Russian Journal of Organic Chemistry, Vol. 41, No. 7, 2005, pp. 1016–1022. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 7, 2005, pp. 1039–1045.

Synthesis and Structure of Diisopropyl 6-Hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxylates and Their Reactions with Nucleophilic Reagents

V. L. Gein[1], N. V. Nosova[1], K. D. Potemkin[1], Z. G. Aliev[2], and A. P. Kriven'ko[3]

[1] *Perm State Pharmaceutical Academy, ul. Lenina 48, Perm, 614990 Russia*
e-mail: perm@pfa.ru

[2] *Institute of Chemical Physics Problems, Russian Academy of Sciences, Chernogolovka, Moscow oblast, Russia*

[3] *Saratov State University, Saratov, Russia*

Received July 20, 2004

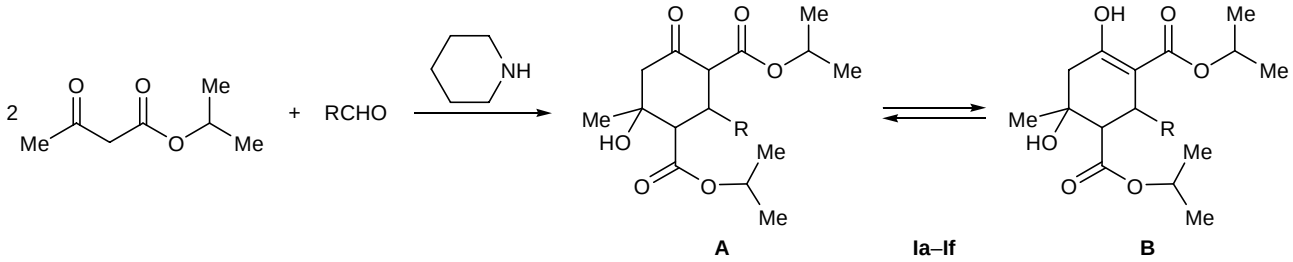
Abstract—Base-catalyzed reactions of isopropyl acetoacetate with aromatic and heterocyclic aldehydes afforded the corresponding diisopropyl 6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxylates which were brought into reactions with mono- and difunctional nitrogen-containing nucleophiles. According to the X-ray diffraction data, diisopropyl 4-oxocyclohexane-1,3-dicarboxylates in crystal exist in the ketone form.

With the goal of elucidating the effect of alkyl radical in the alkoxycarbonyl group on the reactivity of 1,3-bis(alkoxycarbonyl)-substituted cyclohexanones (cyclic β-hydroxy ketones) [1–6] we synthesized 2-substituted diisopropyl 6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxylates and studied their structure and reactions with mono- and difunctional nitrogen-containing nucleophiles. Compounds **Ia**–**If** were obtained by the known method, namely by diketone condensation of isopropyl acetoacetate with aromatic and heterocyclic aldehydes under conditions of base catalysis [1] (in the presence of piperidine; Scheme 1).

Cyclohexanedicarboxylates **Ia**–**If** were isolated as colorless crystalline substances which are soluble in dimethyl sulfoxide, dimethylformamide, and acetone and insoluble in water. Their IR spectra contained absorption bands due to stretching vibrations of the ester (1722–1735 and 1737–1745 cm^{-1}) and ketone carbonyl groups (1700–1710 cm^{-1}) and hydroxy group (3450–3504 cm^{-1}). In the ^1H NMR spectra of **Ia**–**If** we observed a singlet at δ 1.18–1.30 ppm from protons of the methyl group on C^6, a singlet at δ 4.58–4.91 ppm from the hydroxy proton, doublet signals at δ 3.15–3.42 and 3.67–4.05 ppm (J = 12 Hz) from protons in positions *1* and *3* of the cyclohexane ring, a triplet at δ 3.73–4.04 ppm from the 2-H proton, and two doublets (*AB* system) from the C^5H_2 methylene group at δ 2.25–2.40 and 2.82–3.02 ppm (J = 14 Hz).

Compounds **Ia**–**If** can exist as ketone (**A**) and enol tautomers (**B**). The ^1H NMR spectra of **Ia**–**If** contain a signal at δ 12 ppm, which may be attributed to proton of the hydroxy group in the enol tautomer. The fraction of the enol form depends on the substituent R in position *2* of the cyclohexane ring. Electron-acceptor groups in the aryl substituent, e.g., nitro group, favor

Scheme 1.



R = Ph (**a**), 4-$CH_3OC_6H_4$ (**b**), 4-BrC_6H_4 (**c**), 4-$O_2NC_6H_4$ (**d**), 3-$O_2NC_6H_4$ (**e**), 2-pyridyl (**f**).

1070-4280/05/4107-1016

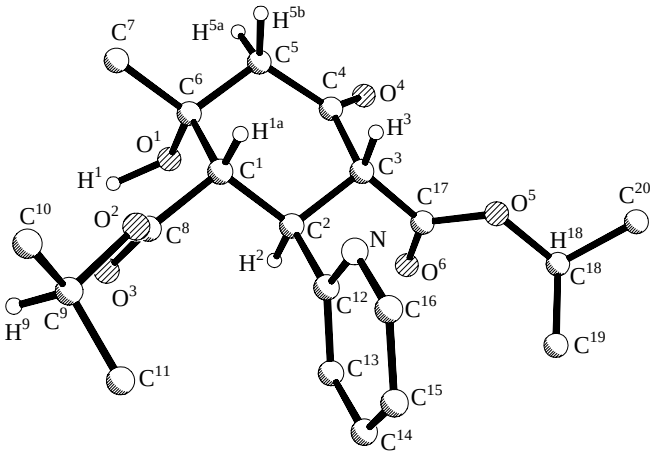
enolization, and the fraction of the enol tautomer attains 5%; the fractions of the enol form in compounds **Ia** and **If** are 3.7 and 3.3%, respectively.

Compounds **Ia**–**If** turn dark yellow on treatment with iron(III) chloride; on storage, the solution gradually darkens and acquires dark red color, presumably as a result of displacement of the tautomeric equilibrium toward the enol form. Thus the color test with iron(III) chloride and the ^{1}H NMR data suggest that compounds **Ia**–**If** in solution exist as mixtures of ketone (**A**) and enol tautomers (**B**).

The structure of compound **If** in crystal was studied by the X-ray diffraction method. A single crystal of **If** suitable for X-ray analysis was obtained by slow crystallization from an alcoholic solution. The structure of molecule **If** is shown in figure; for the sake of simplicity, some hydrogen atoms are not shown. It is seen that compound **If** in crystal exists exclusively as ketone form **A**. The cyclohexane ring adopts a *chair* conformation. The three bulky substituents (two alkoxycarbonyl groups and benzene ring) occupy equatorial positions. The bond lengths and bond angles in molecule **If** have their usual values and require no comments. Probably, molecules **If** in crystal are linked through a very weak hydrogen bond O^1–$N^1\cdots O^3$ [$d(O^1\cdots O^3)$ = 3.146 Å, $d(H^1\cdots O^3)$ = 2.331 Å, $\angle O^1N^1O^3$ = 165.58°] to give centrosymmetric dimers.

We examined reactions of diisopropyl cyclohexanedicarboxylates **Ia**–**If** with aromatic amines, hydrazines, phenylhydrazine, and hydroxylamine in order to elucidate how the nature of the alkoxycarbonyl group affects the reactivity of these compounds. We previously showed [2] that dimethyl 4-oxocyclohexane-1,3-dicarboxylates react with aromatic amines on heating in boiling benzene in the presence of a catalytic amount of acetic acid. The reaction is accompanied by elimination of water with formation of arylaminocyclohexadienes [2]. Under analogous conditions, diethyl 6-hydroxy-4-oxocyclohexane-1,3-dicarboxylates give rise to the corresponding arylaminocyclohexenes, and the hydroxy group on C^6 remains intact [3, 4].

Diisopropyl 6-hydroxy-4-oxocyclohexane-1,3-dicarboxylates were brought into reactions with *p*-toluidine and *p*-anisidine. However, the procedures reported in [2, 3] turned out to be inapplicable. When the reactions were performed by heating of the reactants in boiling benzene or toluene, the process was accompanied by strong tarring, and we failed to isolate the desired amination products. Our further experiments showed that compounds **Id** and **Ie** successfully reacted with aromatic amines on heating in boiling isopropyl alcohol in the presence of acetic acid. As a result, we isolated the corresponding 2-substituted diisopropyl 4-arylamino-6-hydroxy-6-methyl-3-cyclohexene-1,3-dicarboxylates **IId** and **IIe** in high yields (Scheme 2). Isopropyl alcohol was selected as solvent in order to avoid transesterification of initial compounds **I**.

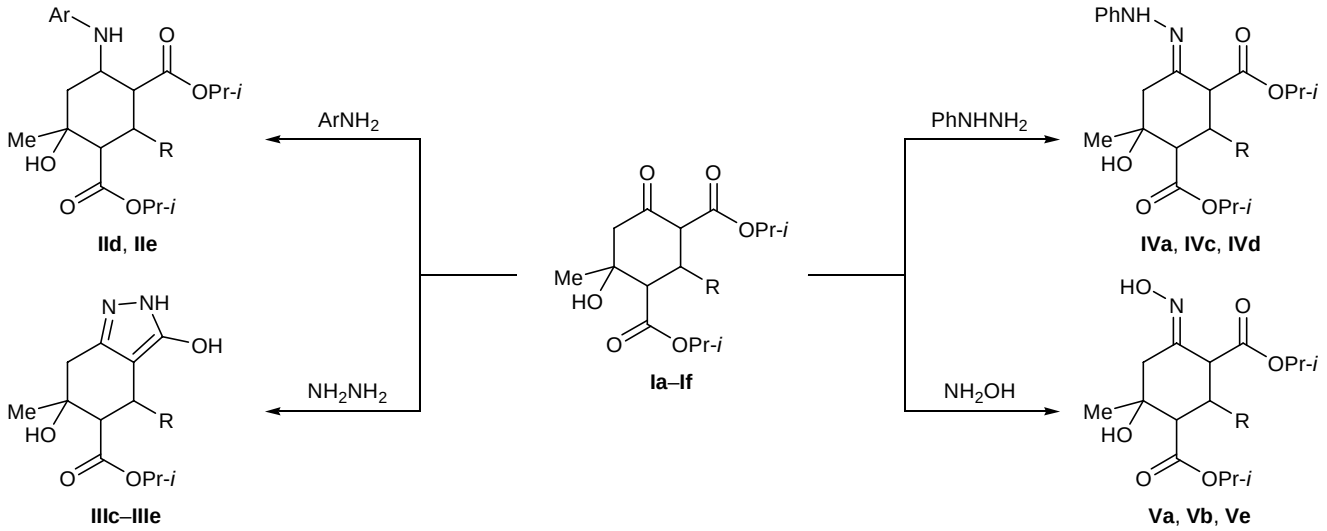


Structure of the molecule of diisopropyl 6-hydroxy-6-methyl-4-oxo-2-(2-pyridyl)cyclohexane-1,3-dicarboxylate (**If**) according to the X-ray diffraction data.

Compounds **IId** and **IIe** are yellow crystalline substances which are soluble in DMSO, DMF, acetone, toluene, and benzene and insoluble in water. The IR spectra of crystalline samples of **IId** and **IIe** contained absorption bands due to stretching vibrations of the N–H (3150–3210 cm^{-1}), O–H (3450–3520 cm^{-1}), and C=C bonds (1650–1665 cm^{-1}). Compounds **IId** and **IIe** contained a singlet from the hydroxy proton (δ 4.58–4.60 ppm), doublets from two CH protons in positions *1* and *2* of the cyclohexane ring (δ 4.16–4.23 and 2.48–2.52 ppm, respectively, J = 11 Hz), and a singlet from the NH proton (δ 10.72–10.78 ppm). The spectral data indicate that compounds **IId** and **IIe** exist in the enamino form.

Reactions of cyclic hydroxy ketones containing methoxy- or ethoxycarbonyl groups in positions *1* and *3* of the cyclohexane ring are known to react with hydrazine hydrate at the 1,3-dioxo fragment; the subsequent heterocyclization gives the corresponding tetrahydroindazoles [5, 6]. Under similar conditions, bis(*tert*-butoxycarbonyl)-substituted analogs are converted into 6-hydrazones [5]. Diisopropyl 6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxylates **Ic**–**Ie** reacted with hydrazine hydrate at a ratio of 1 : 1 in

Scheme 2.



IVa, **Va**, R = Ph; **Vb**, R = 4-$CH_3OC_6H_4$; **IIIc**, **IVc**, R = 4-BrC_6H_4; **IId**, **IIId**, **IVd**, R = 4-$O_2NC_6H_4$; **IIe**, **IIIe**, **Ve**, 3-$O_2NC_6H_4$; **IId**, Ar = 4-$CH_3OC_6H_4$; **IIe**, Ar = 4-$CH_3C_6H_4$.

alcohol on heating on a water bath in the absence of a catalyst. As with dimethyl and diethyl esters, the products were isopropyl 3,6-dihydroxy-6-methyl-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxylates **IIIc**–**IIIe** (Scheme 2) but their formation required a longer time (by a factor of 3–4), presumably due to stronger electron-donor effect of the isopropyl group as compared to ethyl. When the reaction time was shorter, we isolated mixtures of initial hydroxy ketones, intermediate hydrazones, and cyclization products, but we failed to terminate the process at the stage of formation of the corresponding hydrazones.

Indazoles **IIIc**–**IIIe** are colorless crystalline substances readily soluble in DMS and DMF, poorly soluble in dioxane and alcohol, and insoluble in water. Compounds **IIIc**–**IIIe** give rise to an intense cherry color on treatment with a solution of iron(III) chloride. The IR spectra of crystalline indazoles **IIIc**–**IIIe** contained absorption bands due to stretching vibrations of the 6-OH (3435–3500 cm^{-1}) and NH groups (3255–3280 cm^{-1}). In the ^1H NMR spectra of **IIIc**–**IIIe**, doublets from the 4-H and 5-H protons were located at δ 2.48–2.58 and 3.95–4.18 ppm, respectively (J = 11 Hz), and the NH and 3-OH protons gave a broadened singlet in the δ region 8–12 ppm with an intensity of 2H. The IR and ^1H NMR data, in combination with the color test with iron(III) chloride, suggest that compounds **IIIc**–**IIIe** in crystal and in solution exist in the enol form, in keeping with published data for structurally related indazoles [7] which were studied by X-ray analysis.

The reactions of compounds **Ia**–**Ie** with phenylhydrazine and hydroxylamine afforded the corresponding diisopropyl 6-hydroxy-6-methyl-4-phenylhydrazonocyclohexane-1,3-dicarboxylates **IVa**, **IVc**, and **IVd** and diisopropyl 6-hydroxy-4-hydroxyimino-6-methylcyclohexane-1,3-dicarboxylates **Va**, **Vb**, and **Ve** (Scheme 2). No subsequent cyclization occurred, regardless of the reaction time. Presumably, the nucleophilicity of the nitrogen atom in the phenylhydrazine residue and of the oxygen atom in the hydroxylamine residue is insufficient to ensure heterocyclization.

Phenylhydrazones **IVa**, **IVc**, and **IVd** are colorless crystalline substances which are soluble in DMSO, poorly soluble in alcohols, and insoluble in water. Their IR spectra contained absorption bands due to stretching vibrations of the O–H (3442–3505 cm^{-1}), N–H (3370–3380 cm^{-1}), and C=N bonds (1689–1700 cm^{-1}). Phenylhydrazones **IVa**, **IVc**, and **IVd** displayed in the ^1H NMR spectra doublets from protons in positions *1* and *3* of the cyclohexane ring (δ 3.04–3.15 and 3.64–3.75 ppm, respectively, J = 12 Hz), a triplet from the 2-H proton at δ 3.66–3.83 ppm, and a singlet from the NH proton at δ 9.05–9.09 ppm.

Oximes **Va**, **Vb**, and **Ve** are colorless crystalline substances which are readily soluble in DMSO and DMF, poorly soluble in alcohol, and insoluble in water. Their IR spectra contained absorption bands at 3480–3540, 3280–3284, and 1690–1695 cm^{-1}, which were assigned to stretching vibrations of the 6-hydroxy group, N-OH group, and C=N bond, respectively. In

the ^{1}H NMR spectra of **Va**, **Vb**, and **Ve** we observed doublets from protons in positions *1* and *3* of the cyclohexane ring (δ 2.95–3.18 and 3.50–3.70 ppm, respectively, J = 12 Hz), a triplet from the 2-H proton at δ 3.56–3.80 ppm, and a singlet from the oxime hydroxy proton at δ 10.62–10.74 ppm.

EXPERIMENTAL

The IR spectra were recorded from samples dispersed in mineral oil on UR-20 and Specord 80 spectrometers. The ^{1}H NMR spectra were measured on Bruker AM-300 (300 MHz) and Bruker DRX-400 (400 MHz) instruments from solutions in DMSO-d_6 using HMDS as internal reference. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using benzene–ethyl acetate (5:1) as eluent.

Diisopropyl 6-hydroxy-6-methyl-4-oxo-2-phenylcyclohexane-1,3-dicarboxylate (Ia). Isopropyl acetoacetate, 0.046 mol, and benzaldehyde, 0.023 mol, were dissolved in 6 ml of isopropyl alcohol (on heating if necessary). Piperidine, 1 ml, was added to the solution, and the mixture was kept for 1–3 days at room temperature. The precipitate was filtered off and recrystallized from isopropyl alcohol. Yield 70%, mp 180–181°C. IR spectrum, ν, cm^{-1}: 1700 (CO, ketone); 1722, 1737 (CO, ester); 3450 (OH). ^{1}H NMR spectrum, δ, ppm: 0.70 d, 0.88 d, 1.00 d, and 1.02 d [3H each, CH(C**H**$_3$)$_2$]; 1.25 s (3H, CH_3); 2.32 d (1H, 5-H$_B$ or 5-H$_A$, J = 14 Hz); 2.86 d (1H, 5-H$_A$ or 5-H$_B$, J = 14 Hz); 3.24 d (1H, 1-H, J = 12 Hz); 3.79 t (1H, 2-H); 3.85 d (1H, 3-H, J = 12 Hz); 4.66 m and 4.72 m [1H each, C**H**(CH$_3$)$_2$]; 4.77 s (1H, OH); 7.20 m (5H, C_6H_5). Found, %: C 67.19; H 7.54. $C_{21}H_{28}O_6$. Calculated, %: C 67.00; H 7.49.

Compounds **Ib**–**If** were synthesized according to a similar procedure.

Diisopropyl 6-hydroxy-2-(4-methoxyphenyl)-6-methyl-4-oxocyclohexane-1,3-dicarboxylate (Ib). Yield 72%, mp 164–166°C. IR spectrum, ν, cm^{-1}: 1715 (CO, ketone); 1737, 1742 (CO, ester); 3532 (OH). ^{1}H NMR spectrum, δ, ppm: 0.68 d, 0.83 d, 0.94 d, and 0.97 d [3H each, CH(C**H**$_3$)$_2$]; 1.18 s (3H, CH_3); 2.25 d (1H, 5-H$_A$ or 5-H$_B$, J = 14 Hz); 2.82 d (1H, 5-H$_B$ or 5-H$_A$, J = 14 Hz); 3.15 d (1H, 1-H, J = 12 Hz), 3.78 t (1H, 2-H); 3.67 d (1H, 3-H, J = 12 Hz); 3.63 s (3H, 4-C**H**$_3$OC$_6$H$_4$); 4.58 m and 4.65 m [1H each, C**H**(CH$_3$)$_2$]; 4.70 s (1H, OH); 6.75 d and 7.14 d (2H each, 4-CH$_3$OC$_6$**H**$_4$). Found, %: C 65.09; H 7.29. $C_{22}H_{30}O_7$. Calculated, %: C 65.01; H 7.44.

Diisopropyl 2-(4-bromophenyl)-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxylate (Ic). Yield 76%, mp 173–174°C. IR spectrum, ν, cm^{-1}: 1710 (CO, ketone); 1732, 1745 (CO, ester); 3490 (OH). ^{1}H NMR spectrum, δ, ppm: 0.70 d, 0.83 d, 0.94 d, and 0.97 d [3H each, CH(C**H**$_3$)$_2$]; 1.18 s (3H, CH_3); 2.27 d (1H, 5-H$_A$ or 5-H$_B$, J = 14 Hz); 2.83 d (1H, 5-H$_B$ or 5-H$_A$, J = 14 Hz); 3.20 d (1H, 1-H, J = 12 Hz); 3.73 t (1H, 2-H); 3.86 d (1H, 3-H; J = 12 Hz); 4.56 m and 4.65 m [1H each, C**H**(CH$_3$)$_2$]; 4.82 s (1H, OH); 7.20 d and 7.42 d (2H each, 4-BrC_6H_4). Found, %: C 53.62; H 5.75. $C_{21}H_{27}BrO_6$. Calculated, %: C 53.74; H 5.80.

Diisopropyl 6-hydroxy-6-methyl-2-(4-nitrophenyl)-4-oxocyclohexane-1,3-dicarboxylate (Id). Yield 83%, mp 186–188°C. IR spectrum, ν, cm^{-1}: 1695 (CO, ketone); 1727, 1732 (CO, ester); 3510 (OH). ^{1}H NMR spectrum, δ, ppm: 0.77 d, 0.92 d, 1.05 d, and 1.08 d [3H each, CH(C**H**$_3$)$_2$]; 1.27 s (3H, CH_3); 2.38 d (1H, 5-H$_A$ or 5-H$_B$, J = 14 Hz); 2.83 d (1H, 5-H$_B$ or 5-H$_A$, J = 14 Hz); 3.30 d (1H, 1-H, J = 12 Hz); 4.02 t (1H, 2-H); 3.97 d (1H, 3-H, J = 12 Hz); 4.67 m and 4.75 m [1H each, C**H**(CH$_3$)$_2$]; 4.58 s (1H, OH); 7.60 d and 8.12 d (2H each, 4-O$_2$NC_6H_4). Found, %: C 59.77; H 6.64; N 3.29. $C_{21}H_{27}NO_8$. Calculated, %: C 59.85; H 6.46; N 3.32.

Diisopropyl 6-hydroxy-6-methyl-2-(3-nitrophenyl)-4-oxocyclohexane-1,3-dicarboxylate (Ie). Yield 81%, mp 174–176°C. IR spectrum, ν, cm^{-1}: 1712 (CO, ketone); 1731, 1738 (CO, ester); 3523 (OH). ^{1}H NMR spectrum, δ, ppm: 0.75 d, 0.90 d, 1.00 d, and 1.04 d [3H each, CH(C**H**$_3$)$_2$]; 1.30 s (3H, CH_3); 2.40 d (1H, 5-H$_A$ or 5-H$_B$, J = 14 Hz); 2.94 d (1H, 5-H$_B$ or 5-H$_A$, J = 14 Hz); 3.42 d (1H, 1-H, J = 12 Hz); 3.98 t (1H, 2-H); 4.05 d (1H, 3-H, J = 12 Hz); 4.63 m and 4.75 m [1H each, C**H**(CH$_3$)$_2$]; 4.90 s (1H, OH); 7.60 t, 7.79 d, 8.11 d, and 8.22 s (1H each, 3-O$_2$NC_6H_4). Found, %: C 59.91; H 6.39; N 3.27. $C_{21}H_{27}NO_8$. Calculated, %: C 59.85; H 6.46; N 3.32.

Diisopropyl 6-hydroxy-6-methyl-4-oxo-2-(2-pyridyl)cyclohexane-1,3-dicarboxylate (If). Yield 37%, mp 122–124°C. IR spectrum, ν, cm^{-1}: 1704 (CO, ketone); 1734, 1742 (CO, ester); 3504 (OH). ^{1}H NMR spectrum, δ, ppm: 0.76 d, 0.89 d, 0.99 d, and 1.01 d [3H each, CH(C**H**$_3$)$_2$]; 1.27 s (3H, CH_3); 2.32 d (1H, 5-H$_A$ or 5-H$_B$, J = 14 Hz); 3.02 d (1H, 5-H$_B$ or 5-H$_A$, J = 14 Hz); 3.32 d (1H, 1-H, J = 12 Hz); 4.04 t (1H, 2-H); 4.00 d (1H, 3-H, J = 12 Hz); 4.65 m and 4.72 m [1H each, C**H**(CH$_3$)$_2$]; 4.91 s (1H, OH); 7.12 d, 7.22 t, 7.68 t, and 8.51 d (1H each, 2-pyridyl). Found, %:

C 63.44; H 7.31; N 3.84. $C_{20}H_{27}NO_6$. Calculated, %: C 63.65; H 7.21; N 3.71.

Diisopropyl 6-hydroxy-4-(4-methoxyphenylamino)-6-methyl-2-(4-nitrophenyl)-3-cyclohexene-1,3-dicarboxylate (IId). A solution of 0.005 mol of compound **Id**, 0.005 mol of *p*-anisidine, and 0.4 ml of acetic acid (2% by volume) in 20 ml of 2-propanol was heated for 9–16 h under reflux. The mixture was cooled and evaporated, and the residue was recrystallized from isopropyl alcohol. Yield 49%, mp 148–150°C. IR spectrum, ν, cm^{-1}: 1665 (C=C), 1710 (CO), 3210 (NH), 3450 (OH). ^{1}H NMR spectrum, δ, ppm: 0.39 d, 0.74 d, 0.88 d, and 1.00 d [3H each, CH(C**H**$_3$)$_2$]; 1.10 s (3H, CH_3); 2.20 d (1H, 5-H$_A$ or 5-H$_B$, J = 17 Hz); 2.90 d (1H, 5-H$_B$ or 5-H$_A$, J = 17 Hz); 2.48 d (1H, 2-H, J = 11 Hz); 4.23 d (1H, 1-H, J = 11 Hz); 3.77 s (3H, 4-C**H**$_3$OC$_6$H$_4$); 4.58 s (1H, OH); 4.65 m and 4.78 m [1H each, C**H**(CH$_3$)$_2$]; 6.97 d and 7.12 d (2H each, 4-CH$_3$OC$_6$**H**$_4$); 7.62 d and 8.17 d (2H each, 4-NO$_2$C$_6$H$_4$); 10.72 s (1H, NH). Found, %: C 63.72; H 6.39; N 5.41. $C_{28}H_{34}N_2O_8$. Calculated, %: C 63.87; H 6.51; N 5.32.

Diisopropyl 6-hydroxy-6-methyl-4-(4-methylphenylamino)-2-(3-nitrophenyl)-3-cyclohexene-1,3-dicarboxylate (IIe) was synthesized in a similar way. Yield 60%, mp 127–129°C. IR spectrum, ν, cm^{-1}: 1650 (C=C), 1700 (CO), 3150 (NH), 3520 (OH). ^{1}H NMR spectrum, δ, ppm: 0.31 d, 0.77 d, 0.98 d, and 1.03 d [3H each, CH(C**H**$_3$)$_2$]; 1.09 s (3H, CH_3); 2.19 d (1H, 5-H$_A$ or 5-H$_B$, J = 17 Hz); 2.97 d (1H, 5-H$_B$ or 5-H$_A$, J = 17 Hz); 2.25 s (3H, 4-C**H**$_3$C$_6$H$_4$); 2.52 d (1H, 2-H, J = 11 Hz); 4.16 d (1H, 1-H, J = 11 Hz); 4.57 s (1H, OH); 4.59 m and 4.73 m [1H each, C**H**(CH$_3$)$_2$]; 7.00 d and 7.14 d (2H each, 4-CH$_3$C$_6$**H**$_4$); 7.50 t, 7.59 d, 7.91 s, and 7.99 d (1H each, 3-O$_2$NC$_6$H$_4$); 10.78 s (1H, NH). Found, %: C 65.96; H 6.62; N 5.42. $C_{28}H_{34}N_2O_7$. Calculated, %: C 65.87; H 6.71; N 5.49.

Isopropyl 4-(4-bromophenyl)-3,6-dihydroxy-6-methyl-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxylate (IIIc). Hydrazine hydrate, 0.005 mol, was added to a mixture of 0.005 mol of compound **Ic** and 20 ml of 2-propanol. The mixture was heated for 3–5 h on a boiling water bath and cooled, and the precipitate was filtered off and recrystallized from 2-propanol. Yield 88%, mp 290–291°C. IR spectrum, ν, cm^{-1}: 1731 (CO), 3260 (NH), 3435 (OH). ^{1}H NMR spectrum, δ, ppm: 0.77 d and 1.03 d [3H each, CH(C**H**$_3$)$_2$], 1.18 s (3H, CH_3), 2.42 d (1H, 7-H$_A$ or 7-H$_B$, J = 15 Hz), 2.69 d (1H, 7-H$_B$ or H$_A$, J = 15 Hz), 2.48 d (1H, 4-H, J = 11 Hz), 3.95 d (1H, 5-H, J = 11 Hz), 4.38 s (1H, OH), 4.73 m [1H, C**H**(CH$_3$)$_2$], 6.98 d and 7.34 d (2H each, 4-BrC$_6$H$_4$), 8–12 br.s (2H, NH, OH). Found, %: C 52.65; H 5.03; N 6.73. $C_{18}H_{21}BrN_2O_4$. Calculated, %: C 52.82; H 5.17; N 6.84.

Isopropyl 3,6-dihydroxy-6-methyl-4-(4-nitrophenyl)-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxylate (IIId) was synthesized in a similar way. Yield 56%, mp 272–274°C. IR spectrum, ν, cm^{-1}: 1720 (CO), 3280 (NH), 3500 (OH). ^{1}H NMR spectrum, δ, ppm: 0.80 d and 1.09 d [3H each, CH(C**H**$_3$)$_2$], 1.26 s (3H, CH_3), 2.49 d (1H, 7-H$_A$ or 7-H$_B$, J = 15 Hz), 2.80 d (1H, 7-H$_B$ or 7-H$_A$, J = 15 Hz), 2.58 d (1H, 4-H, J = 11 Hz), 4.18 d (1H, 5-H, J = 11 Hz), 4.56 s (1H, OH), 4.76 m [1H, C**H**(CH$_3$)$_2$], 7.39 d and 8.12 d (2H each, 4-O$_2$NC$_6$H$_4$), 8–12 br.s (2H, NH, OH). Found, %: C 57.70; H 5.56; N 11.25. $C_{18}H_{21}N_3O_6$. Calculated, %: C 57.59; H 5.64; N 11.19.

Isopropyl 3,6-dihydroxy-6-methyl-4-(3-nitrophenyl)-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxylate (IIIe) was synthesized in a similar way. Yield 85%, mp 289–291°C. IR spectrum, ν, cm^{-1}: 1732 (CO), 3255 (NH), 3440 (OH). ^{1}H NMR spectrum, δ, ppm: 0.73 d and 1.02 d [3H each, CH(C**H**$_3$)$_2$]; 1.20 s (3H, CH_3); 2.53 d (1H, 7-H$_A$ or 7-H$_B$, J = 15 Hz); 2.76 d (1H, 7-H$_B$ or 7-H$_A$, J = 15 Hz); 2.56 d (1H, 4-H, J = 11 Hz); 4.14 d (1H, 5-H, J = 11 Hz); 4.49 s (1H, OH); 4.73 m [1H, C**H**(CH$_3$)$_2$]; 7.51 t, 7.49 d, 7.87 s, and 8.00 d (1H each, 3-O$_2$NC$_6$H$_4$); 8–12 br.s (2H, NH, OH). Found, %: C 57.73; H 5.75; N 11.27. $C_{18}H_{21}N_3O_6$. Calculated, %: C 57.59; H 5.64; N 11.19.

Diisopropyl 6-hydroxy-6-methyl-2-phenyl-4-phenylhydrazonocyclohexane-1,3-dicarboxylate (IVa). Phenylhydrazine, 0.005 mol, was added to 0.005 mol of compound **Ia** in 20 ml of 2-propanol, the mixture was heated for 1 h on a boiling water bath and cooled, and the precipitate was filtered off and recrystallized from isopropyl alcohol. Yield 59%, mp 210–212°C. IR spectrum, ν, cm^{-1}: 1689 (C=N), 1725 (CO), 3370 (NH), 3442 (OH). ^{1}H NMR spectrum, δ, ppm: 0.66 d, 0.93 d, 1.00 d, and 1.02 d [3H each, CH(C**H**$_3$)$_2$]; 1.30 s (3H, CH_3); 2.17 d (1H, 5-H$_A$ or 5-H$_B$, J = 15 Hz); 3.17 d (1H, 5-H$_B$ or 5-H$_A$, J = 15 Hz); 3.03 d (1H, 1-H, J = 12 Hz); 3.66 t (1H, 2-H); 3.64 d (1H, 3-H, J = 12 Hz); 4.59 m and 4.74 m [1H each, C**H**(CH$_3$)$_2$]; 4.41 s (1H, OH); 7.96 m (10H, C$_6$H$_5$); 9.05 s (1H, NH). Found, %: C 69.44; H 7.49; N 6.08. $C_{27}H_{34}N_2O_5$. Calculated, %: C 69.51; H 7.34; N 6.00.

Diisopropyl 2-(4-bromophenyl)-6-hydroxy-6-methyl-4-phenylhydrazonocyclohexane-1,3-dicar-

boxylate (IVc) was synthesized in a similar way. Yield 75%, mp 216–218°C. IR spectrum, ν, cm^{-1}: 1700 (C=N), 1735 (CO), 3380 (NH), 3505 (OH). ^1H NMR spectrum, δ, ppm: 0.73 d, 0.95 d, 1.00 d, and 1.04 d [3H each, CH(C**H**$_3$)$_2$]; 1.30 s (3H, CH_3); 2.16 d (1H, 5-H_A or 5-H_B, J = 14 Hz); 3.17 d (1H, 5-H_B or 5-H_A, J = 15 Hz); 3.04 d (1H, 1-H, J = 12 Hz); 3.66 t (1H, 2-H); 3.64 d (1H, 3-H, J = 12 Hz); 4.60 m and 4.76 m [1H each, C**H**(CH$_3$)$_2$]; 4.48 s (1H, OH); 7.28 d and 7.49 d (2H each, 4-BrC_6H_4); 6.86 m (5H, C_6H_5); 9.06 s (1H, NH). Found, %: C 59.58; H 5.98; N 5.09. $C_{27}H_{33}BrN_2O_5$. Calculated, %: C 59.45; H 6.10; N 5.13.

Diisopropyl 6-hydroxy-6-methyl-2-(4-nitrophenyl)-4-phenylhydrazonocyclohexane-1,3-dicarboxylate (IVd) was synthesized in a similar way. Yield 66%, mp 209–211°C. IR spectrum, ν, cm^{-1}: 1690 (C=N), 1722 (CO), 3375 (NH), 3500 (OH). ^1H NMR spectrum, δ, ppm: 0.71 d, 0.93 d, 0.99 d, and 1.03 d [3H each, CH(C**H**$_3$)$_2$]; 1.32 s (3H, CH_3); 2.21 d (1H, 5-H_A or 5-H_B, J = 15 Hz); 3.20 d (1H, 5-H_B or 5-H_A, J = 15 Hz); 3.15 d (1H, 1-H, J = 12 Hz); 3.83 t (1H, 2-H); 3.75 d (1H, 3-H, J = 12 Hz); 4.60 m and 4.74 m [1H each, C**H**(CH$_3$)$_2$]; 4.62 s (1H, OH); 7.60 d and 8.18 d (2H each, 4-$O_2NC_6H_4$); 6.96 m (5H, C_6H_5); 9.09 s (1H, NH). Found, %: C 63.49; H 6.34; N 8.15. $C_{27}H_{33}N_3O_7$. Calculated, %: C 63.39; H 6.50; N 8.21.

Diisopropyl 6-hydroxy-4-hydroxyimino-6-methyl-2-phenylcyclohexane-1,3-dicarboxylate (Va). A solution of 0.006 mol of potassium hydroxide in 5 ml of 2-propanol was added to a solution of 0.006 mol of hydroxylamine hydrochloride in 6 ml of 2-propanol. The precipitate was filtered off, and 0.004 mol of compound **Ia** was added to the filtrate. The mixture was heated for 1 h on a boiling water bath and cooled, and the precipitate was filtered off and recrystallized from 2-propanol. Yield 61%, mp 225–226°C. IR spectrum, ν, cm^{-1}: 1690 (C=N), 1719 (CO), 3284 (NOH), 3480 (OH). ^1H NMR spectrum, δ, ppm: 0.66 d, 0.77 d, 0.95 d, and 0.97 d [3H each, CH(C**H**$_3$)$_2$]; 1.23 s (3H, CH_3); 1.98 d (1H, 5-H_A or 5-H_B, J = 14 Hz); 3.29 d (1H, 5-H_B or 5-H_A, J = 14 Hz); 3.00 d (1H, 1-H, J = 12 Hz); 3.62 t (1H, 2-H); 3.58 d (1H, 3-H, J = 12 Hz); 4.57 m and 4.62 m [1H each, C**H**(CH$_3$)$_2$]; 4.36 s (1H, 4-OH); 7.18 m (5H, C_6H_5); 10.65 s (1H, NOH). Found, %: C 64.35; H 7.58; N 3.65. $C_{21}H_{29}NO_6$. Calculated, %: C 64.43; H 7.47; N 3.58.

Diisopropyl 6-hydroxy-4-hydroxyimino-2-(4-methoxyphenyl)-6-methylcyclohexane-1,3-dicarboxylate (Vb) was synthesized in a similar way. Yield 82%, mp 211–212°C. IR spectrum, ν, cm^{-1}: 1690 (C=N), 1725 (CO), 3280 (NOH), 3500 (OH). ^1H NMR spectrum, δ, ppm: 0.71 d, 0.81 d, 0.97 d, and 0.99 d [3H each, CH(C**H**$_3$)$_2$]; 1.22 s (3H, CH_3); 1.95 d (1H, 5-H_A or 5-H_B, J = 14 Hz); 3.28 d (1H, 5-H_B or 5-H_A, J = 14 Hz); 2.95 d (1H, 1-H, J = 12 Hz); 3.56 t (1H, 2-H); 3.50 d (1H, 3-H, J = 12 Hz); 3.68 s (3H, 4-C**H**$_3$OC_6H_4); 4.60 m and 4.65 m [1H each, C**H**(CH$_3$)$_2$]; 4.30 s (1H, 4-OH); 6.80 d and 7.16 d (2H each, 4-CH_3OC_6**H**$_4$); 10.62 s (1H, NOH). Found, %: C 62.77; H 7.30; N 3.42. $C_{22}H_{31}NO_7$. Calculated, %: C 62.69; H 7.41; N 3.32.

Diisopropyl 6-hydroxy-4-hydroxyimino-6-methyl-2-(3-nitrophenyl)cyclohexane-1,3-dicarboxylate (Ve) was synthesized in a similar way. Yield 71%, mp 215–216°C. IR spectrum, ν, cm^{-1}: 1695 (C=N), 1735 (CO), 3280 (NOH), 3540 (OH). ^1H NMR spectrum, δ, ppm: 0.71 d, 0.80 d, 0.94 d, and 0.96 d [3H each, CH(C**H**$_3$)$_2$]; 1.27 s (3H, CH_3); 2.04 d (1H, 5-H_A or 5-H_B, J = 14 Hz); 3.32 d (1H, 5-H_B or 5-H_A, J = 14 Hz); 3.18 d (1H, 1-H, J = 12 Hz); 3.80 t (1H, 2-H); 3.70 d (1H, 3-H, J = 12 Hz); 4.58 m and 4.66 m [1H each, C**H**(CH$_3$)$_2$]; 4.56 s (1H, 4-OH); 7.60 t, 7.77 d, 8.10 d, and 8.20 s (1H each, 3-$O_2NC_6H_4$); 10.74 s (1H, NOH). Found, %: C 57.86; H 6.32; N 6.33. $C_{21}H_{28}N_2O_8$. Calculated, %: C 57.79; H 6.47; N 6.42.

X-Ray analysis of diisopropyl 6-hydroxy-6-methyl-4-oxo-2-(2-pyridyl)cyclohexane-1,3-dicarboxylate (If). Unit cell parameters: a = 9.838(2), b = 18.578(4), c = 5.976(1) Å; α = 86.21(3), β = 74.85(3), γ = 76.04(3)°; V = 1023.1(3) $Å^3$; M 377.43; d_{calc} = 1.225 g/cm^3; Z = 2; space group P-1. A set of experimental reflections was acquired on a KM-4 (KUMA Diffraction) automatic four-circle diffractometer with a χ-geometry (ω/2Θ scanning, monochromatic MoK_α irradiation, 2Θ ≤ 52.1°). Total of 3171 independent reflections were measured. No correction for absorption was introduced (μ 0.090 mm^{-1}). The structure was solved by the direct method using SIR92 program [8], followed by calculation of the electron density maps. The positions of hydrogen atoms in the methyl and aromatic groups were set from the geometry considerations, and the positions of the other hydrogen atoms were determined from difference synthesis of electron density. The structure was refined by the least-squares procedure in full-matrix anisotropic approximation for non-hydrogen atoms using SHELXL-97 program [9] until R_1 = 0.0787, wR_2 = 0.2410 [from 2040 reflections

with $I \geq 2\sigma(I)$] and $R_1 = 0.1144$, $wR_2 = 0.2653$ (from all 3171 reflections); GooF = 1.113.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 04-03-96042).

REFERENCES

1. Finar, I.L., *J. Chem. Soc*., 1961, p. 674.
2. Gein, V.L., Gein, N.V., Voronina, E.V., and Kriven'ko, A.P., *Khim.-Farm. Zh*., 2002, vol. 36, no. 3, p. 23.
3. Sorokin, V.V., Kuz'min, M.V., Smirnova, N.S., Kozhevnikova, N.I., and Kriven'ko, A.P., *Zh. Org. Khim*., 1994, vol. 30, p. 528.
4. Kriven'ko, A.P. and Sorokin, V.V., *Russ. J. Org. Chem*., 1999, vol. 35, p. 1097.
5. Gein, V.L., Gein, N.V., Potemkin, K.D., and Kriven'ko, A.P., *Russ. J. Gen. Chem*., 2004, vol. 74, p. 1564.
6. Sorokin, V.V., Grigor'ev, A.V., Ramazanov, A.K., and Kriven'ko, A.P., *Khim. Geterotsikl. Soedin*., 1999, p. 757.
7. Usova, E.B., Lysenko, L.I., Krapivin, G.D., Zavodnik, V.E., and Kul'nevich, V.G., *Khim. Geterotsikl. Soedin*., 1997, p. 1459.
8. Altomare, A., Cascarano, G., Giacovazzo, C., and Gualardi, A., *J. Appl. Crystallogr*., 1993, vol. 26, p. 343.
9. Sheldrick, G.M., *SHELX97. Programs for Crystal Structure Analysis*, Gottingen: Univ. of Gottingen, Germany, 1998, p. 2332.