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MOLECULAR AND CRYSTAL STRUCTURE OF 2,4-DIETHOXYCARBONYL-5-HYDROXY-5-METHYL-3-PHENYL-N-(3-CHLOROPHENYL)-1-CYCLOHEXENYLAMINE

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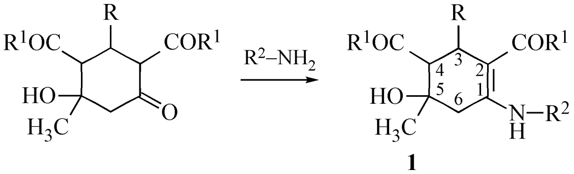
Arylamination of 2,4-diethoxycarbonyl-5-hydroxy-5-methyl-3-phenylcyclohexanone affords 2,4-diethoxycarbonyl-5-hydroxy-5-methyl-3-phenyl-N-(3-chlorophenyl)-1-cyclohexenylamine. A distorted *semi-chair* conformation with psedoequatorial orientation of all substituents except the pseudoaxial OH-group is established based on the spectral and single crystal XRD data. The presence of an intramolecular N–H…O=C hydrogen bond is noted.

Keywords: X-ray structural analysis, enaminoesters, cyclohexenes.

Earlier we have prepared a number of 3-Ar-2,4-diethoxycarbonyl-5-hydroxy-5-methylcyclohexenyl-N-R-amines by the interaction of aryl-, cyclohexyl-, benzylamines with diethoxy-substituted cyclohexanolones [1]. This work presents the data on the synthesis and structural examination of a new member of these series: 2,4-diethoxycarbonyl-5-hydroxy-5-methyl-3-phenyl-N-(3-chlorophenyl)-1-cyclohexenylamine (**1**).

Experimental. Compound **1** was prepared by amination of 2,4-diethoxycarbonyl-5-hydroxy-5-methyl-3-phenyl-cyclohexanone with *m*-chloroaniline in boiling benzene solution under a ketol:amine ratio of 1:2 with addition of a catalytic amount of acetic acid



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A solution of 0.01 mole of 2,4-diethoxycarbonyl-5-hydroxy-5-methyl-3-phenyl-cyclohexanone and 0.013 mole of *m*-chloroaniline in 50 ml of benzene was added with 1 ml of glacial acetic acid. The reaction mixture was boiled for 18 h; light-gray crystals of **1** precipitated on cooling. T_m 161-162°C (from ethanol). Yield 2.32 g (68%). Found, %: C 66.15, H 6.32, N 3.27, Cl 8.05. $C_{25}H_{28}N_1O_5Cl$. Calculated, %: C 65.57, H 6.12, N 3.06, Cl 7.76.

The IR spectra of the compounds were recorded on a Fourier spectrometer FSM-1201 (thin layer: Vaseline oil, hexachlorobutadiene). The ^{1}H NMR spectra were measured on a Bruker AC-300 spectrometer (300 MHz for ^{1}H) in DMSO-d_6

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TABLE 1. Positional (×10^4) and Equivalent Isotropic Thermal Parameters (Å^2×10^3) of Non-Hydrogen Atoms in the Structure of **1**

Atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*(eq)*	Atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*(eq)*
Cl	5000	2819(2)	5000	89(1)	C(10)	5619(5)	1302(7)	4025(13)	59(3)
O(1)	2494(3)	526(4)	1217(9)	58(2)	C(11)	5619(5)	468(8)	3305(14)	64(3)
O(2)	1690(4)	–494(4)	1772(9)	55(2)	C(12)	5022(6)	45(7)	2745(13)	54(3)
O(3)	2334(4)	–3554(4)	4291(9)	64(2)	C(13)	2344(6)	–265(7)	1668(13)	49(3)
O(4)	3079(4)	–4224(4)	2770(9)	67(2)	C(14)	1179(5)	170(7)	1269(15)	82(4)
O(5)	3324(4)	–1983(4)	5530(9)	51(2)	C(15)	503(5)	–307(8)	1216(16)	120(6)
N	3753(4)	101(5)	2340(11)	43(2)	C(16)	2103(5)	–2266(6)	893(11)	40(3)
C(1)	3501(5)	–765(6)	2575(11)	39(2)	C(17)	2343(5)	–2186(6)	–658(12)	55(3)
C(2)	2818(5)	–956(6)	2139(11)	37(3)	C(18)	1956(6)	–2573(7)	–1979(14)	71(4)
C(3)	2544(5)	–1914(7)	2387(12)	41(3)	C(19)	1356(6)	–2994(7)	–1800(13)	73(4)
C(4)	3101(5)	–2634(6)	2852(12)	42(3)	C(20)	1113(6)	–3075(8)	–273(15)	83(4)
C(5)	3630(5)	–2240(6)	4108(13)	42(3)	C(21)	1492(5)	–2679(7)	1026(13)	63(3)
C(6)	3997(4)	–1440(6)	3369(11)	44(3)	C(22)	2774(5)	–3500(7)	3362(13)	48(3)
C(7)	4396(5)	475(6)	2904(13)	44(3)	C(23)	2848(6)	–5131(6)	3238(14)	80(4)
C(8)	4388(5)	1342(6)	3612(12)	49(3)	C(24)	3472(6)	–5696(7)	3516(15)	106(5)
C(9)	5013(6)	1720(6)	4193(14)	60(3)	C(25)	4175(5)	–2980(6)	4623(11)	53(3)

*U(eq) is defined as one third of the trace of the orthogonalized tensor U_{ij}.

(TMS as internal standard). The reaction course and product purity were monitored by TLC on Silufol UV-254 foils, eluent: hexane–ethylacetate–chloroform 2:2:1, iodine staining, UV radiation.

X-ray diffraction data for unit cell refinement and structure solution of compound **1** were collected by the standard method at room temperature on an Enraf-Nonius CAD-4 automatic diffractometer (λMoK_α, graphite monochromator, $\omega/2\theta$-scanning with variable scan rate, $2\theta \leq 55°$) from a prismatic crystal with a size of 0.10×0.15×0.52 mm. The compound crystallizes in the monoclinic crystal system; chemical formula $C_{25}H_{28}NOCl$, $M = 457.93$; space group *Cc*; $a = 19.606(2)$ Å, $b = 14.646(2)$ Å, $c = 8.304(2)$ Å; $\beta = 94.55(1)°$, $V = 2377.0(7)$ Å^3, $Z = 4$, $d_{calc} = 1.280$ g/cm^3. Absorption correction was not applied because of a small linear extinction coefficient ($\mu = 0.196$ mm^{-1}).

The structure was solved by the direct method and refined with full-matrix least squares techniques in the anisotropic approximation for non-hydrogen atoms using the SHELXTL-97 program package [2]. Almost all hydrogen atoms were located from the difference Fourier syntheses and refined with isotropic thermal parameters. Final convergence factors for 300 parameters and 4 restraints on the C–H, N–H, O–H distances were: $R(F) = 0.0405$, $wR(F^2) = 0.0526$ for 782 observed reflections [$I > 2\sigma(I)$]; $R(F) = 0.1169$, $wR(F^2) = 0.0790$ for all 1953 reflections; goodness-of-fit $S = 0.742$.

The refined positional parameters of independent atoms and equivalent isotropic thermal parameters are listed in Table 1; intramolecular bond distances and angles are in Table 2. Crystallographic information has been deposited to the Cambridge Structural Database, deposition number CCDC 719586, address deposit@ccdc.cam.ac.uk.

Results and discussion. The IR spectrum of enamine **1** exhibits stretching vibrations of a secondary amine group (3310 cm^{-1}), hydroxyl (3568 cm^{-1}) and non-conjugated carbonyl groups (1710 cm^{-1}). The bathochromic shift of the carbonyl group vibration at 1639 cm^{-1} is due to the conjugation and intramolecular C=O…H–N hydrogen bonding, similarly to structurally analogous compounds [3, 4].

The ^{1}H NMR spectrum exhibits the signals of protons of the hydroxyl (3.24 ppm), amine (11.71 ppm) functions, geminal protons of the C^6 carbon at 2.63 ppm as a doublet of doublets, 1H each, SSCC J_{6ea} 17.7 Hz indicating their magnetic non-equivalence. Relying on the non-equivalence of the geminal protons and according to the work [5], we accepted the distorted semi-chair confirmation of the cyclohexene ring with the pseudoaxial hydroxyl group.

TABLE 2. Bond Lengths *d*, Å and Angles φ, deg in the Molecule of **1**

Distance	*d*	Distance	*d*	Distance	*d*	Distance	*d*
C(1)–C(2)	1.39(1)	C(5)–C(6)	1.53(1)	C(11)–C(12)	1.37(1)	C(18)–C(19)	1.38(1)
C(1)–N	1.38(1)	C(5)–O(5)	1.42(1)	C(12)–C(7)	1.39(1)	C(19)–C(20)	1.39(1)
C(1)–C(6)	1.50(1)	C(5)–C(25)	1.56(1)	C(13)–O(1)	1.26(1)	C(20)–C(21)	1.39(1)
C(2)–C(3)	1.52(1)	N–C(7)	1.42(1)	C(13)–O(2)	1.34(1)	C(21)–C(16)	1.35(1)
C(2)–C(13)	1.41(1)	C(7)–C(8)	1.40(1)	O(2)–C(14)	1.43(1)	C(22)–O(3)	1.20(1)
C(3)–C(4)	1.54(1)	C(8)–C(9)	1.39(1)	C(14)–C(15)	1.50(1)	C(22)–O(4)	1.33(1)
C(3)–C(16)	1.54(1)	C(9)–C(10)	1.35(1)	C(16)–C(17)	1.41(1)	O(4)–C(23)	1.47(1)
C(4)–C(5)	1.53(1)	C(9)–Cl	1.74(1)	C(17)–C(18)	1.40(1)	C(23)–C(24)	1.48(1)
C(4)–C(22)	1.50(1)	C(10)–C(11)	1.36(1)				

Angle	φ	Angle	φ	Angle	φ
C(2)–C(1)–C(6)	124(1)	C(4)–C(5)–C(25)	110(1)	O(2)–C(13)–C(2)	115(1)
N–C(1)–C(2)	120(1)	C(6)–C(5)–C(25)	108(1)	C(13)–O(2)–C(14)	118(1)
N–C(1)–C(6)	116(1)	C(1)–C(6)–C(5)	112(1)	O(2)–C(14)–C(15)	107(1)
C(1)–C(2)–C(13)	122(1)	C(1)–N–C(7)	129(1)	C(21)–C(16)–C(17)	118(1)
C(1)–C(2)–C(3)	120(1)	C(12)–C(7)–C(8)	119(1)	C(21)–C(16)–C(3)	122(1)
C(13)–C(2)–C(3)	118(1)	C(12)–C(7)–N	124(1)	C(17)–C(16)–C(3)	120(1)
C(2)–C(3)–C(16)	112(1)	C(8)–C(7)–N	117(1)	C(18)–C(17)–C(16)	119(1)
C(2)–C(3)–C(4)	114(1)	C(9)–C(8)–C(7)	118(1)	C(19)–C(18)–C(17)	121(1)
C(16)–C(3)–C(4)	108(1)	C(10)–C(9)–C(8)	123(1)	C(18)–C(19)–C(20)	120(1)
C(22)–C(4)–C(5)	114(1)	C(10)–C(9)–Cl	120(1)	C(21)–C(20)–C(19)	118(1)
C(22)–C(4)–C(3)	110(1)	C(8)–C(9)–Cl	117(1)	C(16)–C(21)–C(20)	123(1)
C(5)–C(4)–C(3)	110(1)	C(9)–C(10)–C(11)	119(1)	O(3)–C(22)–O(4)	123(1)
O(5)–C(5)–C(4)	111(1)	C(10)–C(11)–C(12)	122(1)	O(3)–C(22)–C(4)	126(1)
O(5)–C(5)–C(6)	112(1)	C(11)–C(12)–C(7)	120(1)	O(4)–C(22)–C(4)	111(1)
C(4)–C(5)–C(6)	109(1)	O(1)–C(13)–O(2)	120(1)	C(22)–O(4)–C(23)	118(1)
O(5)–C(5)–C(25)	106(1)	O(1)–C(13)–C(2)	125(1)	O(4)–C(23)–C(24)	106(1)

Figure 1 shows a general view of the molecule of **1**. The cyclohexene ring has the shape of a distorted *semi-chair*. The fragment of the ring near the double bond is almost planar: the C(6)–C(1)–C(2)–C(3) torsion angle is 3°. The configuration of the "saturated" part of the ring approaches to the cyclohexane one: the C(3)–C(4)–C(5)–C(6) torsion angle is 64°.

The aryl substituent at C^3 (C(3) in Fig. 1) and ester substituents are in the pseudo-equatorial positions. The angles between the plane of the aryl substituent at C^3 and the planes defined by C(3), C(4), C(5) and C(1), C(2), C(3) atoms are 110° and 120° respectively. The C(4)–C(3)–C(16)–C(21) and C(2)–C(3)–C(16)–C(21) torsion angles are 99° and 134° respectively. Therefore, the aryl substituent is positioned almost perpendicularly to the "plane" of the cyclohexene ring. The molecule has an intramolecular hydrogen bond between the amine hydrogen and oxygen of the ester function at C^2. The O(1)…H(1) distance is 1.86(6) Å; O(1)…N is 2.64(9) Å; N–H(1) is 0.82(4) Å; the O(1)…H(1)–N(1) angle is 159(6)°. The hydroxyl group is pseudo-axial. The torsion angle between the vicinal trans-diequatorial ester group and the phenyl substituent (C(16)–C(3)–C(4)–C(22)) equals to 54(1)°, evidencing the diaxial arrangement of the methine hydrogens at C(3) and C(4). The torsion angle between the vicinal trans-diequatorial ester group and the methyl substituent (C(22)–C(4)–C(5)–C(25)) is 54(1)°. The N-aryl cycle is not coplanar to the enaminocarbonyl fragment, though not perpendicular to it (C(1)–N(1)–C(7)–C(12) torsion angle is 49(2)°) admitting partial conjugation.

Therefore, the molecule of compound **1** is geometrically similar to the molecule of 2,4-diacetyl-5-hydroxy-5-methyl-3-(2-chlorophenyl)-N-(4-methylphenyl)-1-cyclohexenylamine that we described previously in the work [6].

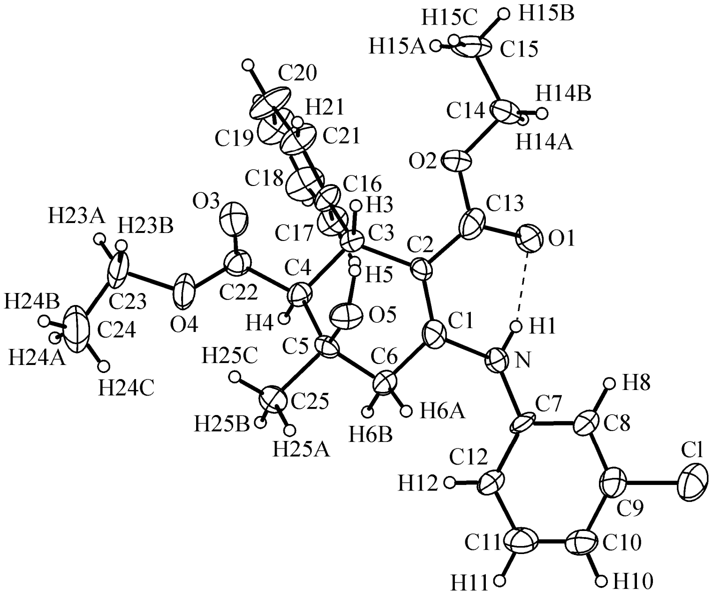

Fig. 1. Geometry of the molecule of **1** according to XRD data.

A difference in the substituents (acetyl, ethoxycarbonyl) does not significantly affect the overall geometry of the molecule: the shape of the cyclohexene ring, twist angles of the aryl groups at the nitrogen and carbon atoms. The dissimilarity consists in the absence of the intramolecular hydrogen bond between the hydroxyl and the adjacent ester group in enamine **1** caused by the switching of the H(5) atom of the hydroxyl group to the intermolecular bond with the O(1) oxygen atom of the ester function. The O(1)…H(5′), O(1)…O(5′), and O(5′)–H(5′) distances are 2.15(9) Å, 2.77(1) Å, and 0.96(4) Å respectively; the O(1)…H(5′)–O(5′) angle is 119(5)°. The presence of this intermolecular hydrogen bond strengthens molecular packing in the structure along the *c* axis.

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