonds in the solid phase manifests itself as a broad ν(OH) band at a lower frequency (3400 cm^{-1}) compared to that of **1b**. The high-frequency position of the ν(C=O) band (1704 cm^{-1} in contrast to that of ketol **1b** (1691 cm^{-1}), KBr) and the broad ν(OH) band are indicative of the involvement of the OH groups in intermolecular OH...OH hydrogen bonds.

Taking into account the possibility of the difference in molecular conformations observed in the crystal phase and solutions, we performed conformational analysis of model stereoisomeric structures **2a** and **2b** by the molecular mechanics method. The results of the analysis demonstrate the conformational features of isolated molecules of the compounds under study in an inert weakly polar medium.



2a: 1*R*,2*S*,4*S*,1'*S*

2b: 1*R*,2*R*,4*S*,1'*S*

The values of the steric energy (E_{ster}), enthalpy of formation (ΔH_{form}), strain energy (E_{str}), and selected torsion angles for the most probable conformations **A**—**C** of the model structures are given in Table 4. These conformations differ by either the orientation of substituents at positions 1, 2, and 4 of the cyclohexanone ring (the φ_1 — φ_3 torsion angles) or the rotation about the exocyclic C(2)—C(11) bond (φ_4 and φ_5). The geometric parameters of the conformation actually observed in crystals of compound **1a** agree rather well with the calculated data for the **B** conformer of model compound **2a**. However, according to the calculation, this conformer is not energetically most favorable for isolated molecules. The preferred conformation is the **A** conformation, which differs from the **B** conformation by the orientation of substituents in the cyclohexanone ring: the methyl and isopropyl groups are in axial positions, while the most bulky 2-(1'-aryl-1'-hydroxy)methyl substituent is in an equatorial position. The conformation of the exocyclic fragment, which is determined by the rotation about the C(2)—C(11) bond, is nearly identical in the **A** and **B** conformers (see φ_4 and φ_5). In both cases, formation of intramolecular hydrogen bonds is impossible, unlike β-hydroxyketone **1b** studied previously[8,9] and model compound **2b**, because intramolecular distances between the O(1) and H(O) atoms are rather large (4.70 and 5.07 Å for the **A** and **B** conformers, respectively). Energy preference of the **A** conformer

Table 4. Results of conformational analysis of model structures **2a** and **2b**

Parameter	Structure			
	2a			**2b**
	A	**B**	**C**	
E_{ster}	25.24	25.76	26.23	23.49
ΔH_{form}	−98.01	−98.24	−96.76	−99.76
E_{str}	18.04	18.56	19.03	16.28
Torsion angles:				
φ_1 C(7)C(1)C(2)C(3)	+71	+178	+72	+177
φ_2 C(8)C(4)C(3)C(2)	+73	−176	+79	−174
φ_3 C(11)C(2)C(3)C(4)	−174	+74	−176	+171
φ_4 C(3)C(2)C(11)C(12)	+59	+45	−178	−63
φ_5 C(3)C(2)C(11)O(2)	−179	+166	−51	−64
φ_6 C(2)C(11)O(2)H(O)	−178	−170	+68	−64
φ_7 C(11)O(2)H(O)O(1)	—	—	−42	+24
φ_8 O(2)H(O)O(1)C(3)	—	—	−4	+22
φ_9 H(O)O(1)C(3)C(2)	—	—	+22	−22
φ_{10} O(1)C(3)C(2)C(11)	+6	−107	+2	−10

following from the results of calculations corresponds to the general concept of the conformational analysis,[13] according to which the bulkiest substituent in the cyclohexanone ring occupies predominantly an equatorial position. Note also that both in the structure of **1a** and in the case of the **B** conformation of model compound **2a**, no substantially shortened contacts between atoms of the axial substituent at position 2 and the axial H(4) and H(6b) atoms, which would characterize axial-axial interactions, are observed: the shortest intramolecular distances of this type, C(11)...H(4), C(11)...H(6b), and H(11)...H(6b), are 2.78, 2.88, and 2.35 Å, respectively.

When the bulkiest 2-(1'-aryl-1'-hydroxy)methyl substituent occupies an equatorial position, the **C** form is possible in addition to the energetically most favorable **A** conformation; the **C** form differs in orientation of fragments of this bulky substituent with respect to the cyclohexanone ring (see φ_4 and φ_5, Table 4). In the **C** conformer, the *gauche* orientation of the C(11)—O(2) bond with respect to the C(2)—C(3) bond of the cyclohexanone ring provides the possibility of formation of an intramolecular hydrogen bond between the hydroxyl group and the carbonyl oxygen atom (the O(1)...H(O) and O(1)...O(2) distances are 2.01 and 2.69 Å, respectively; the O(1)...H(O)—O(2) angle is 127°). The pseudocycle containing an intramolecular hydrogen bond, which is annelated with the cyclohexanone ring, adopts an O(2),H(O)-half-boat conformation (φ_5—φ_{10}, Table 4). The steric energy of the **C** conformer (taking into account the energy of the intramolecular hydrogen bond) is 1 kcal mol^{-1} larger than that of the most favorable **A** form and ~0.5 kcal mol^{-1} larger than that of the **B** conformer, which corresponds to the molecular structure of β-hydroxyketone **1a** in crystals. The same difference was obtained also for the calculated values of the strain energy of the conformation under consideration. This may be determined by steric hindrances between the aryl group and the C(1)HCH$_3$ fragment owing to their proximity in the **C** conformer. The calculated shortened H(1)...C(12) (2.70 Å), C(1)...C(12) (3.04 Å), and C(7)...C(11) (3.16 Å) contacts between atoms of the above-mentioned fragments can be considered as a manifestation of these nonbonded interactions in the **C** conformation. In the **A** and **B** conformations, these shortened contacts are absent. Similar differences in the energies of conformers with aryl groups in different orientations with respect to the cyclohexanone ring, which are caused by analogous reasons, were observed[9] (according to the results of calculations) also for stereoisomeric ketols with the *1R,2R,4S,1'S* (**1b**) and *1R,2R,4S,1'R* configurations.

The rotation of the isopropyl group causes the possibility of the existence of three rotamers for each of the conformers **A**—**C**. In all cases, the preferred rotamers are those with the *trans* arrangement of the C(4)—H(4) and C(8)—H(8) bonds: the H(4)C(4)C(8)H(8) torsion angle is 169—173°. It is this conformation of the isopropyl fragment that is actually observed in crystals. In the case of the **B** conformer with the equatorial arrangement of the 1-methyl and 4-isopropyl substituents, the *gauche* forms are energetically less favorable (by 0.6 kcal mol^{-1}) than the *trans* rotamer. For the conformers with the axial 1,4-alkyl groups, this difference is substantially larger: 3.0 and 2.4 kcal mol^{-1} in the case of **A** and 2.1 kcal mol^{-1} for both *gauche* rotamers of the **C** form. A comparison of these data with the results of the other studies[4—9,14,15] allows a conclusion that the rotameric equilibrium of the isopropyl fragment of the derivatives of *p*-menthan-3-ones depends substantially on their structural features: configurations of chiral centers, orientations of substituents with respect to the cyclohexanone ring, and the presence of additional sp^2-carbon atoms in the cycles.

Therefore, the results of molecular mechanics calculations allow a conclusion that conformational nonuniformity of β-hydroxyketone under study is possible. In solutions, including solutions in liquid crystalline solvents, the possibility of coexistence of at least three different conformations of the types **A**—**C** should be taken into account. The ratio of these conformers would depend on the temperature as well as the basic properties of the solvent. In highly basic solvents, some liquid crystalline media (for example, 4-methoxybenzylidene-4'-(*n*-butyl)aniline) being also such solvents, the conformation equilibrium can be shifted toward the **A** and **B** forms because of their stabilization through intermolecular hydrogen bonds.

Generally, knowledge of conformations existing in solutions can be obtained from the ^{1}H NMR data. In the spectrum of ketol **1a** recorded at 200 MHz, the doublet H(11) signal at 5.15 ppm with a spin-spin coupling constant of 7.5 Hz caused by interaction with the vicinal H(2) proton can be identified. The H(2) resonance: dd at 3.08 ppm, $^3J_{H(11)}$ = 7.5 Hz and $^3J_{H(1)}$ = 4.9 Hz. The hydroxyl proton manifests itself as a broadened signal at 2.61 ppm. A large diamagnetic shift of this signal compared to the corresponding signal in the spectrum of stereoisomeric ketol **1b** (4.30 ppm[9]) may result primarily from the involvement of the hydroxyl group of the stereoisomers under study in different types of H bonds: intermolecular —O—H...O—H hydrogen bonds in **1a** and intramolecular —O—H...O=C< hydrogen bond in **1b**. The possible shielding effect of the circular currents of the aryl group[16] on the hydroxyl proton in stereoisomeric compounds **1a** and **1b** should be considered approximately equal. According to the results of molecular mechanics calculations, the difference in the orientation of this proton with respect to the nearest benzene ring in predominant conformations of compounds **1a** and **1b** is insignificant.

A substantial paramagnetic shift of the H(11) signal in the spectrum of **1a** compared to that of **1b** (δ 4.91)[9] corresponds well to the position of this proton nearly in the plane of the benzene ring at the distance r = 3.5 Å from its center in the **A** and **B** conformers, whereas in

Tables 5. Calculated torsion angles and values of ^3J of selected protons for possible conformers of model ketol **2a**

Parameter	Conformer		
	A	**B**	**C**
Concentration at 25 °C, mole fractions	0.62	0.26	0.12
H(1)C(1)C(2)H(2)/deg	−57	+50	−58
$^3J_{H(1),H(2)}$/Hz	4.4	5.4	4.4
H(2)C(2)C(11)H(11)/deg	−179	+167	−49
$^3J_{H(2),H(11)}$/Hz	12.7	12.1	5.6

compound **1b** with the same value of r, the angle between the ring plane and the direction of r is 15°.

Table 5 gives the torsion angles (according to the results of molecular mechanics calculations) and vicinal spin-spin coupling constants of the H(1) and H(2), H(2) and H(11) protons calculated using Durette—Horton's equation (1)[17] for alternative **A**—**C** conformations of ketol **1a**.

$$^3J_{HH} = (7.8 - \cos\varphi + 5.6\cos 2\varphi)(1 - 0.1\,\Sigma\Delta\chi_i) \quad (1)$$

where φ is the torsion angle and $\Delta\chi_i$ is the difference in electronegativities of the substituent in the ethane fragment and the hydrogen atom.

The weighted-mean values of $^3J_{H(1),H(2)}$ and $^3J_{H(2),H(11)}$ calculated with the use of these data are 4.6 and 11.7 Hz. The first of these constants agrees well with the experimental value of 4.9; the second constant is substantially overestimated (7.5 Hz in the spectrum). A substantial steric strain of the studied compound, which is not taken into account by equation (1), may be responsible for this discrepancy. According to the X-ray structural data, the H(11)C(11)C(2) bond angle has a larger value (115(3)°) compared to the standard value for the sp^3 carbon atom, which can cause a decrease in the spin-spin coupling constant (see Ref. 16). However, a high error in determining this angle makes it impossible to unambiguously judge the set of factors determining the observed values of $^3J_{H(2),H(11)}$ and, correspondingly, to estimate the preferred conformations of ketol **1a** in solutions from ^{1}H NMR spectra.

In the ^{1}H NMR spectrum of β-hydroxyketone **1a** under study, a substantial difference in chemical shifts of protons of two methyl groups of the isopropyl fragment (δ 0.46 and 0.89) is observed; the signal of one of this groups undergoes a large diamagnetic shift compared to that in the spectrum of stereoisomeric compound **1b** (δ 0.74 and 0.81).[9] This effect is in agreement with the characteristic features of the mutual orientation of the isopropyl and aryl fragments in the most probable conformations of this ketol. The molecular mechanics calculations demonstrate that for a number of energetically most favorable rotamers of the **A** and **B** conformers, protons of the nearest methyl group are at a distance of 3.4—4.4 Å from the center of the benzene ring at an angle of 15—45° to the normal, *i.e.*, these protons are located in the region of shielding by the circular currents of the aromatic system.[16] In the alternative rotamers of ketol **1b**, these protons are at a greater distance from the benzene ring (4.4—5.4 Å).

The presence of conformers with intramolecular hydrogen bonds in diluted solutions of ketol **1a** in CCl_4 is evidenced by the data of IR spectroscopy. In the spectrum of a 0.01 mol L^{-1} ketol **1a** solution, the narrow ν(OH) band at 3615 cm^{-1} and a slightly broader band at 3532 cm^{-1} (the ratio of peak intensities is 1:1) are observed. The high-frequency band corresponds to absorption of a free OH group, while the low-frequency band is attributable to absorption of conformers with intramolecular hydrogen bonds. This is confirmed by the fact that when a solution is diluted tenfold, the position and the ratio of intensities of these bands remain unchanged. The character of carbonyl absorption of solutions of ketol **1a** is also consistent with this interpretation: unlike stereoisomer **1b**, the ν(CO) band has a doublet structure, components of which have approximately equal intensities (1707 cm^{-1} and low-frequency bend at 1695 cm^{-1}). These results agree well with the predictions made by the molecular mechanics method that the conformation equilibrium is present in solutions of ketol **1a**.

Study of the twisting power of stereoisomeric ketols **1a** and **1b** in liquid crystalline systems demonstrated that the twisting power depends strongly on the nature of these chiral additives (Table 6). In the studied induced cholesteric systems based on the nematic compound of the azomethine type (4-methoxybenzylidene-4'-(*n*-butyl)aniline) as well as the derivative of 4-cyanobiphenyl (4-(*n*-pentyl)-4'-cyanobiphenyl), the absolute value |β| for ketol **1a** is smaller than that for its stereoisomer **1b**. A particularly large difference in the values of β is observed in 4-methoxybenzylidene-4'-(*n*-butyl)aniline. Moreover, the studied systems differ substantially in the character of the temperature dependence of the helical pitch P. In 4-(*n*-pentyl)-4'-cyanobiphenyl, regardless of the chiral additive used (**1a** or **1b**), the helical pitch is almost independent of the temperature. By contrast, in the 4-methoxybenzylidene-4'-(*n*-butyl)aniline—**1a** system, a substantial increase in P is observed as the temperature increases, and in the 4-methoxybenzylidene-4'-(*n*-butyl)aniline—**1b** system, this change in P is very small.

Table 6. Twisting power (β) of stereoisomeric β-hydroxyketones **1a**,**b** in induced cholesteric systems

Nematic solvent	$\lvert\beta\rvert/\mu m^{-1}$ ppm^{-1}	
	1a	**1b**
4-Methoxybenzylidene-4'-(*n*-butyl)aniline	2.1±0.9	33.8±1.7
4-(*n*-Pentyl)-4'-cyanobiphenyl	15.0±1.1	23.2±0.8

The observed regularities are determined by the difference in physical and chemical properties of nematic components of the systems under study as well as by the conformational characteristics of the structure and the ability of chiral ketols **1a** and **1b** to form H complexes. First of all, it is important that according to the results of the study by IR spectroscopy and molecular mechanics calculations,[9] ketol **1b** exists in the systems under study almost completely in the form of a conformer stabilized by an intramolecular hydrogen bond. The high twisting power of this conformer in 4-methoxybenzylidene-4'-(*n*-butyl)aniline according to the general concepts of Refs. 18—20 may result from the presence of the extended π electron biphenylyl fragment and the chiral C(11) center with a unique orientation with respect to this fragment; this chiral center is involved in the rather rigid pseudocycle with an intramolecular hydrogen bond, which is in turn annelated with the conformationally uniform cyclohexanone ring of the chiral *p*-menthanone fragment. This conformational stability of chiral additive **1b** apparently provides also a very weak temperature dependence of the helical pitch in liquid crystalline systems containing this additive. A slight decrease in the twisting power of ketol **1b** when passing from 4-methoxybenzylidene-4'-(*n*-butyl)aniline to 4-(*n*-pentyl)-4'-cyanobiphenyl may result from, like the other types of chiral additives,[21] the difference in elastic properties and the parameter of the order of these nematic compounds.

A different situation arises with stereoisomeric chiral additives **1a**. It follows from the results of molecular mechanics calculations that this compound is conformationally labile owing to a small difference in energy of the forms appearing as a result of the inversion of the cycle (the **A** and **B** conformers) as well as the internal rotation about the C(2)—C(11) bond (the **A** and **C** conformers) (Table. 4). An important point is that all alternative conformations of this chiral ketol are characterized by a low molecular anisometry, and therefore, none of them can be stabilized substantially through the effect of an orientationally ordered medium. Besides, at the used concentrations of chiral additives in liquid crystalline systems (0.01÷0.02 mole fractions), the competition of self-association of ketol **1a**, for example, through the formation of cooperative H bonds, which occur in crystals, and formation of H complexes with a nematic compound would be expected. The latter phenomenon is particularly essential in the case of 4-methoxybenzylidene-4'-(*n*-butyl)aniline, which is a rather strong base. Equilibrium processes between different forms of associates as well as conformational transitions of molecules **1a** may cause a strong disordering effect in liquid crystalline systems, which, apparently, impair the formation of a helical supramolecular structure. Analogous effects are proposed also for other conformationally labile chiral compounds with a low molecular anisometry.[19,22,23]

Experimental

***1R,2S,4S,1'S*-2-(1'-Biphenyl-4-yl-1'-hydroxy)methyl-*p*-menthan-3-one (1a).** The synthesis was performed under a dry argon atmosphere. Diethyl ether, diisopropylamine, toluene, and pentane were dried and distilled over sodium just prior to use. A solution of styrene (1.1 mL, 9.6 mmol) in 2 mL of ether was added dropwise to a suspension of lithium (0.131 g, 18.8 mmol) in a boiling mixture of diethyl ether (10 mL) and diisopropylamine (2.7 mL, 19.3 mmol). The mixture was boiled for 1 h (until lithium was completely dissolved) and cooled to −70 °C, and then a solution of (−)-menthone (2.8 mL, 16.2 mmol) in 5 mL of ether was added dropwise. The mixture was stirred for 30 min at −70÷−80 °C, and then a solution of chloro(triisopropyloxy)titanium[24] (4.907 g, 18.8 mmol) in 7 mL of pentane was added dropwise; the mixture was kept for 30 min at the same temperature, and then a solution of 4-phenylbenzaldehyde (3.441 g, 18.9 mmol) in 10 mL of toluene was added dropwise for 5 min. The reaction mixture was kept for 1 h 15 min at −80 °C, and then the mixture was decomposed with a solution of NH_4F (5 g) in 40 mL of water and filtered; the precipitate was washed with ether (20 mL); the aqueous layer was extracted with ether (3 × 10 mL); the organic extracts were combined, washed with water, dried with anhydrous $MgSO_4$, and evaporated. An oily product was obtained in a yield of 4.126 g; according to TLC (Silufol UV-254, $CHCl_3$), the product contained ~50 % of the initial aldehyde, and the other portion was a mixture of ketols: R_f = 0.40 (identical to **1b** obtained previously[8]) and R_f = 0.23 (**1a**). The fraction enriched with ketol **1a** with R_f = 0.23 was isolated by column chromatograhy (silica gel—benzene). Ketol **1a** (0.062 g), m. p. 133.5—134 °C, was isolated from hexane

Table 7. Atomic coordinates (×10⁴) and equivalent isotropic temperature factors B_{eq} in the structure of **1a**

Atom	*x*	*y*	*z*	B_{eq}/Å²
C(1)	4022(13)	2626(3)	3350(3)	4.18(2)
C(2)	4657(10)	1919(3)	3817(2)	3.24(2)
C(3)	5353(10)	1194(3)	3402(2)	3.08(2)
C(4)	3384(10)	876(3)	2974(2)	3.55(2)
C(5)	2783(15)	1579(4)	2526(2)	5.05(2)
C(6)	2103(14)	2356(3)	2890(3)	4.90(2)
O(1)	7409(7)	943(2)	3393(2)	4.66(1)
O(2)	2525(8)	2329(2)	4771(2)	4.18(1)
C(7)	3380(16)	3430(3)	3672(3)	6.24(3)
C(8)	4005(11)	74(3)	2637(3)	4.11(2)
C(9)	2012(16)	−202(4)	2199(4)	8.21(4)
C(10)	4548(16)	−622(4)	3091(4)	6.90(3)
C(11)	2679(12)	1701(3)	4292(2)	3.32(2)
C(12)	3058(9)	875(3)	4611(2)	3.08(2)
C(13)	1386(12)	272(4)	4575(3)	4.82(2)
C(14)	1679(13)	−466(3)	4881(3)	4.74(2)
C(15)	3662(11)	−630(3)	5241(2)	3.16(2)
C(16)	5347(12)	−20(3)	5289(3)	5.53(3)
C(17)	5065(12)	701(3)	4966(3)	4.97(2)
C(18)	3986(12)	−1425(3)	5578(2)	3.63(2)
C(19)	2261(13)	−2044(3)	5520(3)	4.50(2)
C(20)	2465(15)	−2772(3)	5835(3)	5.29(2)
C(21)	4457(12)	−2917(3)	6213(3)	4.11(2)
C(22)	6159(13)	−2322(4)	6280(3)	4.74(2)
C(23)	5897(13)	−1587(3)	5966(3)	4.58(2)

Table 8. Atomic coordinates for hydrogens ($\times 10^3$) in the structure of **1a**

Atom	*x*	*y*	*z*
H(1)	570(4)	270(1)	310(1)
H(2)	609(4)	206(1)	404(1)
H(4)	178(4)	75(1)	323(1)
H(5a)	142(4)	144(2)	223(1)
H(5b)	406(4)	168(2)	221(1)
H(6a)	182(4)	279(2)	257(1)
H(6b)	58(4)	226(2)	313(1)
H(7a)	341(5)	382(2)	339(2)
H(7b)	188(5)	324(2)	388(1)
H(7c)	443(5)	356(2)	407(2)
H(8)	540(4)	22(1)	247(1)
H(9a)	245(5)	−71(2)	200(1)
H(9b)	162(5)	21(2)	191(2)
H(9c)	58(5)	−7(2)	233(2)
H(10a)	311(4)	−60(2)	335(2)
H(10b)	477(5)	−115(2)	283(2)
H(10c)	577(4)	−40(2)	329(2)
H(11)	116(4)	169(1)	414(1)
H(13)	4(4)	32(1)	431(1)
H(14)	55(4)	−89(1)	480(1)
H(16)	688(4)	−15(1)	546(1)
H(17)	607(4)	107(1)	501(1)
H(19)	83(4)	−199(1)	527(1)
H(20)	152(5)	−316(1)	577(1)
H(21)	473(4)	−344(1)	639(1)
H(22)	770(4)	−245(1)	654(1)
H(23)	721(4)	−119(1)	604(1)
H(O)	408(4)	238(1)	495(1)

Note. Isotropic temperature factors B_{iso} are 5 Å^2.

by fractional crystallization. Colorless needle-like single crystals suitable for X-ray structural analysis were obtained by slow evaporation of a solution of **1a** in *p*-xylene.

The IR spectra were recorded on a Specord-75 IR spectrometer. The ^{1}H NMR spectrum was recorded on a Gemini-200 BB spectrometer ($CDCl_3$).* The conformational analysis was performed by the molecular mechanics method using the MM2 force field taking into account π electron interactions.[25]

Crystals of compound 1a are orthorhombic, a = 5.519(2) Å, b = 16.365(7) Å, c = 21.217(8) Å, V = 1916.2(14) Å^3, M = 336.5 ($C_{23}H_{28}O_2$), the space group is $P2_12_12_1$, Z = 4, d_{calc} = 1.166 g cm^{-3}, μ(Mo-K_α) = 0.07 mm^{-1}.

X-ray diffraction study was performed on an automated Siemens P3/PC diffractometer (Mo-K_α radiation, graphite monochromator, θ/2θ scanning technique up to $2\theta_{max} \leq 50°$). Intensities of 929 independent reflections with $I > 3\sigma$ were measured. The structure was solved by the direct method. The positions of hydrogen atoms were located from successive difference electron density syntheses. The structure was refined anisotropically by the full-matrix least-squares method (isotropically for hydrogen atoms) to R = 0.036, R_w = 0.040, S = 1.02. Calculations were performed using the SHELXTL PLUS/PC program package. Atomic coordinates are given in Tables 7 and 8.

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