Conformational analysis and steric effects of substituents in derivatives of 3-oxo-, 3-imino-, and 3-methylenecyclohexene

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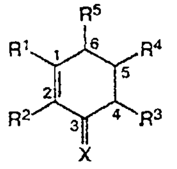
The equilibrium conformations and the inversion barriers of the rings in 3-oxo-, 3-imino-, and 3-methylenecyclohexenes and in their methyl, *tert*-butyl, and phenyl derivatives were calculated by molecular mechanics. The unsubstituted molecules adopt a sofa conformation. The nonbonded interactions between substituents at positions 2 and 4 and the exocyclic double bond lead to a change in the conformation of the ring to a half-chair. The effect is enhanced as the volume of the substituent increases in the series of the oxo, imino, and methylene derivatives. Substituents at other positions of the ring affect only slightly the equilibrium conformation. The results of calculations were confirmed by X-ray structural analysis of 2-(4-benzoyloxybenzyl)-6-isopropyl-3-methylcyclohex-2-enone.

Key words: 3-oxo-, 3-imino-, and 3-methylenecyclohexenes, conformational analysis, X-ray structural analysis, molecular mechanics.

Cyclohexenes belong to a class of organic compounds many of which exhibit high biological activity and enter into the composition of natural products.[1] Studies of the characteristic features of the three-dimensional structures and the conformational behavior of these molecules are of importance not only for the general stereochemistry of the cyclic systems but for an understanding of the mechanism of their biological action as well.

The major characteristic features of the structures and dynamics of cyclohexene and its substituted derivatives have been well studied (see, for example, Refs. 2 and 3). However, systematic studies of 3-oxo-, 3-imino-, and 3-methylenecyclohexenes have not been carried out yet. The known data on the molecular structures concern mainly polysubstituted molecules,[4—7] and they do not allow one to unambiguously reveal the factors that affect the equilibrium conformation of the ring.

The aim of this work was to carry out conformational analysis of 3-oxo-, 3-imino-, 3-methylenecyclohexenes and their methyl, *tert*-butyl, and phenyl derivatives **1—23**.



X = O (**1—6**, **19—23**); NH (**7—12**); CH_2 (**13—18**)

1—23

1, 7, 13: $R^1 = R^2 = R^3 = R^4 = R^5 = H$
2, 8, 14: $R^2 = R^3 = R^4 = R^5 = H$,
R^1 = Me (**a**), Bu^t (**b**), Ph (**c**)
3, 9, 15: $R^1 = R^3 = R^4 = R^5 = H$,
R^2 = Me (**a**), Bu^t (**b**), Ph (**c**), CH_2Ph (**3d**)
4, 10, 16: $R^1 = R^2 = R^4 = R^5 = H$,
R^3 = Me (**a**), Bu^t (**b**), Ph (**c**)
5, 11, 17: $R^1 = R^2 = R^3 = R^5 = H$,
R^4 = Me (**a**), Bu^t (**b**), Ph (**c**)
6, 12, 18: $R^1 = R^2 = R^3 = R^4 = H$,
R^5 = Me (**a**), Bu^t (**b**), Ph (**c**), Pr^i (**6d**)
19: $R^3 = R^4 = R^5 = H$, R^1 = Me, $R^2 = CH_2Ph$
20: $R^1 = R^4 = R^5 = H$, $R^2 = CH_2Ph$, $R^3 = Pr^i$
21: $R^2 = R^4 = R^5 = H$, R^1 = Me, $R^3 = Pr^i$
22: $R^4 = R^5 = H$, R^1 = Me, $R^2 = CH_2Ph$, $R^3 = Pr^i$
23: $R^4 = R^5 = H$, R^1 = Me, $R^2 = CH_2C_6H_4OCOPh$, $R^3 = Pr^i$

Experimental

Calculations of molecules **1—22** were carried out by the molecular mechanics method with the MMX force field.[8] The inversion barriers were calculated by scanning the =C—C—C—C(=X) torsion angles with a step of 5°. The results of calculations are given in Table 1.

The equilibrium conformation of the ring was characterized by the puckering parameters.[9]

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2-(4-Hydroxybenzyl)-6-isopropyl-3-methylcyclohex-2-enone (31). A mixture of 1*R*,4*R*-2-(4-methoxybenzylidene)-*p*-menthan-3-one (3 g) and pyridinium chloride (21 g) was kept under an atmosphere of nitrogen at 200 °C for 3.5 h. After cooling under a stream of nitrogen, the reaction mixture crystallized. Water was added, and the reaction mixture was extracted with benzene. The extract was washed with dilute H_2SO_4 and H_2O, dried over $MgSO_4$, and concentrated. The residue (2.9 g) was crystallized from a hexane—CCl_4 mixture. The colorless product was obtained in a yield of 2.3 g, m.p. 87—89 °C. IR (CCl_4): ν(OH) 3440, ν(C=O) 1665, ν(C=C) 1632, ν(Ar) 1600 cm^{-1}.

2-(4-Benzoyloxybenzyl)-6-isopropyl-3-methylcyclohex-2-enone (23). Benzoyl chloride (1.5 g) was added to a solution of compound **31** (2.9 g) in pyridine (15 mL). The reaction mixture warmed up, and a white precipitate formed. After 5 h, the reaction mixture was poured into a mixture of H_2SO_4 with ice and extracted with benzene. The extract was washed with H_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was crystallized from hexane. Compound **23** was obtained as a white finely crystalline powder in a yield of 2.3 g (58%), m.p. 88—95 °C. IR (in KBr): ν(C=O) 1664 and 1742, ν(C=C) 1632, ν(Ar) 1602 cm^{-1}.

Single crystals suitable for X-ray structural analysis were obtained by crystallization from MeOH.

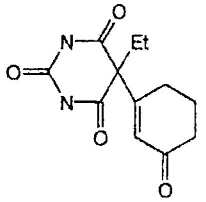
X-ray structural analysis of compound 23. Crystals of $C_{23}H_{26}O_3$ are triclinic. At 20 °C, a = 9.116(3), b = 9.143(3), c = 13.182(4) Å, α = 79.54(3)°, β = 73.68(3)°, γ = 72.23(6)°, V = 998.5(6) $Å^3$, d_{calc} = 1.205 g cm^{-3}, μ = 0.08 mm^{-1}, space group $P\bar{1}$, Z = 2. The unit cell parameters and intensities of 4566 independent reflections (R_{int} = 0.03) were measured on a four-circle automated Siemens P3/PC diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scanning technique, $2\theta_{max}$ = 60°).

The structure was solved by the direct method using the SHELXTL PLUS program package.[10] The positions of the hydrogen atoms were located from difference electron density syntheses and refined isotropically using the riding model with variable U_{iso} parameters. The refinement based on F^2 with anisotropic thermal parameters for nonhydrogen atoms using 3124 reflections converged to R_1 = 0.064 (for 2371 reflections with $F > 4\sigma(F)$), wR_2 = 0.177, S = 1.02. The coordinates and equivalent isotropic thermal parameters of nonhydrogen atoms are given in Table 2. The bond lengths, bond angles, and selected torsion angles are listed in Tables 3—5, respectively.

Results and Discussion

The equilibrium conformation of the ring in the unsubstituted molecules of derivatives of 3-oxo-, 3-imino-, and 3-methylenecyclohexenes is determined, on the one hand, by conjugation between two double bonds and 1,2-allylic interactions along the C(1)—C(6) and C(3)—C(4) bonds, which force the molecule to be planar, and, on the other hand, by the bending strain that occurs owing to the deformation of the endocyclic bond angles at the saturated carbon atoms in the planar conformation of the ring and the tendency to a staggered conformation along the C(sp^3)—C(sp^3) bonds, which favor the nonplanar geometry of the ring. The results of calculations demonstrated that the ring in molecules **1**, **7**, and **13** adopts a sofa conformation with the C(5) atom deviating from the plane through the remaining atoms of the ring by 0.37 (**1**), 0.36 (**7**), and 0.39 Å (**13**). The change in the nature of the exocyclic double bond affects only slightly the geometry of the ring in the unsubstituted molecules.

An increase in the volume of the substituent at the C(1) atom leads to a slight twist of the ring (Table 1) owing to the strengthening of the nonbonded interactions with the H atoms of the adjacent methylene group. The results of the calculations agree well with the data of X-ray structural analysis of compounds **24** and **25**.[11,12]



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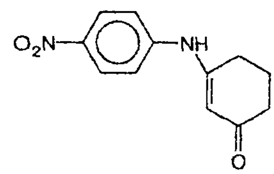
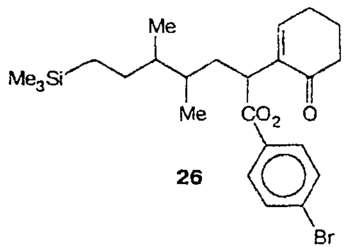


25

	S	θ	ψ
24	0.66	36.6°	6.4°
25	0.71	42.2°	6.8°

In 2-substituted derivatives **3**, **9**, and **15**, the degree of twisting of the ring is determined by the repulsion between the substituent and the exocyclic double bond. An increase in the volume of the substituents and the change in the character of the C=X bond in the series X = O, NH, and CH_2 lead to a substantial distortion of the C=C—C=X fragment from planarity and, as a consequence, the conformation of the ring changes to a half-chair. Analogous effects were observed experimentally[13,14] in molecules **26** and **27**.



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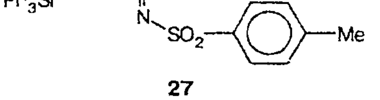


27

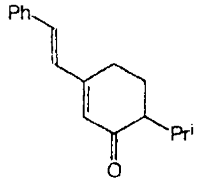
	S	θ	ψ
26	0.60	37.5°	16.0°
27	0.70	40.7°	18.4°

Nonbonded interactions between the R^3 substituents and the exocyclic double bond have a pronounced effect on the conformations of 4-substituted derivatives **4**, **10**, and **16**. An increase in the steric repulsion between these groups leads to destabilization of the equatorial conformer and to its substantial twisting as the volume of the R^3 substituent increases in the series X = O, NH, and CH_2 (see Table 1). The change in the conformation of the ring to a half-chair with the axial orientation of the alkyl group in the case of R^3 = Bu^t is, apparently, attributable to nonbonded interactions between the substituents and the remaining atoms of the ring. The results of the calculations agree well with the data of X-ray structural analysis of compounds **28** and **29**.[15,16]

Table 1. Puckering parameters of the tetrahydrocycle, the relative stabilities of the conformers, and the inversion barriers of the ring in compounds **1**—**22**

Compound	X	R*	Conformation	Puckering parameters			$\Delta E_{e/a}$	ΔE_{inv}
				S	θ	ψ	kcal mol^{-1}	
					deg			
1	O	H		0.70	39.7	0.2		6.70
2a	O	1-Me		0.70	39.3	0.4		6.01
2b	O	1-Bu^t		0.71	42.1	1.5		7.47
2c	O	1-Ph		0.71	40.4	7.6		6.97
3a	O	2-Me		0.72	39.6	0.1		7.63
3b	O	2-Bu^t		0.72	41.2	2.5		5.57
3c	O	2-Ph		0.72	37.3	10.4		5.35
4a	O	4-Me	*a*	0.68	40.0	0.6	1.60	8.13
			e	0.71	38.7	6.9	0	
4b	O	4-Bu^t	*a*	0.69	38.7	19.4	0.98	6.50
			e	0.72	38.0	10.3	0	
4c	O	4-Ph	*a*	0.70	40.3	2.2	0.57	7.23
			e	0.72	38.8	7.3	0	
5a	O	5-Me	*a*	0.70	39.0	0.9	1.17	7.42
			e	0.70	39.5	0.3	0	
5b	O	5-Bu^t	*a*	0.70	38.1	6.1	2.62	7.73
			e	0.69	40.3	2.3	0	
5c	O	5-Ph	*a*	0.65	39.8	3.5	3.81	8.71
			e	0.70	40.6	11.1	0	
6a	O	6-Me	*a*	0.68	42.1	12.8	0.55	7.19
			e	0.71	40.6	3.4	0	
6b	O	6-Bu^t	*a*	0.67	44.3	15.3	1.26	6.92
			e	0.70	40.4	1.9	0	
6c	O	6-Ph	*a*	0.68	41.1	0.3	0.87	7.06
			e	0.70	40.4	1.2	0	
7	NH	H		0.69	41.1	3.6		6.76
8a	NH	1-Me		0.69	43.8	5.2		6.89
8b	NH	1-Bu^t		0.71	44.8	7.0		8.01
8c	NH	1-Ph		0.72	42.7	11.7		8.17
9a	NH	2-Me		0.69	44.8	6.2		6.80
9b	NH	2-Bu^t		0.72	56.7	17.8		6.52
9c	NH	2-Ph		0.70	39.4	3.2		6.86
10a	NH	4-Me	*a*	0.68	40.2	0.2	0.16	7.64
			e	0.69	44.0	5.9	0	
10b	NH	4-Bu^t	*a*	0.69	39.2	13.9	0	6.67
			e	0.68	50.4	19.3	1.50	
10c	NH	4-Ph	*a*	0.68	43.0	3.3	0.82	7.93
			e	0.69	43.3	3.4	0	
11a	NH	5-Me	*a*	0.69	42.7	4.3	1.25	7.52
			e	0.69	43.3	4.9	0	
11b	NH	5-Bu^t	*a*	0.69	41.3	0.6	2.86	8.15
			e	0.67	43.8	7.0	0	
11c	NH	5-Ph	*a*	0.63	44.3	11.7	6.12	9.37
			e	0.69	43.3	4.6	0	
12a	NH	6-Me	*a*	0.67	43.8	8.2	0.40	7.27
			e	0.69	43.3	6.0	0	
12b	NH	6-Bu^t	*a*	0.67	45.3	14.8	0.96	6.97
			e	0.69	43.4	1.9	0	
12c	NH	6-Ph	*a*	0.68	43.5	3.1	1.10	7.55
			e	0.69	43.1	6.2	0	
13	CH_2	H		0.72	39.1	2.8		7.71
14a	CH_2	1-Me		0.72	40.1	6.8		7.71
14b	CH_2	1-Bu^t		0.72	41.8	5.9		8.15
14c	CH_2	1-Ph		0.74	39.8	5.1		7.94
15a	CH_2	2-Me		0.72	42.4	6.1		7.40
15b	CH_2	2-Bu^t		0.74	59.2	21.8		3.73
15c	CH_2	2-Ph		0.74	35.6	16.8		6.27
16a	CH_2	4-Me	*a*	0.70	38.9	4.5	0	8.78
			e	0.72	39.5	1.5	0.45	
16b	CH_2	4-Bu^t	*a*	0.71	37.8	21.8	0	6.73
			e	0.71	37.0	22.2	4.25	
16c	CH_2	4-Ph	*a*	0.70	40.1	1.4	0.51	8.18
			e	0.70	42.2	5.3	0	
17a	CH_2	5-Me	*a*	0.71	38.5	3.5	1.17	8.39
			e	0.72	39.1	2.8	0	
17b	CH_2	5-Bu^t	*a*	0.72	37.6	13.2	2.38	8.67
			e	0.71	39.0	3.5	0	
17c	CH_2	5-Ph	*a*	0.65	40.2	5.2	6.36	10.22
			e	0.72	39.0	2.8	0	
18a	CH_2	6-Me	*a*	0.70	39.6	2.6	0.66	7.30
			e	0.72	39.4	0.2	0	
18b	CH_2	6-Bu^t	*a*	0.68	42.8	12.1	1.35	8.0
			e	0.72	39.3	1.4	0	
18c	CH_2	6-Ph	*a*	0.71	39.4	1.9	1.08	8.59
			e	0.72	39.0	0.3	0	
19	O	1-Me, 2-$PhCH_2$		0.71	43.0	5.9		
20	O	2-$PhCH_2$, 4-Pr^i	*a*	0.72	64.8	23.7	1.38	
			e	0.72	39.6	6.4	0	
21	O	1-Me, 4-Pr^i	*a*	0.74	38.3	19.2	0.30	8.15
			e	0.72	39.3	9.2	0	
22	O	1-Mc, 2-$PhCH_2$ 4-Pr^i	*a*	0.74	64.7	22.4		1.23
			e	0.72	43.7	9.3		0

* R is the substituent in the cyclohexene ring (R = R^1, R^2, R^3, R^4, or R^5 depending on the structure, see p. 1891). S is the degree of puckering, and θ and ψ are polar angles that describe the conformational type. The angles for the ideal conformations are as follows: θ = 45° and ψ = 0° for a sofa; and θ = 45° and ψ = 30° for a half-chair.



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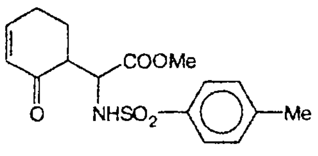


29

	S	θ	ψ
28	0.67	55.3°	29.9°
29	0.73	38.2°	18.7°

The ability of the Ph group to decrease unfavorable nonbonded interactions through rotation about the C(sp^3)—C(Ar) bond makes the regularities under consideration substantially less pronounced in 4-phenyl-substituted derivatives **4b**, **10b**, and **16b**. In these compounds, the equatorial conformer is more stable than the axial one (although the difference in the energy between them is almost halved in going from X = O to X = NH and CH$_2$), and it virtually has no twist.

The removal of the substituent at the C(5) atom from the exocyclic double bond determines the relative stability of the conformational characteristics of the rings in compounds **5**, **11**, and **17** as the volume of the substituent increases or when the nature of the C=X bond changes (see Table 1). In all the cases, the equatorial conformer predominates, and the ring has a sofa conformation.

The introduction of a substituent at the C(6) atom leads to a substantial increase in the 1,2-allylic strain along the C(1)—C(6) bond. The relative stabilities of the conformers of compounds **6**, **12**, and **18** are caused by nonbonded interactions between the alkyl (phenyl) group and the hydrogen atoms at the C(1) and C(5) atoms. An increase in these interactions as the volume of the substituent increases leads to relative destabilization of the equatorial conformer compared to 5-substituted derivatives and to substantial twisting of the axial conformers. The exceptions are the phenyl derivatives in which the ring has a sofa conformation (see Table 1).

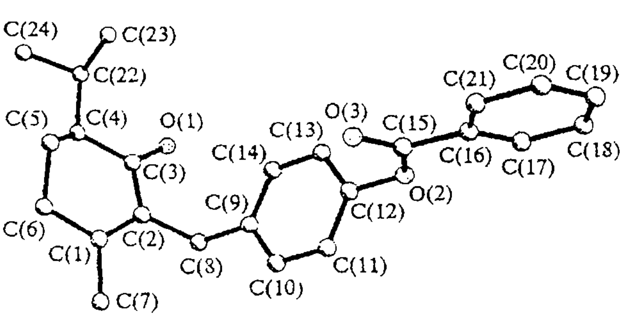
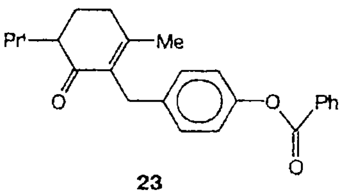


Fig. 1. Structure of molecule **23** (hydrogen atoms are omitted).

To test the results of calculations, we carried out X-ray structural analysis of compound **23** (Fig. 1, Tables 3—5).



23

Table 2. Coordinates (×10^4) and equivalent isotropic thermal parameters (×10^3/Å) of nonhydrogen atoms in the structure of **23**

Atom	x	y	z	U_{eq}
O(1)	2857(2)	7843(3)	4205(2)	75(1)
C(1)	−1273(3)	8263(3)	4687(2)	57(1)
O(2)	2838(2)	3907(2)	199(1)	64(1)
C(2)	234(3)	8196(3)	4126(2)	51(1)
C(3)	1526(3)	7740(3)	4680(2)	54(1)
O(3)	1708(3)	2281(2)	1418(2)	90(1)
C(4)	1156(3)	7278(3)	5886(2)	57(1)
C(5)	−214(3)	6552(4)	6192(2)	65(1)
C(6)	−1632(3)	7644(4)	5834(2)	66(1)
C(7)	−2696(4)	9012(4)	4231(3)	86(1)
C(8)	689(3)	8695(3)	2945(2)	57(1)
C(9)	1228(3)	7378(3)	2244(2)	49(1)
C(10)	353(3)	7294(3)	1583(2)	64(1)
C(11)	859(4)	6122(3)	911(2)	68(1)
C(12)	2266(3)	5038(3)	923(2)	54(1)
C(13)	3180(3)	5097(3)	1573(2)	64(1)
C(14)	2662(3)	6253(3)	2237(2)	60(1)
C(15)	2475(3)	2543(3)	540(2)	53(1)
C(16)	3115(3)	1463(3)	−292(2)	48(1)
C(17)	4061(3)	1805(3)	−1267(2)	55(1)
C(18)	4641(3)	742(3)	−2013(2)	65(1)
C(19)	4256(3)	−637(3)	−1780(2)	65(1)
C(20)	3316(4)	−981(3)	−810(2)	70(1)
C(21)	2741(3)	69(3)	−64(2)	61(1)
C(22)	2623(4)	6351(3)	6284(3)	72(1)
C(23)	3208(5)	4708(4)	6013(4)	103(1)
C(24)	2334(5)	6410(5)	7480(3)	98(1)

Table 3. Bond lengths in compound **23**

Bond	d/Å	Bond	d/Å
O(1)—C(3)	1.223(3)	C(9)—C(14)	1.394(4)
C(1)—C(2)	1.354(4)	C(10)—C(11)	1.399(4)
C(1)—C(6)	1.496(4)	C(11)—C(12)	1.363(4)
C(1)—C(7)	1.503(4)	C(12)—C(13)	1.370(4)
O(2)—C(15)	1.353(3)	C(13)—C(14)	1.381(4)
O(2)—C(12)	1.414(3)	C(15)—C(16)	1.483(3)
C(2)—C(3)	1.472(4)	C(16)—C(17)	1.374(3)
C(2)—C(8)	1.516(3)	C(16)—C(21)	1.378(3)
C(3)—C(4)	1.537(4)	C(17)—C(18)	1.390(4)
O(3)—C(15)	1.196(3)	C(18)—C(19)	1.370(4)
C(4)—C(5)	1.512(4)	C(19)—C(20)	1.367(4)
C(4)—C(22)	1.524(4)	C(20)—C(21)	1.382(4)
C(5)—C(6)	1.509(4)	C(22)—C(23)	1.506(5)
C(8)—C(9)	1.527(3)	C(22)—C(24)	1.531(5)
C(9)—C(10)	1.362(4)		

Table 4. Bond angles (φ) in compound **23**

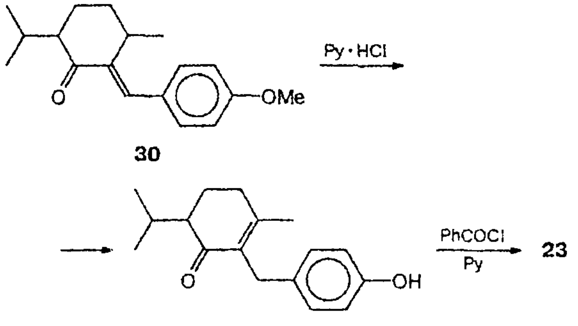
Angle	φ/deg	Angle	φ/deg
C(2)—C(1)—C(6)	121.3(2)	C(12)—C(11)—C(10)	118.8(3)
C(2)—C(1)—C(7)	123.3(3)	C(11)—C(12)—C(13)	120.8(2)
C(6)—C(1)—C(7)	115.4(3)	C(11)—C(12)—O(2)	119.3(2)
C(15)—O(2)—C(12)	117.4(2)	C(13)—C(12)—O(2)	119.7(2)
C(1)—C(2)—C(3)	119.9(2)	C(12)—C(13)—C(14)	119.7(2)
C(1)—C(2)—C(8)	123.9(2)	C(13)—C(14)—C(9)	120.8(3)
C(3)—C(2)—C(8)	116.0(2)	O(3)—C(15)—O(2)	122.2(2)
O(1)—C(3)—C(2)	120.5(2)	O(3)—C(15)—C(16)	125.4(2)
O(1)—C(3)—C(4)	119.8(2)	O(2)—C(15)—C(16)	112.4(2)
C(2)—C(3)—C(4)	119.4(2)	C(17)—C(16)—C(21)	119.6(2)
C(5)—C(4)—C(22)	115.8(2)	C(17)—C(16)—C(15)	122.4(2)
C(5)—C(4)—C(3)	109.0(2)	C(21)—C(16)—C(15)	118.0(2)
C(22)—C(4)—C(3)	113.1(2)	C(16)—C(17)—C(18)	119.9(2)
C(6)—C(5)—C(4)	110.3(2)	C(19)—C(18)—C(17)	120.0(3)
C(1)—C(6)—C(5)	114.0(2)	C(20)—C(19)—C(18)	120.3(3)
C(2)—C(8)—C(9)	114.2(2)	C(19)—C(20)—C(21)	120.0(3)
C(10)—C(9)—C(14)	118.0(2)	C(16)—C(21)—C(20)	120.3(2)
C(10)—C(9)—C(8)	121.2(2)	C(23)—C(22)—C(4)	113.2(3)
C(14)—C(9)—C(8)	120.8(2)	C(23)—C(22)—C(24)	111.0(3)
C(9)—C(10)—C(11)	121.8(2)	C(4)—C(22)—C(24)	111.0(3)

Table 5. Selected torsion angles (ω) in compound **23**

Angle	ω/deg
C(1)—C(2)—C(3)—C(4)	2.6(3)
C(2)—C(3)—C(4)—C(5)	30.3(3)
C(3)—C(4)—C(5)—C(6)	−56.3(3)
C(4)—C(5)—C(6)—C(1)	51.7(3)
C(5)—C(6)—C(1)—C(2)	−17.6(4)
C(6)—C(1)—C(2)—C(3)	−10.0(4)
O(3)—C15)—C(16)—C(21)	3.4(4)

In this case, it is of interest to elucidate the characteristic features of the structure of the cyclohexene ring as well as the structure of phenyl benzoate (the degree of coplanarity of the benzene rings and the conformation of the ester group). This is associated with the presence and the important role of this fragment in molecules of liquid-crystalline compounds with various types of mesomorphism.

Compound **23** was prepared in an attempt to demethylate 1*R*,4*R*-2-(4-methoxybenzylidene)-*p*-menthan-3-one[18] (**30**), which is used as an efficient admixture to liquid-crystalline systems, according to a known procedure[17] (by the reaction with pyridinium chloride at high temperature). However, the spectral characteristics of the resulting hydroxy derivative (the decreased stretching vibration frequency of the carbonyl group (ν(C=O) is 1664 cm^{-1}) and the increased frequency of the low-intensity ν(C=C) band at 1632 cm^{-1}), which differ substantially from those of 1*R*,4*R*-2-arylidene-*p*-menthan-3-ones[19] (for compound **30**, ν(C=O) is 1674 cm^{-1}, and ν(C=C) is 1598 cm^{-1}), indicate that in this case demethylation of the methoxy group is accompanied by a change in the structure of the cyclic fragment. Based on the above-mentioned spectral characteristics, it can be suggested that the C=O and C=C double bonds in the resulting compound have an *s-trans* configuration, which corresponds to the rearrangement product (with transfer of the exocyclic double bond to the six-membered ring) that formed under the reaction conditions. Analogous transformations have been observed for some 2-arylidenecyclohexanones upon heating with HCl. [20,21]



The results of X-ray structural analysis of compound **23**, which is the benzoyl derivative of alcohol **31**, confirm the occurrence of this rearrangement in the studied 2-arylidene-*p*-menthan-3-ones.

The cyclohexene ring in compound **23** adopts a twisted-sofa conformation (the puckering parameters are as follows: S = 0.72, θ = 46.1°, and ψ = 10.5°). This is also evidenced by the values of the endocyclic torsion angles (see Table 5) and the deviations of the C(5) and C(4) atoms from the mean plane through the remaining atoms of the ring (−0.59 and 0.12 Å, respectively). The isopropyl group at the C(4) atom has the equatorial orientation (the C(22)—C(4)—C(5)—C(6) torsion angle is 175.0(2)°) with the *sc* arrangement* of the hydrogen atoms at the C(22) and C(4) atoms (the H(4)—C(4)—C(22)—H(22) torsion angle is −73(1)°). The C(9)...C(14) phenyl group is almost perpendicular to the C(2)—C(8) bond (the C(1)—C(2)—C(8)—C(9) torsion angle is −95.8(3)°).

The O(2), O(3), and C(15) atoms and the C(16)...C(21) phenyl ring are almost coplanar (the O(3)—C(15)—C(16)—C(17), C(12)—O(2)—C(15)—O(3), and O(3)—C(15)—C(16)—C(21) torsion angles are 176.4(3)°, 0.3(4)°, 3.4(4)°, respectively) in spite of the shortened O(2)...H(17) intramolecular contact (2.42 Å; the sum of their van der Waals radii[22] is 2.45 Å), and are perpendicular to the plane of the C(9)...C(14) benzene ring (the C(15)—O(2)—C(12)—C(13) torsion angle is 90.9(3)°).

The enone fragment in molecule **23** is nonplanar (the C(1)—C(2)—C(3)—O(1) torsion angle is

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* *sc* is the synclinal arrangement of the atoms.

−171.6(2)°), which is, apparently, due to the shortened intermolecular contacts (O(1)...H(8B), 2.42 Å; H(8A)...H(7B), 1.96 Å (2.32 Å); C(7)...H(8A), 2.63 Å (2.87 Å); and C(8)...H(7B) 2.57 Å). Apparently, this is also the cause of the increase in the C(2)—C(1)—C(7) and C(1)—C(2)—C(8) bond angles (123.3(3)° and 123.9(2)°, respectively) compared to the C(6)—C(1)—C(7) and C(3)—C(2)—C(8) angles (115.4(3)° and 116.0(2)°, respectively).

A comparison of the experimental geometry of the ring with the results of calculations for compounds **2**—**4** and **19**—**22** demonstrated that the characteristic features of the di- and trisubstituted derivatives are similar to those of the monoalkyl derivatives. In all the cases, the equatorial orientation of the Pr^i group is more favorable (see Table 1). The agreement between the experimental geometry of compound **23** and the results of calculations for molecule **22** allows one to conclude that intermolecular interactions in the crystal affect only slightly the conformation of the ring.

According to the results of calculations, the inversion of the ring in the compounds under consideration, as in the case of cyclohexene,[3] proceeds through nonplanar conformations. The transition state of the process is characterized by a boat conformation. The values of the inversion barriers in molecules **1** and **7** are close to that in cyclohexene.[23—25] The substantial increase in the barrier in methyl derivative **13** is, apparently, associated with substantial destabilization of the transition state. An analogous effect was observed in methylenecyclohexane.[26]

The influence of the steric effects of the substituents on the energies of the conformational transitions is determined by the character of nonbonded interactions with their participation in the ground and transition states. A decrease in the steric repulsion, for example, in 1-, 4-, and 5-substituted derivatives, leads to higher destabilization of the transition state and, as a result, to an increase in the inversion barrier. When a substituent is present at position 2 or 4, the inverse dependence is observed, which is caused by unfavorable nonbonded interactions between the alkyl (phenyl) group and the exocyclic double bond. These interactions decrease in the boat conformation. An analogous (but substantially less pronounced) effect is also observed in 6-substituted derivatives. In this case, the decrease in the inversion barriers of the ring is, apparently, associated with the decrease in repulsion between the substituents and the vicinal hydrogen atoms in the transition state.

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