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# Reaction of Dialkyl 2-Aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylates with Aliphatic Amines

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**Abstract**—Benzylamine, phenethylamine, and homoveratrylamine reacted with dialkyl 2-aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylates at the endocyclic carbonyl group with conservation of the enolic hydroxy group to give dialkyl 4-alkylamino-2-aryl-6-hydroxy-6-methylcyclohex-3-ene-1,3-dicarboxylates. The reaction of dimethyl 4-hydroxy-4-methyl-6-oxo-2-phenylcyclohexane-1,3-dicarboxylate with tryptamine was accompanied by dehydration with formation of dimethyl 4-[2-(1*H*-indol-3-yl)ethylamino]-6-methyl-2-phenylcyclohexa-3,5-diene-1,3-dicarboxylate, presumably due to basic properties of the indole nitrogen atom.

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We previously described in detail reactions of dialkyl 2-aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylates with aromatic amines in the presence of acid catalyst (2% of acetic acid or 1% of *p*-toluenesulfonic acid). It was found that nucleophile attacks the endocyclic carbonyl carbon atom to give the corresponding arylaminocyclohexenedicarboxylates [1–6]. The reactions with dimethyl 6-oxocyclohexane-1,3-dicarboxylates were accompanied by dehydration with formation of arylaminocyclohexadienedicarboxylates; the dehydration process was also favored by increased concentration of the acid catalyst (9% of acetic acid) [2, 7].

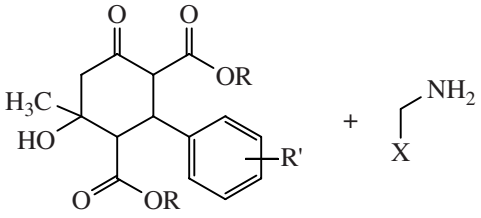
There are almost no published data on reactions of dialkyl 4-oxocyclohexane-1,3-dicarboxylates with aliphatic amines. It was reported that bis(ethoxycarbonyl)-substituted cyclohexanones reacted with benzylamine and cyclohexenylamine in the presence of a catalytic amount of acetic acid to produce the corresponding *N*-benzyl(cyclohexyl)cyclohexenamines [8]. The reaction with benzylamine successfully occurred in the absence of catalyst.

With a view to examine the reactivity of dialkyl oxocyclohexane-1,3-dicarboxylates, as well as to obtain new potential biologically active compounds, in the present work we performed reactions of dimethyl, diisopropyl, diallyl, and di-*tert*-butyl 2-aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylates **I–IV** with benzylamine, phenethylamine, homoveratrylamine [2-(3,4-dimethoxyphenyl)ethanamine], and tryptamine. It is known that some derivatives of the above amines exhibit strong physiological activity; furthermore, such compounds as adrenalin and serotonin are biogenic amines.

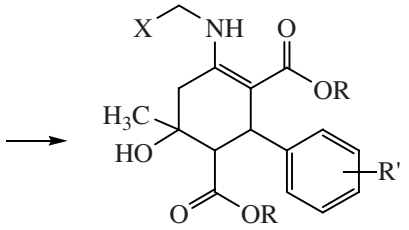
Dialkyl oxocyclohexane-1,3-dicarboxylates **I–IV** successfully reacted with benzylamine, phenethylamine, and homoveratrylamine on heating for a short time in boiling alcohol containing a catalytic amount of acetic acid, and the products were the corresponding dialkyl 4-alkylamino-2-aryl-6-hydroxy-6-methylcyclohex-3-ene-1,3-dicarboxylates **Va–Vf**, **Va**, **VIIa–VIId**, **VIIg–VIIi**, and **VIIIa** (Scheme 1, Table 1). The reactions with dimethyl 4-oxocyclohexane-1,3-dicarboxylates **Ia–Ic** required no catalyst. In both cases, regardless of the presence or absence of acetic acid in the reaction medium, the hydroxy group in position *4* of the cyclohexane ring remained unchanged.

Dimethyl cyclohex-3-ene-1,3-dicarboxylate **Vc** was also synthesized by independent method. While studying three-component condensation of methyl acetoacetate with *p*-nitrobenzaldehyde and benzylamine, we found that the product was not the corresponding Hantzsch dihydropyridine but dimethyl 4-benzylamino-6-hydroxy-6-methyl-2-(4-nitrophenyl)-cyclohex-3-ene-1,3-dicarboxylate (**Vc**) which was formed in a high yield (Scheme 2). Samples of **Vc** had

**Scheme 1.**



**Ia–Ic, IIa, IIIa, IVa–IVd**



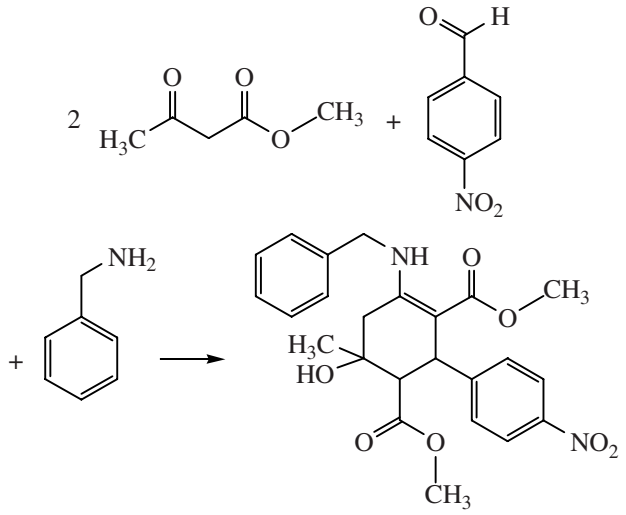
**Va–Vf, VIa, VIIa–VIId, VIIg–VIIi, VIIIa**

**Va–Vc**, **VIa**, **VIIa**, **VIIb**, X = Ph; **Vd**, **VIIc**, **VIId**, **VIIg**, X = $PhCH_2$; **Vf**, **VIIh**, **VIIi**, **VIIIa**, X = 3,4-$(MeO)_2C_6H_3CH_2$; **Ia–Ic**, **Va–Vd**, **Vf**, R = Me; **IIa**, **VIa**, R = *i*-Pr; **IVa–IVc**, **VIIa–VIId**, **VIIg–VIIi**, R = *t*-Bu; **IIIa**, **VIIIa**, R = $CH_2$=$CHCH_2$; **Ia**, **IIIa**, **IVa**, **Va**, **Vd**, **Vf**, **VIIa**, **VIIc**, **VIIh**, **VIIIa**, R′ = H; **Ib**, **Vb**, R′ = 4-MeO; **Ic**, **IIa**, **IVb**, **Vc**, **VIa**, **VIIb**, R′ = 4-$O_2N$; **IVc**, **VIId**, R′ = 3-$O_2N$; **IVd**, **VIIg**, **VIIi**, R′ = 4-Cl.

**Table 1.** Yields, melting points, and elemental analyses of dialkyl 4-alkylamino-2-aryl-6-hydroxy-6-methylcyclohex-3-ene-1,3-dicarboxylates **Va–Vf**, **VIa**, **VIIa–VIIi**, and **VIIIa**

| Comp. no. | Yield, % | mp, °C | Found N, % | Formula | Calculated N, % |
|---|---|---|---|---|---|
| **Va** | 43 | 169–171 | 3.35 | $C_{24}H_{27}NO_5$ | 3.42 |
| **Vb** | 50 | 176–177 | 3.22 | $C_{25}H_{29}NO_6$ | 3.18 |
| **Vc** | 54 | 155–157 | 6.19 | $C_{24}H_{26}N_2O_7$ | 6.16 |
| **Vd** | 30 | 134–136 | 3.24 | $C_{25}H_{29}NO_5$ | 3.31 |
| **Ve** | 35 | 182–183 | 5.21 | $C_{29}H_{34}N_2O_7$ | 5.36 |
| **Vf** | 57 | 158–159 | 2.93 | $C_{27}H_{33}NO_7$ | 2.95 |
| **VIa** | 30 | 123–125 | 5.56 | $C_{28}H_{34}N_2O_7$ | 5.48 |
| **VIIa** | 59 | 184–185 | 2.76 | $C_{30}H_{39}NO_5$ | 2.84 |
| **VIIb** | 85 | 202–204 | 5.29 | $C_{30}H_{38}N_2O_7$ | 5.20 |
| **VIIc** | 70 | 176–177 | 2.88 | $C_{31}H_{41}NO_5$ | 2.76 |
| **VIId** | 31 | 130–132 | 5.00 | $C_{31}H_{40}N_2O_7$ | 5.07 |
| **VIIe** | 90 | 164–166 | 4.71 | $C_{33}H_{41}ClN_2O_5$ | 4.82 |
| **VIIf** | 40 | 170–172 | 4.74 | $C_{34}H_{44}N_2O_6$ | 4.85 |
| **VIIg** | 62 | 176–178 | 2.60 | $C_{31}H_{40}ClNO_5$ | 2.58 |
| **VIIh** | 68 | 183–185 | 2.54 | $C_{33}H_{45}NO_7$ | 2.51 |
| **VIIi** | 55 | 148–150 | 2.28 | $C_{33}H_{44}ClNO_7$ | 2.32 |
| **VIIIa** | 20 | 131–133 | 2.57 | $C_{31}H_{37}NO_7$ | 2.61 |

**Scheme 2.**



**Vc**

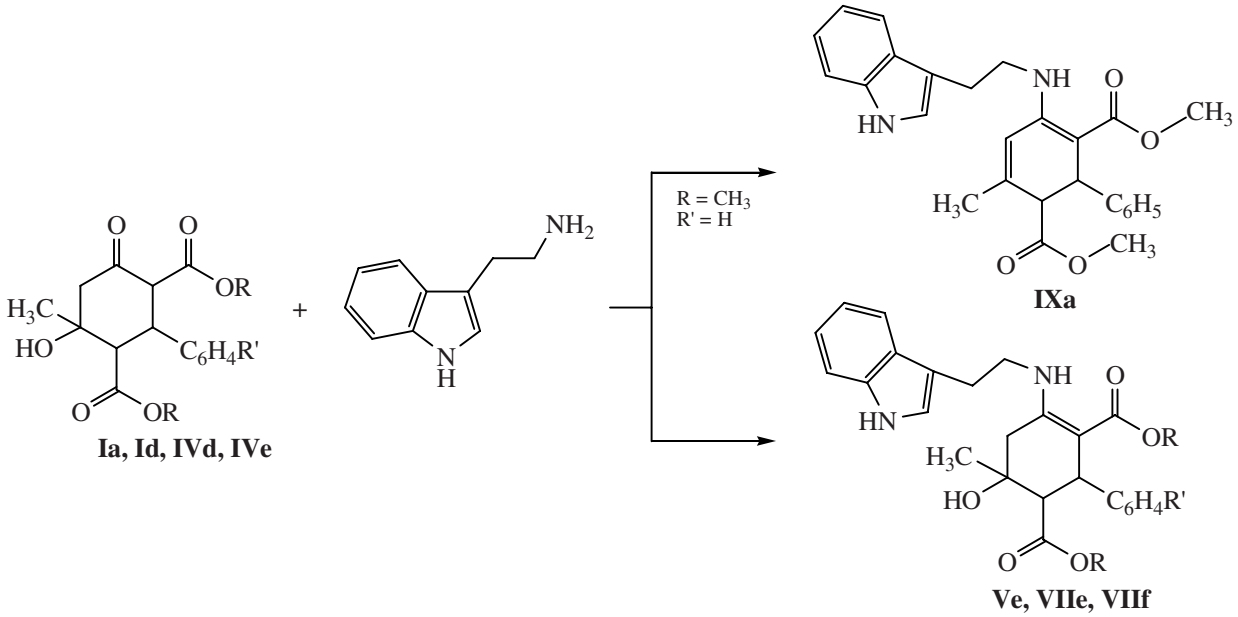
similar spectral properties and showed no depression of the melting point on mixing. Presumably, the process involves intermediate formation of cyclic β-hydroxy ketone, where benzylamine acts as base catalyst. In the next step, the resulting cyclohexanone reacts with benzylamine as nucleophile.

The reaction of dimethyl 4-hydroxy-4-methyl-6-oxo-2-phenylcyclohexane-1,3-dicarboxylate (**Ia**) with tryptamine was accompanied by dehydration of the amination product with formation of dimethyl 4-[2-(1*H*-indol-3-yl)ethylamino]-6-methyl-2-phenylcyclohexa-3,5-diene-1,3-dicarboxylate (**IXa**). In the reactions of diesters **Id**, **IVd**, and **IVe** with tryptamine under analogous conditions, the hydroxy group remained unchanged, and the products were dimethyl and di-*tert*-butyl 2-aryl-6-hydroxy-4-[2-(1*H*-indol-3-yl)ethylamino]-6-methylcyclohex-3-ene-1,3-dicarboxylates **Ve**, **VIIe**, and **VIIf**, respectively (Scheme 3, Table 1).

Presumably, dehydration of the amination product of compound **Ia** is favored by basic properties of the indole nitrogen atom which is capable of binding proton in position *5* of the cyclohexene ring. Di-*tert*-butyl cyclohexene-1,3-dicarboxylates **VIIa** and **VIIf** are more stable: electron-donor properties of the *tert*-butyl group hamper the elimination of proton from $C^5$ in the cyclohexene ring, and no dehydration is observed.

Compounds **Va–Vf**, **VIa**, **VIIa–VIIi**, and **VIIIa** are white, off-white, or yellow crystalline substances that are soluble in DMSO, DMF, and acetone and insoluble in water. The IR spectra of crystalline samples of **Va–**

**Scheme 3.**




**Ia**, **Id**, **Ve**, R = Me; **IVd**, **IVe**, **VIIe**, **VIIf**, R = *t*-Bu; **Ia**, R′ = H; **Id**, **Ve**, R′ = 3,4-$(MeO)_2$; **IVd**, **VIIe**, R′ = 4-Cl; **IVe**, **VIIf**, R′ = 4-MeO.

**Vf**, **VIa**, **VIIa**–**VIIi**, and **VIIIa** contained absorption bands in the regions 3490–3565 ($\nu_{OH}$), 3240–3285 ($\nu_{NH}$), and 1644–1660 $cm^{-1}$ (C=C) (Table 2). In the $^1H$ NMR spectra of these compounds, the hydroxy proton resonated as a singlet at δ 4.12–4.65 ppm, two CH protons in positions *1* and *2* of the cyclohexene ring gave doublets at δ 3.85–4.25 and 2.09–2.58 ppm with a coupling constant *J* of 10 Hz, two doublets at δ 2.40–2.59 and 2.44–2.70 ppm with a coupling constant *J* of 17 Hz were assigned to the $C^5H_2$ group, and the NH signal was a triplet at δ 8.80–9.30 ppm (Table 2). Compound **Vd** displayed in the mass spectrum the molecular ion peak with *m*/*z* 423, ion peaks with *m*/*z* 405 $[M - H_2O]^+$, 346 $[M - H_2O - COOCH_3]^+$, and 300 $[M - H_2O - (CH_2)_2C_6H_5]^+$, and other fragment ion peaks, which were consistent with the assumed

**Table 2.** IR and $^1H$ NMR spectra of dialkyl 4-alkylamino-2-aryl-6-hydroxy-6-methylcyclohex-3-ene-1,3-dicarboxylates **Va**–**Vf**, **VIa**, **VIIa**–**VIIi**, and **VIIIa**

| Comp. no. | IR spectrum, ν, $cm^{-1}$ | $^1H$ NMR spectrum, δ, ppm |
|---|---|---|
| **Va** | 1657 (C=C), 1715 (COO), 3250 (NH), 3510 (OH) | 1.13 s (3H, $CH_3$), 2.45 d (1H, $C^2H$, *J* 10 Hz), 2.58 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.59 d (1H, $C^5H_AH_B$, *J* 17 Hz), 3.14 s, 3.45 s (3H each, $2CH_3O$), 4.11 d (1H, $C^1H$, *J* 10 Hz), 4.46 m (2H, $CH_2$), 4.49 s (1H, OH), 7.07 m, 7.19 m, 7.40 m (10H, $2C_6H_5$), 9.18 t (1H, NH) |
| **Vb** | 1660 (C=C), 1710 (COO), 3285 (NH), 3505 (OH) | 1.12 c (3H, $CH_3$), 2.37 d (1H, $C^2H$, *J* 10 Hz), 2.48 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.55 d (1H, $C^5H_AH_B$, *J* 17 Hz), 3.21s, 3.43 s (3H each, $2CH_3O$), 3.71 c (3H, 4-$CH_3OC_6H_4$), 4.02 d (1H, $C^1H$, *J* 10 Hz), 4.44 m (2H, $CH_2$), 4.23 s (1H, OH), 6.67 d, 6.93 d (4H, 4-$CH_3OC_6H_4$), 7.30 m (5H, $C_6H_5$), 9.17 t (1H, NH) |
| **Vc** | 1644 (C=C), 1725 (COO), 3283 (NH), 3517 (OH) | 1.16 s (3H, $CH_3$), 2.51 d (H, $C^2H$, *J* 10 Hz), 2.59 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.70 d (1H, $C^5H_AH_B$, *J* 17 Hz), 3.15 s, 3.46 s (3H each, $2CH_3O$), 4.25 d (1H, $C^1H$, *J* 10 Hz), 4.48 m (2H, $CH_2$), 4.65 s (1H, OH), 7.35 m (5H, $C_6H_5$, 2H, 4-$NO_2C_6H_4$), 8.09 d (2H, 4-$NO_2C_6H_4$), 9.28 t (1H, NH) |
| **Vd** | 1648 (C=C), 1720 (COO), 3255 (NH), 3565 (OH) | 1.07 s (3H, $CH_3$), 2.32 d (1H, $C^2H$, *J* 10 Hz), 2.50 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.53 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.79 t (2H, $PhCH_2$), 3.06 s, 3.37 s (3H each, $2CH_3O$), 3.25 m (2H, $CH_2NH$), 4.01 d (1H, $C^1H$, *J* 10 Hz), 4.40 s (1H, OH), 7.10 m (10N, $2C_6H_5$), 8.80 t (1H, NH) |
| **Ve** | 1650 (C=C), 1723 (COO), 3265 (NH), 3400 (NH), 3540 (OH) | 1.06 c (3H, $CH_3$), 2.34 d (1H, $C^2H$, *J* 10 Hz), 2.48 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.51 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.90 t (2H, $CH_2$), 3.11 s, 3.41 s (3H each, $2CH_3O$), 3.60 s, 3.62 s [3H each, 3,4-$(CH_3O)_2C_6H_4$], 3.28 m (2H, $CH_2NH$), 3.95 d (1H, $C^1H$, *J* 10 Hz), 4.36 s (1H, OH), 6.48 m, 6.68 d, 6.97 m, 7.15 s , 7.28 d, 7.52 d [8H, 3,4-$(CH_3O)_2C_6H_3$, indole], 8.82 t (1H, NH), 10.83 s [1H, NH (indole)] |

**Table 2.** (Contd.)

| Comp. no. | IR spectrum, ν, $cm^{-1}$ | $^1H$ NMR spectrum, δ, ppm |
|---|---|---|
| **Vf** | 1650 (C=C), 1710 (COO), 3250 (NH), 3540 (OH) | 1.31 s (3H,$CH_3$); 2.37 d (1H, $C^2H$, *J* 10 Hz), 2.50 d (1H, $C^5H_AH_B$, *J* 15 Hz), 2.60 d (1H,$C^5H_AH_B$, *J* 15 Hz), 2.78 t (2H, $CH_2$), 3.08 s, 3.27 s (3H each, $2CH_3O$), 3.39 m (2H,$CH_2NH$), 3.67 s, 3.70 s (3H each, $2OCH_3$), 4.02 d (1H, $C^1H$, *J* 10 Hz), 4.40 s (1H, OH), 6.73 m, 7.02 m [8H, $C_6H_5$, 3,4-$(CH_3O)_2C_6H_3$], 8.87 t (1H, NH) |
| **VIa** | 1652 (C=C), 1728 (COO), 3255 (NH), 3490 (OH) | 0.69 d, 0.85 d, 0.99 d, 1.06 d [6H each, $2CH(CH_3)_2$], 1.30 s (3H, $CH_3$), 2.58 d (1H, $C^2H$, *J* 11 Hz), 2.67 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.86 d (1H, $C^5H_AH_B$, *J* 17 Hz), 3.35 d (1H, $C^1H$, *J* 11 Hz), 4.13 m (2H, $CH_2$), 4.26 s (1H, OH), 4.79 m, 4.87 m [1H each, $2CH(CH_3)_2$], 7.41 m (5H, $C_6H_5$), 7.64 d, 8.20 d (4H, 4-$NO_2C_6H_4$), 9.30 s (1H, NH) |
| **VIIa** | 1644 (C=C), 1700 (COO), 3250 (NH), 3500 (OH) | 0.96 s, 1.22 s [9H each, $2(CH_3)_3C$], 1.17 s (3H, $CH_3$), 2.20 d (1H, $C^2H$, *J* 10 Hz), 2.47 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.54 d (1H, $C^5H_AH_B$, *J* 17 Hz), 3.95 d (1H, $C^1H$, *J* 10 Hz), 4.42 m (2H, $CH_2$), 4.23 s (1H, OH), 7.20 m (10H, $2C_6H_5$), 9.11 t (1H, NH) |
| **VIIb** | 1650 (C=C), 1690 (COO), 3240 (NH), 3500 (OH) | 0.97 s, 1.22 s [9H each, $2(CH_3)_3C$], 1.20 s (3H, $CH_3$), 2.25 d (1H, $C^2H$, *J* 10 Hz), 2.51 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.63 d (1H, $C^5H_AH_B$, *J* 17 Hz), 4.11 d (1H, $C^1H$, *J* 10 Hz), 4.44 m (2H, $CH_2$), 4.42 s (1H, OH), 7.36 m (5H, $C_6H_5$, 2H, 4-$NO_2C_6H_4$), 8.15 d (2H, 4-$NO_2C_6H_4$), 9.27 t (1H, NH) |
| **VIIc** | 1640 (C=C), 1690 (COO), 3250 (NH), 3508 (OH) | 0.89 s, 1.16 s [9H each, $2(CH_3)_3C$], 1.12 s (3H, $CH_3$), 2.10 d (1H, $C^2H$, *J* 10 Hz), 2.40 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.44 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.75 t (2H, $PhCH_2$), 3.31 m (2H, $CH_2NH$), 3.85 d (1H, $C^1H$, *J* 10 Hz), 4.15 s (1H, OH), 7.12 m (10H, $2C_6H_5$), 8.81 t (1H, NH) |
| **VIId** | 1655 (C=C), 1705 (COO), 3250 (NH), 3525 (OH) | |
| **VIIe** | 1660 (C=C), 1705 (COO), 3250 (NH), 3420 (NH), 3530 (OH) | 0.95 s, 1.15 s [9H each, $2(CH_3)_3C$], 1.10 s (3H, $CH_3$), 2.09 d (1H, $C^2H$, *J* 10 Hz), 2.44 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.47 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.88 t (2H, $CH_2$), 3.38 m (2H, $CH_2NH$), 3.86 d (1H, $C^1H$, *J* 10 Hz), 4.12 s (1H, OH), 7.20 m (9H, 4-$ClC_6H_4$, indol), 8.90 t (1H, NH), 10.82 s [1H, NH (indole)] |
| **VIIf** | 1650 (C=C), 1720 (COO), 3260 (NH), 3400 (NH), 3540 (OH) | |
| **VIIg** | 1650 (C=C), 1690 (COO), 3230 (NH), 3560 (OH) | 0.96 s, 1.22 s [9H each, $2(CH_3)_3C$], 1.17 c (3H, $CH_3$), 2.20 d (1H, $C^2N$, *J* 10 Hz), 2.47 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.54 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.78 t (2H, $PhCH_2$), 3.95 d (1H, $C^1H$, *J* 10 Hz), 4.12 m (2H, $CH_2NH$), 4.23 s (1H, OH), 7.20 m (9H, $C_6H_5$, 4-$ClC_6H_4$), 9.11 t (1H, NH) |
| **VIIh** | 1650 (C=C), 1710 (COO), 3280 (NH), 3550 (OH) | 0.95 s, 1.20 s [9H each, $2(CH_3)_3C$], 1.25 s (3H, $CH_3$), 2.15 d (1H, $C^2H$, *J* 10 Hz), 2.43 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.65 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.75 t (2H, $CH_2Ar$), 3.39 m (2H, $CH_2NH$), 3.72 s, 3.81 s (3H each, $2OCH_3$), 3.86 d (1H, $C^1H$, *J* 10 Hz), 4.12 s (1H, OH), 6.64 m, 7.19 m [8H, $C_6H_5$, 3,4-$(CH_3O)_2C_6H_3$], 8.73 t (1H, NH) |
| **VIIi** | 1650 (C=C), 1700 (COO), 3230 (NH), 3570 (OH) | 0.97 s, 1.21 s [9H each, $2(CH_3)_3C$], 1.25 s (3H, $CH_3$), 2.11 d (1H, $C^2N$, *J* 10 Hz), 2.33 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.44 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.75 t (2H, $CH_2Ar$), 3.25 s, 3.82 s (3H each, $2OCH_3$), 3.88 d (1H, $C^1H$, *J* 10 Hz), 3.90 m (2H, $CH_2NH$), 4.21 s (1H, OH), 6.92 m, 7.18 m [7H, 4-$ClC_6N_4$, 3,4-$(CH_3O)_2C_6H_3$], 8.83 t (1H, NH) |
| **VIIIa** | 1650 (C=C), 1710 (COO), 3280 (NH), 3520 (OH) | 1.15 s (3H, $CH_3$), 2.47 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.56 d (1H, $C^5H_AH_B$, *J* 17 Hz), 2.62 d (1H, $C^2H$, *J* 10 Hz), 2.72 t (2H, $CH_2Ar$), 3.67 s, 3.70 s (3H each, $2CH_3O$), 4.07 d (1H, $C^1H$, *J* 10 Hz), 4.12 m, 4.40 m (2H each, $CH_2O$), 4.50 s (1H, OH), 4.74 m (2H, $CH_2NH$), 4.87 m, 5.12 m (2H each, $CH_2$=), 5.37 m, 5.69 m (1H each, 2CH=), 6.81 m, 7.24 m [8H, $C_6H_5$, 3,4-$(CH_3O)_2 \cdot C_6H_3$], 8.93 t (1H, NH) |

structure. The mass spectrum of **VIIb** contained peaks from ions with *m/z* 538 $[M]^+$, 520 $[M - H_2O]^+$, and 437 $[M - COOC(CH_3)_3]^+$, and other fragment ions.

Cyclohexadienedicarboxylate **IXa** is a yellow crystalline substance which is soluble in DMSO, DMF, toluene, and benzene and insoluble in water. It showed in the IR spectrum absorption bands due to stretching vibrations of the N–H (3360, 3250 $cm^{-1}$), C=O (1720 $cm^{-1}$), and C=C bonds (1675, 1645 $cm^{-1}$). The $^1H$ NMR spectrum of **IXa** contained signals from aromatic protons, a three-proton singlet at δ 1.69 ppm from the 6-methyl group, a doublet at δ 3.16 ppm ($J$ = 1.3 Hz) from 2-H, a doublet at δ 6.33 ppm ($J$ = 1.3 Hz) from 1-H, a singlet at δ 4.38 ppm from 5-H, a triplet at δ 8.87 ppm from the 4-NH proton, and a singlet at δ 10.83 ppm from the NH proton in the indole ring.

The above spectral data indicate that compounds **Va**–**Vf**, **VIa**, **VIIa**–**VIIi**, **VIIIa**, and **IXa** exist as enamino tautomer which is likely to be stabilized by intramolecular hydrogen bond N–H···O=C.

## EXPERIMENTAL

The IR spectra were recorded from samples dispersed in mineral oil on UR-20 and Specord M80 spectrometers. The $^1H$ NMR spectra were measured from solutions in DMSO-$d_6$ on Bruker AM-300 (300 MHz) and Bruker DRX-400 (400 MHz) instruments using hexamethyldisiloxane as internal reference. The mass spectra (electron impact, 70 eV) were obtained on an MKh-1320 spectrometer. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using hexane–diethyl ether–chloroform (2:2:1) and benzene–ethyl acetate (5:1) as eluents.

**Dimethyl 2-aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylates Ia–Id** *(general procedure).* Methyl acetoacetate, 0.05 mol, and the corresponding aromatic aldehyde, 0.025 mol, were dissolved in 6 ml of methanol or ethanol (if necessary, on heating), 1 ml of piperidine was added, and the mixture was kept for 1–3 days at room temperature. The precipitate was filtered off and recrystallized from ethanol.

**Diisopropyl 4-hydroxy-4-methyl-2-(4-nitrophenyl)-6-oxocyclohexane-1,3-dicarboxylate (IIa).** Isopropyl acetoacetate, 0.05 mol, and 4-nitrobenzaldehyde, 0.025 mol, were dissolved in 6 ml of isopropyl alcohol on heating, 1 ml of piperidine was added, and the mixture was kept for 24 h at room temperature. The precipitate was filtered off and recrystallized from isopropyl alcohol.

**Diallyl 4-hydroxy-4-methyl-6-oxo-2-phenylcyclohexane-1,3-dicarboxylate (IIIa).** Allyl acetoacetate, 0.05 mol, and benzaldehyde, 0.025 mol, were dissolved in 6 ml of isopropyl alcohol, 1 ml of piperidine was added, and the mixture was kept for 24 h at room temperature. The precipitate was filtered off and recrystallized from isopropyl alcohol.

**Di-*tert*-butyl 2-aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylates IVa–IVe** *(general procedure). tert*-Butyl acetoacetate, 0.05 mol, and the corresponding aromatic aldehyde, 0.025 mol, were dissolved in 6 ml of isopropyl or *tert*-butyl alcohol (if necessary, on heating), 1 ml of piperidine was added, and the mixture was kept for 1–3 days at room temperature. The precipitate was filtered off and recrystallized from isopropyl alcohol.

**Dimethyl 2-aryl-4-benzylamino-6-hydroxy-6-methylcyclohex-3-ene-1,3-dicarboxylates Va–Vc** *(general procedure). a*. A solution of 0.005 mol of dimethyl 2-aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylate **Ia**–**Ic** and 0.005 mol of benzylamine in 20 ml of ethanol was heated for 1–3 h under reflux in the absence of a catalyst or in the presence of 1 vol % of acetic acid. The mixture was cooled, and the precipitate was filtered off and recrystallized from ethanol.

**Dimethyl 4-benzylamino-6-hydroxy-6-methyl-2-(4-nitrophenyl)cyclohex-3-ene-1,3-dicarboxylate (Vc).** *b*. A solution of 0.005 mol of methyl acetoacetate, 0.025 mol of 4-nitrobenzaldehyde, and 0.025 mol of benzylamine in 10 ml of ethanol was heated for 3 h under reflux (on a water bath). The mixture was cooled, poured into cold water, and left overnight. The aqueous phase was separated by decanting, and the crystals were washed with ethanol, filtered off, and recrystallized from ethanol. Yield 37%, mp 154–156° C. IR spectrum (mineral oil), ν, $cm^{-1}$: 3515 (OH), 3280 (NH), 1725 (C=O), 1645 (C=C). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 1.15 s (3H, $CH_3$), 2.51 d (1H, 2-H, $J$ = 10 Hz), 2.60 d and 2.70 d (1H each, 5-H, $J$ = 17 Hz), 3.16 s and 3.46 s (3H each, $CH_3O$), 4.25 d (1H, 1-H, $J$ = 10 Hz), 4.47 m (2H, $CH_2$), 4.65 s (1H, OH), 7.35 m (7H, $H_{arom}$), 8.10 d (2H, $C_6H_4$), 9.29 t (1H, NH). Found, %: C 63.50; H 5.88; N 6.82. $C_{24}H_{26}N_2O_7$. Calculated, %: C 63.44; H 5.73; N 6.17.

**Dimethyl, diisopropyl, di-*tert*-butyl, and diallyl-4-alkylamino-2-aryl-6-hydroxy-6-methylcyclohex-3-**

**ene-1,3-dicarboxylates Vd–Vf, VIa, VIIa–VIIi, and VIIIa** *(general procedure).* A solution of 0.005 mol of dimethyl, diisopropyl, diallyl, or di-*tert*-butyl 2-aryl-4-hydroxy-4-methyl-6-oxocyclohexane-1,3-dicarboxylate **Ia**, **Id**, **IIa**, **IIIa**, or **IVa–IVe** and 0.005 mol of the corresponding amine in 20 ml of ethanol containing 1 vol % of acetic acid was heated for 1–3 h under reflux. The mixture was cooled, and the precipitate was filtered off and recrystallized from ethyl or isopropyl alcohol.

**Dimethyl 4-[2-(1*H*-indol-3-yl)ethylamino]-6-methyl-2-phenylcyclohexa-3,5-diene-1,3-dicarboxylate (IXa).** A solution of 0.005 mol of dimethyl 4-hydroxy-4-methyl-6-oxo-2-phenylcyclohexane-1,3-dicarboxylate (**Ia**) and 0.005 mol of tryptamine in 20 ml of ethanol containing a few drops of acetic acid was heated for 2 h under reflux. The mixture was cooled, and the precipitate was filtered off and recrystallized from ethanol. Yield 53%, mp 141–142°C. IR spectrum (mineral oil), ν, $cm^{-1}$: 3360, 3250 (NH); 1720 (C=O); 1675, 1645 (C=C). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 1.69 c (3H, $CH_3$), 2.89 t (2H, $CH_2$), 3.16 d (1H, 2-H, $J$ = 1.3Hz), 3.33 s and 3.57 s (3H each, $CH_3O$), 3.53 m (2H, C$H_2$NH), 4.38 s (1H, 5-H), 6.33 d (1H, 1-H, $J$ = 1.3Hz), 7.16 m (10H, $H_{arom}$), 8.87 t (1H, $CH_2$N*H*), 10.83 s (1H, NH, indole). Found, %: C 72.88; H 6.39; N 6.20. $C_{27}H_{28}N_2O_4$. Calculated, %: C 72.97; H 6.31; N 6.31.

## REFERENCES


1. Sorokin, V.V., Kuz'min, M.V., Smirnova, N.S., Kozhevnikova, N.I., and Kriven'ko, A.P., *Zh. Org. Khim.*, 1994, vol. 30, no. 4, p. 528.
2. Sorokin, V.V., Grigor'ev, A.V., Ramazanov, A.K., and Kriven'ko, A.P., *Russ. J. Org. Chem.*, 2000, vol. 36, no. 6, p. 781.
3. Ramazanov, A.K., Sorokin, V.V., and Kriven'ko, A.P., *Khimiya i komp'yuternoe modelirovanie. Butlerovskie soobshcheniya* (Chemistry and Computer Modeling. Butlerov Reports), Saratov, 2002, no. 6, p. 79.
4. Sorokin, V.V., Kuz'min, M.V., Smirnova, N.S., Kozhevnikova, N.I., and Kriven'ko, A.P., *Khimiya i tekhnologiya furanovykh soedinenii* (Chemistry and Technology of Furan Compounds), Krasnodar, 1995, p. 15.
5. Sorokin, V.V., *Novye dostizheniya v organicheskoi khimii* (New Advances in Organic Chemistry), Kriven'ko, A.P., Ed., Saratov, 1997, p. 59.
6. Gein, V.L., Nosova, N.V., Potemkin, K.D., Aliev, Z.G., and Kriven'ko, A.P., *Russ. J. Org. Chem.*, 2005, vol. 41, no. 7, p. 1016.
7. Gein, V.L., Gein, N.V., Voronina, E.V., and Kriven'ko, A.P., *Khim.-Farm. Zh.*, 2002, vol. 36, no. 3, p. 23.
8. Grigor'eva, E.A., Kriven'ko, A.P., Sorokin, V.V., Ramazanov, A.K., and Inozemtseva, O.A., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 2004, vol. 50, no. 5, p. 131.