Conformations of *Z*- and *E*-isomers of some chiral (1*R*,4*R*)-2-arylidene-*p*-menthan-3-ones

N. S. Pivnenko,[a] V. V. Vashchenko,[a] L. A. Kutulya,[a]★ A. O. Doroshenko,[b] and L. V. Chepeleva[b]

[a]*Institute for Single Crystals, National Academy of Sciences of the Ukraine, 60 prosp. Lenina, 61001 Kharkov, Ukraine. Fax: +7 (057 2) 32 0273. E-mail: kutulya@isc.kharkov.com*
[b]*Karazin National University, 4 pl. Svobody, 61077 Kharkov, Ukraine*

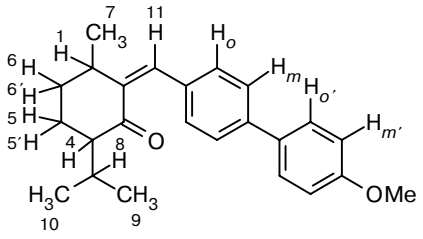
The ^{1}H NMR method in combination with molecular simulation was used to study conformations of *Z*- and *E*-isomers of (1*R*,4*R*)-*cis*-2-(4-methoxyphenyl)benzylidene-*p*-menthan-3-one. In solutions the *Z*-isomer, unlike the conformationally uniform *E*-isomer, is an equilibrium mixture of chair conformers with the substantial predomination of one form with the axially oriented methyl and equatorial isopropyl groups (75—78%). The enone group is more nonplanar in the *Z*-isomer than in the *E*-isomer. For the isopropyl fragment, the equiprobable existence of *trans*- and two *gauche*-rotamers for the *Z*-isomer and a substantial predomination of *gauche*-forms in the case of the *E*-isomer were established.

Key words: *Z*- and *E*-(1*R*,4*R*)-2-(4-methoxyphenyl)benzylidene-*p*-menthan-3-ones, ^{1}H NMR, spin-spin coupling constants, molecular simulation, conformers, rotamers.

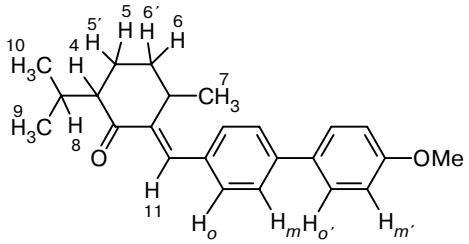
E,*Z*-Isomerization of chiral (1*R*,4*R*)-2-arylidene-*p*-menthan-3-ones has recently attracted attention[1—5] due to a great distinction in the properties of isomers as components of induced cholesteric liquid-crystalline (LC) composites. Compounds with the *Z*-isomeric structure were obtained by the photochemical method.[1,2] For the determination of the configuration of α,β-unsaturated ketones relatively to the double bond (first of all, 2-arylidene derivatives of various cyclohexanones), the chemical shift of the arylidene proton ($\delta_{=CH} > 6.9$ for *E*-isomers and $\delta_{=CH} \approx 6.2$—6.4 for *Z*-forms[1,2,6,7]) is used a reliable criterion.

The steric structure of *E*-isomers of various 2-arylidene-*p*-menthan-3-ones was studied in detail by both spectral methods[8] and X-ray diffraction analysis (see, *e.g.*, Refs. 9—11). However, until presently the suggestions about the specific features of the structure of the corresponding *Z*-forms (degree of nonplanarity of the cinnamoyl group, conformational state of the cyclohexanone fragment) were based only on analysis of spectral (UV, IR) data and some results of simulation by the molecular mechanics (MM) method.[2,3,12] The latter method, as mentioned in Refs. 13 and 14, does not always describe adequately the conformational state of cyclic systems, although in combination with analysis of parameters of ^{1}H NMR spectra it can give quite convincing results.

The knowledge of the conformational state of the *Z*- and *E*-isomers of chiral (1*R*,4*R*)-2-arylidene-*p*-menthan-3-ones is necessary for understanding of both the peculiarities of their photochemical behavior (a much higher efficiency of the $E \rightarrow Z$ process than that of the inverse photoreaction[3,12]) and spectral distinctions of isomers.[2,12] This is also important for revealing reasons for a considerable decrease in the twisting ability of *Z*-isomers compared to the initial *E*-forms in induced cholesteric LC systems[1,3,4] and for the explanation of differences in signs and values of spontaneous polarization of ferroelectric LC composites.[15] Therefore, the task of this work is to study the conformational state of *Z*- and *E*-isomers of (1*R*,4*R*)-2-(4-methoxyphenyl)benzylidene-*p*-menthan-3-one by ^{1}H NMR spectroscopy and molecular simulation.



Z-isomer



E-isomer

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 9, pp. 1519—1527, September, 2001.

Table 1. Chemical shifts (δ) in ^{1}H NMR spectra of *Z*- and *E*-isomers (400 MHz)

Proton	*Z*	*E*	Δ^Z	*Z*	*E*	Δ^Z	*Z* ($\Delta\delta_Z$)	*E* ($\Delta\delta_E$)
	($CDCl_3$)			(C_6D_6)				
H(1)	2.890	3.486	0.596	2.663	3.496	0.833	0.227	−0.010
H(4)	2.306	2.248	−0.058	2.183	2.100	−0.083	0.123	0.148
H(5)	1.987	1.873	−0.114	1.700	1.581	−0.119	0.287	0.292
H(5′)	1.863	1.906	0.043	1.665	1.752	0.087	0.198	0.154
H(6)	1.775	1.801	0.026	1.493	1.506	0.013	0.282	0.295
H(6′)	2.020	1.923	−0.097	1.744	1.687	−0.057	0.276	0.236
H(8)	2.197	2.576	0.379	2.302	2.862	0.560	−0.105	−0.286
H(11)	6.319	7.155	0.836	6.297	7.624	1.327	0.022	−0.469
CH_3(7)	1.134	1.231	0.097	0.930	0.992	0.062	0.104	0.239
CH_3(9, 10)	0.881;	0.911;	0.030;	1.053;	1.124;	0.071;	−0.172;	−0.213;
	0.914	0.974	0.060	0.976	1.079	0.103	−0.062	−0.105
H_o	7.370	7.426	0.056	7.697	7.412	−0.285	−0.327	0.014
H_m	7.454	7.565	0.111	7.544	7.518	−0.026	−0.090	0.047
$H_{o'}$	7.515	7.549	0.034	4.469	7.514	0.045	0.046	0.035
$H_{m'}$	6.956	6.984	0.028	6.894	6.935	0.041	0.062	0.049
OCH_3	3.843	3.856	0.013	3.398	3.421	0.023	0.445	0.435

Note. $\Delta^Z(CDCl_3) = \delta_E(CDCl_3) - \delta_Z(CDCl_3)$; $\Delta^Z(C_6D_6) = \delta_E(C_6D_6) - \delta_Z(C_6D_6)$; $\Delta\delta_Z = \delta_Z(CDCl_3) - \delta_Z(C_6D_6)$; $\Delta\delta_E = \delta_E(CDCl_3) - \delta_E(C_6D_6)$.

With this purpose, we compared the experimental values of vicinal spin-spin coupling constants for protons of the cyclohexanone ring ($^3J_{H,H}$) with their values calculated for alternative conformers by the results of molecular simulation. Using the conformational study of some cyclohexanone derivatives,[13] we showed that the MM method describes satisfactorily the geometry of molecules but gives the relative content of conformers with a substantial error. Therefore, in this work, along with the known MMX method (taking into account π-electron conjugation),[16] we used the semiempirical quantum-chemical AM1[17] and PM3[18] methods. It seems reasonable to verify the validity of the complex approach applied in Refs. 13 and 14 for the characterization of the conformational state of cyclic systems using a new example.

Results and Discussion

The ^{1}H NMR spectra of the compounds under study were obtained in $CDCl_3$ and C_6D_6, which allows one to monitor the dependence of aromatic solvent-induced shifts of signals from protons on their position in the molecule. For example, the distances between multiplets of methylene protons for the *E*-isomer in benzene increase compared to those in the spectrum obtained in $CDCl_3$. The signals mentioned are observed separately, which allowed the application of double resonance methods. The use of these solvents, double resonance, and computer simulation of spin systems (see Experimental) allowed the entire assignment and analysis of multiplets from all protons of the compounds under study. The obtained chemical shifts (δ) and spin-spin coupling constants (*J*) are presented in Tables 1 and 2.

Chemical shifts of the *Z*- and *E*-isomers differ significantly (see Table 1). The highest Δ^Z values are observed for arylidene H(11), methine H(1), and isopropyl H(8) protons. In a solution of C_6D_6 they increase by 0.2—0.4 ppm compared to those in $CDCl_3$. The arylidene H(11) proton in the *E*-isomer lies in the region of deshielding by the carbonyl group, whereas in the *Z*-form this proton is substantially remote from this group and, therefore, its signal is upfield shifted.[19] A similar difference in chemical shifts of the arylidene proton was also observed for several other *E*,*Z*-isomeric pairs.[6,7,20] The diamagnetic shift of the H(1) signal in the *Z*-isomer, as compared to that in the *E*-isomer, corresponds to its distance from the aromatic system. A change in the orientation of the aryl fragment also

Table 2. Experimental spin-spin coupling constants (*J*/Hz) in ^{1}H NMR spectra of the *Z*- and *E*-isomers

Protons	*Z*	*E*	*Z*	*E*
	($CDCl_3$)		(C_6D_6)	
H(5), H(5′)	−13.6	−13.6	−13.5	−13.3
H(6), H(6′)	−13.5	−13.4	−13.5	−13.3
H(1), H(6)	4.6	2.5	4.7	2.5
H(1), H(6′)	4.0	3.8	4.4	3.8
H(4), H(5)	5.9	6.4	5.9	6.3
H(4), H(5′)	10.3	12.4	10.5	12.4
H(5), H(6)	4.9	3.0	5.0	2.9
H(5), H(6′)	5.0	3.9	4.6	3.9
H(5′), H(6)	3.8	3.6	4.0	3.6
H(5′), H(6′)	10.5	13.4	10.3	13.3
H(4), H(8)	6.6	3.4	6.5	3.4
H(1), CH_3(7)	7.0	7.0	7.0	6.8
H(8), CH_3(9, 10)	6.8	6.9	6.7	6.9

results in the diamagnetic shift of resonance of H(8) in the *Z*-isomer compared to that in the *E*-form. Taking into account that the configuration for the *E*-isomer is known from X-ray diffraction data for several related compounds,[9,10] including that for the biphenyl analog,[12] the difference in chemical shifts of protons presented above for the second isomer can evidence the *Z*-configuration of the latter.

Conformational states of the cyclohexanone ring of *Z*- and *E*-isomers. The *J* values of the isomers (see Table 2) depend on the conformational state of molecules. For the most probable conformers differed in orientation of the alkyl groups relatively to the cyclohexanone ring and turning of the isopropyl group, we present the calculated values of steric energy *E* (in the case of MMX calculations) or energy of formation ΔH (in the case of AM1 and PM3 calculations) (Tables 3 and 4). The molar fractions of probable conformers for both isomers (Tables 3 and 4) were calculated using the known correlation (1):

$$m_i = \exp(-E_i/RT)/\Sigma\exp(-E_i/RT), \quad (1)$$

where m_i is the molar fraction of the *i*th conformer in the equilibrium system, E_i is its energy, T is temperature (K), and R is the universal gas constant.

It is seen in Table 3 that the results of simulation of the *Z*-isomer by the MM method indicate a substantial prevailing of the *chair* conformations with the axial methyl and equatorial isopropyl groups (*chair-ae*) (about 97%). In addition, the isopropyl fragment has three hindered rotamers characterized by the torsion angle φ H(8)—C(8)—C(4)—H(4). The rotamer with the *trans*-arrangement of the H(8) and H(4) protons (conformer *A*, see Table 3) is more preferential (42.9%) than each of two alternative *gauche*-forms (*B* and *C*, 23.3 and 30.6%, respectively).

At the same time, a diverse conformational variety of the *Z*-isomer follows from the AM1 and PM3 calculations (see Table 3). Along with the above-indicated conformations *chair-ae*, inverted forms *chair-ea* contribute considerably. According to the PM3 results, conformers of the *chair-ea* type are somewhat more preferential (the overall content of three rotamers D—F is 50%) compared to the conformer *chair-ae* (rotamers A—C, 23%). In addition, both quantum-chemical methods show that several higher-energy *twist*-conformers, whose overall content is about 25% (PM3) and about 10% (AM1), can exist in the equilibrium system.

Table 5 contains the vicinal constants $^3J_{H,H}$ for protons of the ring for the alternative conformers of the *Z*-isomer. They were calculated from the torsion angles (according to the results of molecular simulation) using two modified Karplus—Conroy's equations: Durette—Horton's equation (2) taking into account the

Table 3. Energy parameters (*E*) and some torsion angles for the most probable conformers of the *Z*-isomer*

Conformer	*E* /kcal mol^{-1}	Fraction (%)	Angle/deg										
			φ(4.8)	φ_1	φ_2	φ_3	φ_4	φ_5	φ_6	φ_7	φ_8	φ_9	φ_{10}
					MMX								
*A chair-ae**	45.7	42.9	168	53	−51	52	−56	52	−50	53	39	74	−179
*B chair-ae**	46.1	23.3	−64	50	−49	52	−57	53	−49	50	36	75	−179
*C chair-ae**	45.9	30.6	66	49	−48	51	−59	−54	−49	48	38	75	−177
*D chair-ea***	47.6	1.6	171	−52	49	−52	59	−56	52	−56	80	177	−77
					AM1								
A chair-ae	−3.6	15.8	166	58	−58	55	−54	51	−52	62	−50	72	178
B chair-ae	−3.5	12.8	−63	56	−57	56	−55	51	−52	60	−50	72	177
C chair-ae	−4.2	45.9	75	55	−56	56	−56	52	−51	60	−50	73	177
D chair-ea	−3.5	13.7	176	−56	53	−52	56	−56	55	−61	50	179	−73
E twist	−2.9	4.7	69	58	−35	−24	64	−41	−18	62	−49	106	−163
F twist	−2.5	2.1	173	48	−66	21	37	−56	12	56	−49	135	−169
					PM3								
A chair-ae	−4.7	14.9	174	60	−63	61	−56	48	−50	66	43	75	172
B chair-ae	−3.5	1.9	−63	59	−58	55	−54	50	−53	63	48	71	178
C chair-ae	−4.2	6.1	68	55	−56	56	−56	52	−52	58	56	73	178
D chair-ea	−4.7	15.7	−171	−54	53	−55	61	−59	55	−59	76	178	−69
E chair-ea	−4.4	9.2	−64	−49	43	−45	55	−58	54	−50	−72	178	−86
F chair-ea	−5.0	25.2	63	−48	39	−42	54	−60	56	−49	−75	180	−90
G twist	−4.9	22.5	179	−40	54	−11	−43	57	−15	−41	−61	110	−71

Notes. The data are presented for conformers, whose fraction exceeds 1.5%. φ_1 — C(1)—C(2)—C(3)—C(4), φ_2 — C(2)—C(3)—C(4)—C(5), φ_3 — C(3)—C(4)—C(5)—C(6), φ_4 — C(4)—C(5)—C(6)—C(1), φ_5 — C(5)—C(6)—C(1)—C(2), φ_6 — C(6)—C(1)—C(2)—C(3), φ_7 — OC(3)—C(2)—C(11), φ_8 — C(2)—C(11)—C(12)—C(*ortho*-), φ_9 — C(7)—C(1)—C(2)—C(3), φ_{10} — C(8)—C(4)—C(3)—C(2).

* Conformation *chair* with axial methyl and equatorial isopropyl groups.

** Conformation *chair* with equatorial methyl and axial isopropyl groups.

Table 4. Energy parameters (*E*) and some torsion angles for the most probable conformers of the *E*-isomer*

Conformer	*E* /kcal mol^{-1}	Fraction (%)	Angle/deg									
			φ(4.8)	φ$_1$	φ$_2$	φ$_3$	φ$_4$	φ$_5$	φ$_6$	φ$_7$	φ$_8$	φ$_9$	φ$_{10}$
						MMX							
*A chair-ae**	46.1	27.8	166	53	−50	50	−56	54	−51	56	47	72	−178
*B chair-ae**	46.3	17.9	−67	49	−46	49	−57	55	−51	52	47	73	−176
*C chair-ae**	45.7	52.0	63	47	−43	47	−56	56	−51	49	47	73	−174
						AM1							
A chair-ae	−4.8	32.2	162	49	−51	54	−57	52	−48	49	50	76	−176
B chair-ae	−4.4	14.5	−69	47	−49	54	−57	52	−47	45	50	77	−175
C chair-ae	−5.1	48.3	73	46	−49	55	−58	52	−46	45	50	77	−176
						PM3							
A chair-ae	−6.4	30.4	173	51	−59	62	−59	46	−43	53	54	82	177
B chair-ae	−5.5	7.2	−65	47	−50	55	−57	50	−44	45	54	80	−174
C chair-ae	−6.7	53.1	67	44	−50	58	−59	50	−43	42	55	82	−177
D twist	−4.8	2.1	59	49	−16	−38	64	−32	−22	47	−79	101	−145
E twist	−5.1	3.4	−180	−37	51	−11	−43	57	−17	−37	−76	108	−73

Notes. See Table 3.
* Conformation *chair* with axial methyl and equatorial isopropyl groups.

Table 5. Torsion angles φ(H,H)/deg for possible conformers in the *Z*-form and coupling constants ($^3J_{H,H}$/Hz) calculated using Eqs. (2) and (3)

Conformer, J_{av}, J_{exp}	φ(1,6)	$^3J_{H(1),H(6)}$		φ(1,6′)	$^3J_{H(1),H(6')}$		φ(4,5′)	$^3J_{H(4),H(5')}$		φ(5,6)	$^3J_{H(5),H(6)}$		φ(5′,6′)	$^3J_{H(5'),(6')}$	
		(2)	(3)		(2)	(3)		(2)	(3)		(2)	(3)		(2)	(3)
							MMX								
A	−65	3.2	2.4	52	5.0	4.2	176	12.1	11.8	59	4.2	3.1	−173	10.1	13.4
B	−70	3.2	2.4	52	4.9	4.1	179	12.1	11.8	58	4.2	3.1	−174	12.7	13.4
C	−64	3.3	2.5	53	4.8	4.0	177	12.1	11.8	58	4.3	3.3	−173	12.7	13.4
D	−179	12.1	11.8	−62	3.6	3.1	66	3.0	2.2	177	12.8	13.5	−54	4.9	4.0
$^3J_{av}$		3.3	2.5		4.8	4.0		11.7	11.5		4.3	3.3		12.4	13.1
							AM1								
A	−69	2.8	2.0	48	5.5	4.7	177	12.1	11.8	64	3.6	2.4	−171	12.6	13.3
B	−69	2.8	2.0	49	5.4	4.6	180	12.1	11.8	63	3.7	2.5	−173	12.7	13.4
C	−68	2.8	2.0	49	5.4	4.5	180	12.1	11.8	62	3.7	2.6	−173	12.7	13.4
D	−178	12.1	11.8	−61	3.7	3.2	68	2.9	2.1	174	12.8	13.5	−61	3.9	3.0
E	−161	11.1	10.9	−44	6.2	5.8	100	2.2	1.7	−179	12.9	13.6	−53	5.0	4.3
F	−176	12.1	11.8	−60	3.8	3.3	145	8.9	8.7	155	10.9	11.3	−80	2.1	0.8
$^3J_{av}$		4.8	4.2		5.1	4.4		9.9	9.5		5.7	5.0		10.4	10.6
							PM3								
A	−71	2.6	1.8	45	6.0	5.1	−176	12.1	11.8	60	4.1	3.0	−172	12.7	12.9
B	−68	2.8	2.0	47	5.7	4.8	177	12.1	11.8	62	3.8	2.6	−170	12.5	12.7
C	−68	2.9	2.1	48	5.5	4.6	180	12.1	11.8	61	3.9	2.8	−172	12.7	12.8
D	177	12.1	11.8	−66	3.1	2.6	66	3.1	2.3	178	12.9	13.6	−56	4.5	3.4
E	180	12.1	11.8	−64	3.3	2.8	76	2.2	1.5	171	12.6	13.3	−60	4.0	2.8
F	178	12.1	11.8	−66	3.0	2.6	78	2.1	1.3	170	12.6	13.2	−62	3.8	2.6
G	−63	3.5	2.6	52	4.8	4.0	107	2.9	2.5	72	2.7	1.3	−158	11.4	11.5
$^3J_{av}$		7.7	7.1		4.1	3.5		4.8	4.3		8.1	7.4		7.6	7.0
$^3J_{exp}$		4.6			4.0			10.3			4.9			10.5	

Note. The data are presented for conformers, whose fraction exceeds 1.5%.

electronegativity of α-substituents[21] and Eq. (3) additionally taking into account the orientation of α-substituents relatively to the pair of coupling protons and the electronegativity of β-substituents[22]

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

$$^3J_{H,H} = P_1\cos^2\varphi + P_2\cos\varphi + P_3 + \Sigma\Delta\chi_i[P_4 + P_5\cos^2(\xi_i\varphi + P_6\,|\Delta\chi_i|)], \qquad (3)$$

where φ is the torsion angle, $\Sigma\Delta\chi_i$ is the sum of differences of electronegativities of substituents in the ethane fragment and hydrogen according to Huggins,[23] $P_1 - P_6$

Table 6. Torsion angles φ(H,H) for possible conformers in the *E*-form and coupling constants ($^3J_{H,H}$/Hz) calculated using Eqs. (2) and (3)

Conformer, J_{av}, J_{exp}	φ(1,6)	$^3J_{H(1),H(6)}$		φ(1,6′)	$^3J_{H(1),H(6′)}$		φ(4,5′)	$^3J_{H(4),H(5′)}$		φ(5,6)	$^3J_{H(5),H(6)}$		φ(5′,6′)	$^3J_{H(5′),(6′)}$	
		(2)	(3)		(2)	(3)		(2)	(3)		(2)	(3)		(2)	(3)
							MMX								
A	−64	3.3	2.5	52	4.9	4.0	174	12.0	11.8	59	4.2	3.1	−173	12.7	12.9
B	−63	3.4	2.6	53	4.7	3.8	176	12.1	11.8	58	4.2	3.2	−173	12.7	12.9
C	−62	3.5	2.7	54	4.6	3.7	174	12.0	11.8	59	4.2	3.2	−173	12.7	12.9
$^3J_{av}$		3.4	2.6		4.6	3.8		11.9	11.6		4.2	3.2		12.7	12.9
							AM1								
A	−68	2.8	2.0	49	5.4	4.5	171	12.1	11.8	61	3.8	2.7	−174	12.7	13.4
B	−68	2.9	2.1	50	5.3	4.4	178	12.1	11.8	61	3.9	2.8	−174	12.8	13.5
C	−67	2.9	2.1	49	5.3	4.4	179	12.1	11.8	60	4.0	2.9	−175	12.8	13.5
$^3J_{av}$		2.9	2.2		5.2	4.4		11.6	11.3		4.0	3.0		12.2	12.9
							PM3								
A	−72	2.5	1.7	43	6.3	5.4	−175	12.0	11.7	57	4.4	3.4	−174	12.8	13.5
B	−69	2.7	1.9	46	5.8	4.9	−178	12.1	11.8	59	4.2	3.2	−173	12.7	13.4
C	−69	2.7	2.0	46	5.8	4.9	179	12.1	11.8	58	4.3	3.3	−175	12.8	13.5
D	−51	9.9	9.7	−36	7.4	7.0	85	1.8	1.2	179	12.9	13.6	−52	5.1	4.3
E	−63	3.4	2.6	52	4.9	4.1	106	2.8	2.4	73	2.6	1.3	−157	11.3	11.8
$^3J_{av}$		2.7	2.0		5.8	5.0		11.1	10.8		4.4	3.4		12.1	12.8
$^3J_{exp}$		2.5			3.8			12.4			3.0			13.4	

Note. See Table 5.

are empirical coefficients,[22] ξ is the coefficient that characterizes the orientation of the α-substituent relatively to the pair of coupling protons, and $\Delta\chi_i$ is the electronegativity of the α-substituent calculated taking into account the electronegativity of the β-substituent.

The weighted-mean values ($^3J_{av}$) for each type of coupling constants were calculated using Eq. (4)

$$^3J_{av} = \Sigma^3J_i m_i, \qquad (4)$$

where m_i is the molar fraction of the *i*th conformer obtained from the simulation results (see Table 3).

It is seen in Table 5 that the vicinal constants $^3J_{H(1),H(6)}$, $^3J_{H(4),(5′)}$, and $^3J_{H(5),H(6)}$,$^3J_{H(5′),H(6′)}$, whose $^3J_{ev}$ values obtained by the AM1 simulation agree satisfactorily with experiment (see Table 2 or the last row in Table 5), are conformationally sensitive for the *Z*-isomer. This allows us to believe that the results of simulation by this method reflect the real conformational equilibrium in solutions of the compound under study, *i.e.*, the existence of a mixture of chair-like conformers with a considerable prevailing of *chair-ae* (the overall content of different rotamers of the isopropyl group is approximately 75%).

The vicinal constants $^3J_{av}$ based on the results of PM3 simulation differ considerably from the experimental values (see Tables 5 and 2). Since all simulation methods used almost equally describe the geometry of the molecules (see Table 3), it is natural to assume that for the *Z* compound under study the divergence between the PM3 results and experiment is associated with the nonadequate description of minor energy differences between alternative conformers. A similar situation was

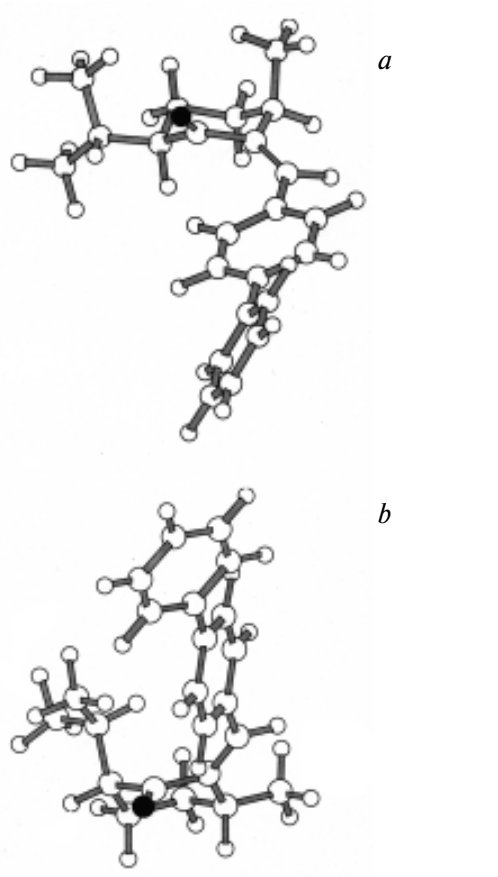


Fig. 1. Most probable alternative chair conformations of two types for the *Z*-isomer with the axial (*a*) and equatorial (*b*) orientation of the methyl group (conformations *A* and *D* in Table 3).

also stated in Ref. 14 for some cyclohexenones. However, the ratio of conformers can be corrected considering the experimental $^3J_{H(1),H(6)}$, $^3J_{H(4),(5')}$, $^3J_{H(5),H(6)}$, and $^3J_{H(5'),H(6')}$ values as weighted-average for three types of conformers according to Eq. (5)

$$^3J_{exp} = {}^3J_{chair\text{-}ae}m_{ae} + {}^3J_{chair\text{-}ea}m_{ea} + {}^3J_{twist}[1 - (m_{ae} + m_{ea})], \quad (5)$$

where m_{ae} and m_{ea} are the molar fractions of inverted chair-like conformers in the equilibrium system; and $^3J_{chair\text{-}ae}$, $^3J_{chair\text{-}ea}$, and $^3J_{twist}$ are the corresponding J constants calculated from Eqs. (1) and (2) for the conformers *chair-ae, chair-ea*, and *twist*, respectively.

The results obtained by the solution of the corresponding systems of equations are presented in Table 7 along with similar results based on the use of the molecular geometry obtained by the MMX method. These estimations and the results of the AM1 method described above show that the *Z*-isomer in solutions is a equilibrium system of chair-like conformers (Fig. 1, *a, b*) with a considerable prevailing form *chair-ae* (on the average 75—78%). At the same time, according to these estimations, the contribution of the *twist*-conformers (on the contrary to the results of AM1 and especially PM3 simulation) is insignificant.

In the case of the *E*-isomer (Tables 4 and 6), all simulation methods used and all calculated $^3J_{av}$ values also indicated the preferential *chair* conformation with the axial methyl and equatorial isopropyl groups (*chair-ae*) (91—98%). Only the PM3 method gives a noticeable content of the *twist*-conformers (in general, approximately 6—7%). Note that the same conformation of molecules is observed in crystals of various *E*-(1*R*,4*R*)-2-arylidene-*p*-menthan-3-ones studied previously by the X-ray diffraction method.[9—11]

Rotameric equilibrium of the isopropyl fragment of isomers. The rotameric equilibrium of the isopropyl fragment with respect to the C(4)—C(8) bond is also of interest. In the case of the *E*-isomer, the constant $^3J_{H(4),H(8)}$ is equal to 3.4 Hz (see Table 2), which corresponds to the predomination of *gauche*-rotamers in equilibrium. The molecular simulation methods give consistent results of rotamer population, also preferring *gauche*-forms (see Table 4). However, the $^3J_{avH(4),H(8)}$ value calculated from the obtained rotamer distribution is overestimated compared to the experimental values in all cases (Table 8, 9). Table 9 also contains the populations of rotamers of the *E*-isomer calculated from the experimental $^3J_{H(4),H(8)}$ value using Eq. (6)

$$^3J_{exp} = {}^3J_{trans}m + {}^3J_{gauche}(1 - m), \quad (6)$$

where m is the molar fraction of the *trans*-rotamer in the equilibrium system, and $^3J_{trans}$ and $^3J_{gauche}$ are the coupling constants calculated by Eqs. (2) and (3) for the

Table 7. Estimation of the conformational state (fractions m_{ae} and m_{ea} of conformers *chair-ae* and *chair-ea*) from $^3J_{exp}$ and $^3J_{calc}$ for alternative conformers* of the *Z*-isomer

Protons	φ_i/deg			$^3J_{calc}$/Hz			$^3J_{exp}$/Hz	m_{ae}	m_{ea}
	Chair		Twist	Chair		Twist		Calculation	
	ae	*ea*		*ae*	*ea*				
				MMX					
H(1), H(6)	−65	−179		2.4	11.8		4.6	0.76	0.24
	−64	−179		2.5	11.8			0.77	0.23
H(4), H(5′)	176	66		11.8	2.2		10.3	0.84	0.16
	177	66		12.1	3.0			0.80	0.20
H(5), H(6)	59	177		3.1	13.5		5.0	0.83	0.17
	58	177		3.3	13.5			0.84	0.16
H(5′), H(6′)	−173	−54		13.4	4.0		10.5	0.69	0.31
	−174	−54		12.7	4.9			0.72	0.28
m_{av}								0.78	0.22
				PM3					
H(1), H(6)	−68	−177	−63	2.1	11.8	2.6	4.6	0.77	0.26
	−71	180	−63	1.8	11.8	2.6			
H(4), H(5′)	−176	66	107	11.8	2.3	2.5	10.3	0.71	0.29
	−179	76	107	11.8	1.5	2.5			
H(5), H(6)	61	171	72	2.8	13.3	1.3	5.0	0.79	0.21
	63	170	72	2.6	13.2	1.3		0.82	0.22
H(5′), H(6)	−170	−62	−158	12.7	2.6	11.5	10.5	0.67	0.24
	−172	−56	−158	12.9	3.4	11.5			
m_{av}								0.75	0.24

Notes. The results obtained using Eq. (2) for the calculation of $^3J_{calc}$ are presented; application of Eq. (3) gives, on the average, similar results. The boundary values of the corresponding torsion angles (φ_i) from the array of those calculated for conformers of this type (*chair-ae*, *chair-ea* or *twist*) differed in turn of the isopropyl group relatively to the cyclohexane ring.

Table 8. Torsion angles (φ(H,H)/deg, vicinal coupling constants ($^3J_{H,H}$/Hz) for possible rotamers of the isopropyl fragment of the *Z*- and *E*-isomers calculated from Eqs. (1) and (2), and fractions (*m*) of the *trans*-rotamer calculated using Eq. (6)

Conformer	MMX				AM1				PM3			
	Fraction (%)	φ/deg	^3J/Hz		Fraction (%)	φ/deg	^3J/Hz		Fraction (%)	φ/deg	^3J/Hz	
			(2)	(3)			(2)	(3)			(2)	(3)
					Z-isomer							
A chair-ae	42.9	169	10.9	10.8	15.8	166	10.8	10.7	14.9	174	11.3	11.1
B chair-ae	23.3	−64	3.1	2.3	12.8	−63	3.2	2.4	1.9	−62	3.2	2.4
C chair-ae	30.6	66	2.9	1.9	45.9	74	2.1	1.1	6.1	67	2.7	1.7
D chair-ea	1.6	171	11.1	11.0	13.7	175	11.3	11.1	15.7	−71	11.1	10.9
E chair-ea									9.2	−63	3.1	2.2
F chair-ea									25.8	63	3.2	2.2
					E-isomer							
A chair-ae	27.8	166	10.8	10.7	32.2	161	10.4	10.3	30.4	173	11.2	11.1
B chair-ae	17.9	−66	2.8	2.0	14.51	−68	2.6	1.8	7.2	−65	2.9	2.1
C chair-ae	52.0	63	3.2	2.2	48.34	72	2.3	1.3	53.1	66	2.8	1.8
E twist									2.1	59	3.6	2.7
F twist									3.4	−79	11.3	11.2

corresponding rotamers. Despite some scatter of the obtained values (Table 8), we can conclude that the *E*-isomer in solutions contains approximately 15% *trans*-rotamer (this is much lower than 28.8—32.0% calculated from the energy characteristics). Therefore, the *E*-isomer in solutions is, most likely, an equilibrium mixture of *trans*- and two *gauche*-rotamers in a ratio of 0.15 : 0.85, respectively.

For the *Z*-isomer, the experimental $^3J_{H(4),H(8)}$ value is double that for the *E*-form, which indicates an increase in the fraction of the transoid rotamer. The calculation from the experimental *J* value gave a content of the *trans*-rotamer of 50% on the average (see Table 9). A similar change in the populations of the rotamers of the isopropyl group was also observed on going from some 2-arylidene- and 2-(O-aroyl)oxymethylene derivatives of (1*R*,4*R*)-*p*-menthan-3-one to their (4*S*)-diastereomers with the conformation lability of the cyclohexanone ring (coexistence of conformers *chair-ae* and *twist*).[24—26] The *trans*-rotamer of the isopropyl fragment is substantially prevailing for β-hydroxyketone, a derivative of (−)-menthone with the (4*S*)-configuration, as can be judged from a $^3J_{H(4),H(8)}$ value of 11.0 Hz obtained in Ref. 25.

Degree of nonplanarity of the enone and arylidene groups of the *Z*- and *E*-isomers. For understanding differences in the properties of *Z*- and *E*-isomers as components of LC systems, it is important to know the structure of their cinnamoyl fragment, in particular, the degree of nonplanarity of the enone and arylidene groups. All three used simulation methods describe almost similarly the geometry of the cyclohexanone rings of identical conformations, whereas substantial differences are observed for the structure of the cinnamoyl fragment (see Tables 3 and 4, torsion angles φ_7 and φ_8). According to the results of MMX calculations, the enone groups in both isomers are aplanar to approximately the same extent (φ_7 = 48—56°), and the benzylidene fragment in the *Z*-form is even somewhat flattened compared to that in the *E*-isomer (φ_8 = 38 and 47°). However, the AM1 and PM3 methods indicate a more considerable distortion of the coplanar character of the carbonyl and double >C=C< bonds (φ_7) and a slightly different "twisting" of the benzylidene group (φ_8) in the case of the *Z*-form.

We attempted to obtain data on the structure of the cinnamoyl group from the experimental results of ^{1}H NMR. As can be seen in Table 1, the difference in the δ values for *ortho*- and *metha*-protons is much lower for the *Z*-isomer than for the *E*-isomer (0.084 and

Table 9. Vicinal coupling constants ($^3J_{H(4),H(8)}$) for possible rotamers of the isopropyl fragment of the *Z*- and *E*-isomers calculated from Eqs. (1) and (2), and fractionc (*m*) of the *trans*-rotamer calculated using Eq. (6)

Parameter	MMX		AM1		PM3	
	(2)	(3)	(2)	(3)	(2)	(3)
			Z-isomer			
$^3J_{av}$	6.6	5.9	5.1	4.4	6.5	5.8
$^3J_{exp}$			6.6			
m_1*	0.45	0.51	0.45	0.51	0.42	0.48
m_2*	0.46	0.53	0.52	0.57	0.45	0.52
m_{av}			0.49			
			E-isomer			
$^3J_{av}$	5.2	4.5	5.0	4.3	5.6	4.9
$^3J_{exp}$			3.4			
m_1*	0.08	0.16	0.11	0.19	0.07	0.14
m_2*	0.16	0.14	0.14	0.23	0.08	0.17
m_{av}			0.14			

* m_1 was obtained using the coupling constant of *gauche* rotamer *B*, m_2 was obtained using the coupling constant of *gauche* rotamer *C*.

0.139 ppm, respectively). This reflects a weakening of the electron interaction of the carbonyl group and benzene ring in the first case, which, in turn, indicates the more nonplanar structure of the *Z*-isomer compared to its *E*-analog. Thus, the experimental ^{1}H NMR data confirm the results of quantum-chemical calculations predicting the more nonplanar structure of the cinnamoyl fragment of the *Z*-isomer under study compared to its *E*-form.

Influence of an aromatic solvent on spectra of *Z*- and *E*-isomers. The studied isomeric unsaturated ketones differ substantially by the influence of the aromatic solvent (benzene) on chemical shifts of the protons H(1), H(11), and H_o (by more than 20-fold, see Table 1, $\Delta\delta_Z$, $\Delta\delta_E$) and H(8), CH_3(7), and H_m (somewhat more than twofold). The changes in the chemical shifts of other protons in the spectra of the *Z*- and *E*-isomers on going from deuteriochloroform to deuteriobenzene are virtually the same. This indicates the specific character of solvation, *i.e.*, the interaction of the π-electronic benzene system with the carbonyl carbon atom bearing a partial positive charge.[27] This representation corresponds sufficiently well to the shielding effect of benzene for protons of the 5- and 6-methylene groups and the methyl group in position 1 of the cyclohexanone fragment. The difference in the observed values of aromatic solvent-induced chemical shifts (ASIS effect[28,29]) for isomeric compounds in the case of protons H(1) and CH_3(7) is related, most likely, to somewhat different steric conditions for the coordination in this fragment (neighborhood of the arylidene proton in the case of the *Z*-isomer or aryl group for the *E*-analog). It is likely that the conformational specific features of the isomers also play a substantial role (the significant content of conformers with the equatorial methyl group in the case of the *Z*-isomer).

However, based on the concept of the type of coordination considered above, we cannot explain the considerably different ASIS effects for the arylidene and *ortho*-protons of the benzene ring nearest to the enone group in isomeric compounds. For example, the H(11) proton of the *E*-isomer in benzene experiences a strong deshielding effect compared to that in a solution of $CDCl_3$ ($\Delta\delta_E$ = −0.469), unlike the *Z*-isomer ($\Delta\delta_Z$ = 0.022). By contrast, the *ortho*-protons of the benzene ring are strongly deshielded by the aromatic solvent in the case of the *Z*-isomer ($\Delta\delta_Z$ = −0.327, see Table 1). These distinctions can be presented as a result of the formation in the studied systems of weak H-complexes of the C—H bond of the benzene ring with lone electron pairs of the carbonyl group. The AM1 calculations indicate the possibility of the formation of such bonds (the C_{ap}—H...O=C distance was estimated as 230—290 pm, see Fig. 2, *a* and *b*). In such H-complexes formed by the *E*-isomer, the arylidene proton is arranged in the plane of the solvating benzene ring at a distance of 400—500 pm experiencing a substantial deshielding.[19] In the case of the *Z*-isomer, a similar situation appears in benzene solutions for protons (especially *ortho*-) nearest to the enone group of the benzene ring (see Fig. 2, *a*).

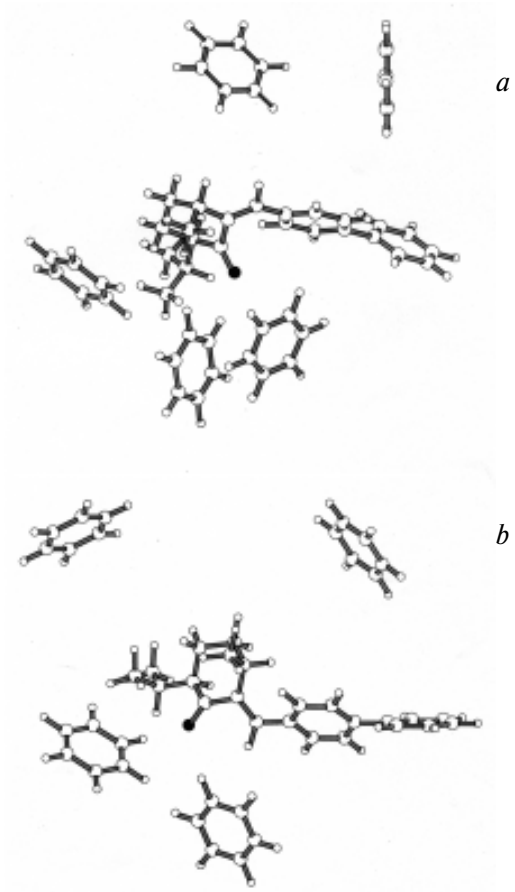


Fig. 2. Possible orientation of benzene molecules relatively to model *Z*-(1*R*,4*R*)-2-(4-phenyl)benzylidene-*p*-menthan-3-one (*a*) and its *E*-isomer (*b*) according to estimations by the AM1 method.

Note that we did not observe any substantial changes in the *J* values between the protons of the cyclohexanone fragment and the $^3J_{H(4),H(8)}$ values for the studied isomeric compounds on going from $CDCl_3$ to C_6D_6 (see Table 2). Therefore, the conformational states of the cyclohexanone fragment of the studied isomeric compounds and the rotameric equilibria of their isopropyl fragment in an aromatic solvent remain unchanged.

Experimental

E-(1*R*,4*R*)-2-(4-Methoxyphenyl)benzylidene-*p*-menthan-3-one was synthesized as described,[2] and the *Z*-isomer was obtained by its photochemical transformation.[2]

^{1}H NMR spectra were obtained on a Jeol JNM-LA 400 FT spectrometer (400 MHz) using Me_4Si as an internal standard. The observed multiplets of protons in the second-order spectra were interpreted using double resonance and confirmed by the computer simulation of spin systems (using the quantum-chemical NUTS 4.35 program). The simulation of multiplets was performed for the seven-spin sys-

tem H(1)H(6)H(6′)H(5)H(5′)H(4)H(8) (see designations in Table 1). The determination accuracy for chemical shifts of the H(1), H(4), H(8), and H(11) protons and protons of the methyl groups and benzene rings was 0.001 ppm; the accuracy of determination of δ values is an order of magnitude lower for protons of the 5- and 6-methylene groups in the spectra recorded in $CDCl_3$. The *J* values were determined from simulation results with an accuracy of 0.1 and 0.3 Hz in the first and second cases, respectively.

Quantum-chemical calculations for alternative conformers were performed by the AM1[17] and PM3[18] methods realized in the MOPAC 6.0 program package. The solvation of the ketones under study was simulated in the framework of the AM1 method by the full optimization of a molecular ensemble composed of a molecule of the solute and five solvent molecules, whose initial arrangement was specified arbitrarily. The calculation was performed for several variants of the initial mutual orientation of solvent molecules. As the calculations showed, the results of optimization of the geometry of molecular ensembles somewhat differed quantitatively but were the same at the qualitative level.

This work was financially supported by the INTAS (Grant 1997-1730). ^{1}H NMR spectra were measured at the Laboratory of Coordinator of the Project Prof. J. W. Goodby (University of Hull, Center of Organic and Biological Chemistry, Great Britain), and the authors are sincerely grateful to him for assistance.

References

1. S. N. Yarmolenko, L. A. Kutulya, V. V. Vashchenko, and L. V. Chepeleva, *Liquid Crystals*, 1994, **16**, 877.
2. S. N. Yarmolenko, L. V. Chepeleva, L. A. Kutulya, V. V. Vashchenko, T. G. Drushlyak, and O. A. Ponomarev, *Zh. Obshch. Khim.*, 1995, **65** (1), 145 [*Russ. J. Gen. Chem.*, 1995, **65** (Engl. Transl.)].
3. L. A. Kutulya, S. N. Yarmolenko, V. V. Vashchenko, L. V. Chepeleva, L. D. Patsenker, and O. A. Ponomarev, *Zh. Fiz. Khim.*, 1995, **69**, 88 [*Russ. J. Phys. Chem.*, 1995, **69** (Engl. Transl.)].
4. P. Van De Witte, J. Carlos Galan, and Johan Lub, *Liquid Crystals*, 1998, **24**, 819.
5. A. Yu. Bobrovskii, N. I. Boiko, and V. P. Shibaev, *Vysokomol. Soedin.*, 1998, **40**, 410 [*Polymer Sci.*, 1998, **40** (Engl. Transl.)].
6. A. Hassner and T. C. Mead, *Tetrahedron*, 1964, **20**, 2201.
7. P. Baas and H. Cerfontain, *Tetrahedron*, 1977, **33**, 1509.
8. L. A. Kutulya, N. S. Pivnenko, I. B. Nemchenok, T. V. Khandrimaidova, G. P. Semenkova, V. I. Biba, and V. G. Tishchenko, *Zh. Obsh. Khim.*, 1987, **57**, 397 [*J. Gen. Chem. USSR*, 1987, **57** (Engl. Transl.)].
9. V. I. Kulishov, L. A. Kutulya, V. E. Kuz′min, I. B. Nemchenok, M. A. Kravers, I. B. Stel′makh, Yu. T. Struchkov, and A. S. Tolochko, *Zh. Obshch. Khim.,* 1991, **61**, 155 [*J. Gen. Chem. USSR*, 1991, **61** (Engl. Transl.)].
10. L. A. Kutulya, V. P. Kuznetsov, V. I. Kulishov, and V. V. Vashchenko, *Kristallografiya,* 1999, **44**, No. 3, 475 [*Crystallography Reports*, 1999, **44**, 435 **(**Engl. Transl.)].
11. A. S. Tolochko, V. I. Kulishov, L. A. Kutulya, V. P. Kuznetsov, and V. V. Vashchenko, *Kristallografiya*, 2001, **46**, No. 2 (in press) [*Crystallography Reports*, 2001, **46** (Engl. Transl.)].
12. L. V. Chepeleva, Ph. D. (Chem.) Thesis, Institute of Single Crystals, National Academy of Sciences of the Ukraine, Khar′kov, 1997, 91 pp. (in Russian).
13. V. V. Vashchenko, N. S. Pivnenko, L. A. Kutulya, A. S. Petrenko, S. V. Iksanova, and J. W. Goodby, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 1221 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 1218 (Engl. Transl.)].
14. W. B. Smith and C. Amezcua, *Magn. Reson. Chem.*, 1998, **36**, S3.
15. L. A. Kutulya, V. V. Vashchenko, A. O. Doroshenko, M. N. Pivnenko, L. V. Chepeleva, N. S. Pivnenko, and N. I. Shkolnikova, in *Nonlinear Optics of Liquid and Photorefractive Crystals, Proceeedings of SPIE* (в печати).
16. K. B. Lipkowitz, A. M. Naylor, and W. B. Melchior, *Tetrahedron Lett.*, 1984, **25**, 2297.
17. M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.
18. J. J. P. Stewart, *J. Comp. Chem.*, 1989, **10**, 221.
19 H. Gunter, *NMR Spectroscopy. An Introduction*, J. Wiley and Sons, Chichester, New York—Brisbane—Toronto, 1980.
20. N. S. Pivnenko, L. A. Pravotorova, N. D. Trusevich, and V. F. Lavrushin, *Vestnik Khar′kovskogo un-ta* [*Bulletin of Khar′kov University*], 1982, No. 236, 56 (in Russian).
21. P. L. Durette and D. Horton, *Org. Magn. Reson.*, 1971, **3**, 417.
22. C. A. G. Haasnoot, F. A. A. M. Leeuw, and C. Altona, *Tetrahedron*, 1980, **36**, 2783.
23. M. L. Huggins, *J. Am. Chem. Soc.*, 1953, **75**, 4123.
24. Yu. E. Shapiro, L. A. Kutulya, A. Z. Kalyuskii, N. S. Pivnenko, S. N. Yarmolenko, and V. V. Vashchenko, *Zh. Obshch. Khim.*, 1993, **63**, 1381 [*Russ. J. Gen. Chem.*, 1993, **63** (Engl. Transl.)].
25. Yu. E. Shapiro, L. A. Kutulya, V. A. Bacherikov, L. D. Patsenker, V. V. Vashchenko, and T. B. Fedorkova, *Zh. Obshch. Khim.*, 1995, **65**, 1357 [*Russ. J. Gen. Chem.*, 1995, **65** (Engl. Transl.)].
26. N. S. Pivnenko, T. G. Drushlyak, L. A. Kutulya, V. V. Vashchenko, A. O. Doroshenko, and J. W. Goodby, *J. Phys. Org. Chem.*, 2001, in press.
27. N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, Holdenday, INC, San Francisco—London—Amsterdam, 1964.
28. J. Ronayne and D. H. Williams, *Annual Rev. NMR Spectra*, 1969, **2**, 83.
29. V. V. Razin, in *YaMR v organicheskoi khimii* [*NMR in Organic Chemistry*], Leningrad, 1974, Issue 1, 61 (in Russian).

Received January 25, 2001;
in revised form March 27, 2001