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Synthesis of *N*,*N*',2-Triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamides and Their Reactions with *p*-Toluidine and Hydrazine Hydrate

V. L. Gein, T. F. Odegova, A. N. Yankin, and N. V. Nosova

Perm State Pharmaceutical Academy, Ministry of Health of the Russian Federation, ul. Polevaya 2, Perm, 614990 Russia
e-mail: geinvl48@mail.ru

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Abstract—Reaction of *N*-arylacetoacetamides with aromatic aldehydes in the presence of piperidine in ethanol afforded *N*,*N*',2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamides. The latter reacted with *p*-toluidine leading to the formation of dehydration products. Reactions of *N*,*N*',2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamides with hydrazine hydrate and cyanoacetic acid hydrazide gave rise to tetrahydroindazoles. Some of the obtained compounds showed antimicrobial activity.

Keywords: cyclohexane-1,3-dicarboxamides, *p*-toluidine, hydrazine hydrate, indazoles, antimicrobial activity

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Cyclohexanones containing in their structure a hydroxy group and two alkoxycarbonyl or acyl moieties are widely used in the syntheses of functionalized carbocyclic or fused heterocyclic compounds [1].

Previously we found for the first time that the base-catalyzed reaction of acetoacetic acid amides with aromatic aldehydes furnished *N*,*N*,*N*',*N*'-tetramethyl- [2], *N*,*N*'-dimethyl- [3], *N*,*N*',2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamides; some of them were found to possess antimicrobial activity [4].

In this work, we obtained new *N*,*N*'-disubstituted 2-aryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamides **Ia**–**Ir** and studied their reactivity and antimicrobial activity. 1,3-Dicarboxamides **Ia**–**Ir** were obtained by reacting acetoacetamides with aromatic aldehydes in ethanol at room temperature in the presence of piperidine in 60–91% yield (Scheme 1).

The obtained compounds **Ia**–**Ir** were white or pale yellow crystalline solids soluble in DMF, DMSO, ethyl acetate and acetic acid, in ethyl alcohol and isopropyl alcohol with heating, and insoluble in water.

The structure of the compounds obtained was confirmed by IR, NMR spectroscopy and mass spectrometry.

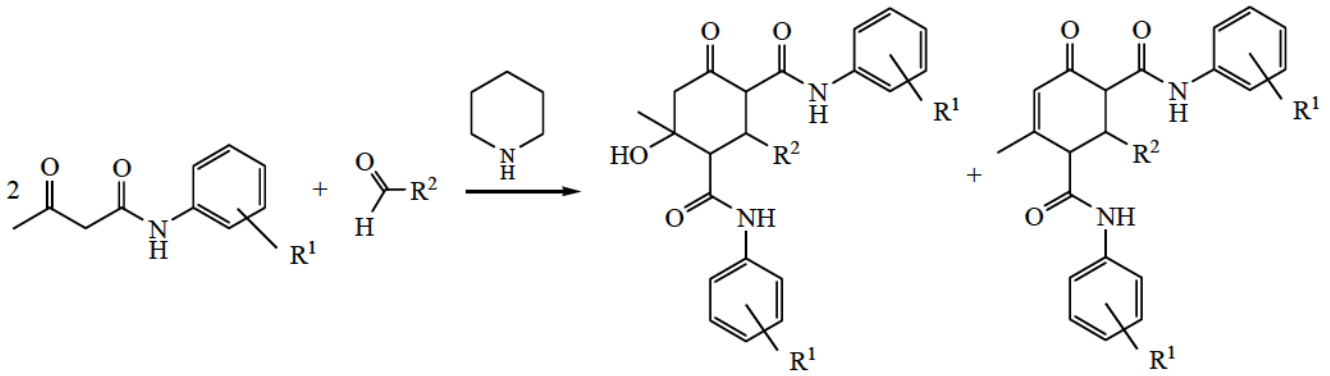
The IR spectra of **Ia**–**Ir** contained absorption bands at 3004–3340 (OH), 3384–3440, 1620–1676 (CONHAr) and 1696–1724 cm^{-1} (CO). In the ^1H NMR spectra there were the signals of aromatic (6.25–8.67 ppm) and ring protons C^6OH (5.02–5.70 ppm), C^5H_2 (*AB*-system, 2.44–2.88 and 2.66–3.19 ppm, *J* 14.0 Hz), C^2H (3.86–4.65 ppm, *J* 12.0 Hz), C^3H (3.84–3.94 ppm, *J* 12.0 Hz), C^1H (3.15–3.39 ppm, *J* 12.0 Hz), C^6CH_3 (1.29–1.40 ppm), and two singlets of NH-protons (8.80–10.02 ppm).

Mass spectrum of **Ia** contained the peaks of molecular ion $[M]^+$ (*m*/*z* 470) and fragment ions, *m*/*z*: 452 $[M - H_2O]^+$, 332 $[M - H_2O - PhNHCO]^+$, 120 $[PhNHCO]^+$, 93 $[PhNH_2]^+$. Mass spectra of other compounds **Ib**–**Ir** were similar.

In some cases, *N*,*N*',2-triaryl-6-methyl-4-oxo-5-cyclohexene-1,3-dicarboxamides **IIa**–**IIc** were isolated along with the target *N*,*N*',2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamides.

In the IR spectra of cyclohexenes **IIa**–**IIc** there were absorption bands at 3280–3384 (NH), 1716–1720 (CO) and 1632–1664 cm^{-1} (CONHAr). Along with the signals of aromatic protons, ^1H NMR spectra of compounds **IIa**–**IIc** contained the proton signals of =CH (6.05–6.08 ppm) and C^6CH_3 moieties (1.98–2.00 ppm), and no signals of hydroxy group and methylene protons C^5H_2 which confirms dehydration process.

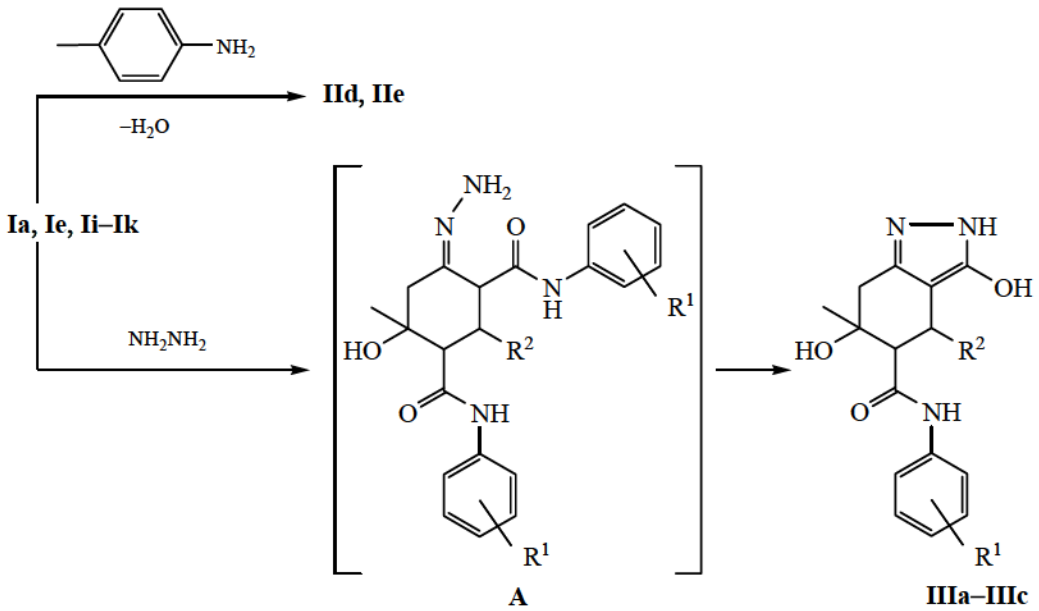
Scheme 1.



Ia–Ir **IIa–IIc**

R^1 = H, R^2 = 4-$C_2H_5C_6H_4$ (**Ia**), 4-$(CH_3)_3CC_6H_4$ (**Ib**), 2-$CH_3OC_6H_4$ (**Ic**), 2,4-$(CH_3O)_2C_6H_3$ (**Id**), 4-$(CH_3)_2NC_6H_4$ (**Ie**), 3-$NO_2C_6H_4$ (**If**, **IIa**), 4-FC_6H_4 (**Ig**, **IIb**), 2-thienyl (**Ih**, **IIc**), 3-pyridyl (**Ii**); R^1 = 2-CH_3O, R^2 = C_6H_5 (**Ij**), 4-$(CH_3)_2NC_6H_4$ (**Ik**), 2-ClC_6H_4 (**Il**), 2-thienyl (**Im**), 3-pyridyl (**In**); R^1 = 2-CH_3, R^2 = 4-$(CH_3)_2NC_6H_4$ (**Io**), 4-$(C_2H_5)_2NC_6H_4$ (**Ip**), 3-pyridyl (**Iq**); R^1 = 2-Cl, R^2 = 4-$(CH_3)_2NC_6H_4$ (**Ir**).

Scheme 2.



A **IIIa–IIIc**

R^1 = 2-CH_3O, R^2 = C_6H_5 (**IId**), 4-$(CH_3)_2NC_6H_4$ (**IIe**); R^1 = H, R^2 = 4-$C_2H_5C_6H_4$ (**IIIa**), 4-$(CH_3)_2NC_6H_4$ (**IIIb**), 3-pyridyl (**IIIc**).

The synthesized compound **Ia**–**Ir**, **IIa**–**IIc** do not react with an alcohol solution of iron(III) chloride, which together with the spectrum data indicates their existence both in solid state and in solution in the ketone form.

In order to investigate the chemical properties of **Ia**–**Ir**, we performed their reactions with *p*-toluidine, hydrazine hydrate, and cyanoacetic acid hydrazide.

Reacting compounds **Ij** and **Ik** with *p*-toluidine dehydration products **IId** and **IIe** were obtained. The reaction is apparently due to the fact that the reactivity of the carbonyl group in the position 4 of alicycle is lowered due to the influence of amide group, and *p*-toluidine acts as a base catalyst for the dehydration.

Spectral characteristics of compounds **IId** and **IIe** were similar to those for compounds **IIa**–**IIc**.

Antimicrobial activity of compounds **Ia–Ir**, **IIId**

Compound	MIC, μg mL^{-1}	
	Escherichia coli	*Staphylococcus aureus*
Ia	250	250
Ib	–	500
Ic	500	1000
Id	500	500
Ie	1000	1000
If	1000	1000
Ig	1000	1000
Ih	500	1000
Ii	1000	1000
Ij	250	1000
Ik	500	500
Il	1000	1000
Im	250	500
In	–	1000
Io	500	1000
Ip	–	1000
Iq	500	1000
Ir	1000	–
IIId	250	500
Furacilin	125	250
Dioxidine	62.5–1000	3.9–62.5

Reactions of *N*,*N*',2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamides **Ia**, **Ie**, and **Ii** (20–40% excess) with hydrazine hydrate proceeded successfully by refluxing in ethanol for 2 h in the absence of catalyst and led to the formation of *N*,4-diaryl-3,6-dihydroxy-6-methyl-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxamides **IIIa–IIIc**. Their formation occurs probably through the intermediate formation of hydrazone **A** (Scheme 2).

Indazoles **IIIa–IIIc** were colorless crystalline substances, soluble in DMSO and DMF, in ethyl alcohol and isopropyl alcohol with heating, insoluble in water.

IR spectra of indazoles **IIIa–IIIc** contained the absorption from the stretching vibrations of C^6OH (3525–3620 cm^{-1}), enol OH groups (3300–3436 cm^{-1}), NH (3260–3330 cm^{-1}), and CONH fragments (1650–1675 cm^{-1}). In the ^{1}H NMR spectra of tetrahydroindazoles **IIIa–IIIc** there were the signals of aromatic (6.92–7.45 ppm) and heterocycle protons NH and C^3OH (10.00–11.50 ppm), CH_3 (1.25–1.33 ppm) and OH groups (4.45-4.63 m. d.), C^4H and C^5H (2.52–2.60, 4.03–4.18 ppm, *J* 10.0–10.5 Hz), C^7H_2 (*AB*-system, 2.57–2.62, 2.65–2.71 ppm, *J* 16.0 Hz), and the singlet of arylamino group (9.52–9.63 ppm).

Mass spectrum of **IIIa** contained the peaks of molecular ion $[M]^+$ (*m*/*z* 392) as well as the peaks of fragment ions, *m*/*z*: 374 $[M - H_2O]^+$, 254 $[M - H_2O - PhNHCO]^+$, 93 $[PhNH_2]^+$.

Compounds **IIIa–IIIc** reacted with an alcohol solution of iron(III) chloride to produce deep cherry color. This fact along with the literature [3, 5] and spectral data indicates the enolization of the carbonyl group in the 3-position of heterocycle.

Reaction of **Ib** with cyanoacetic acid hydrazide in the presence of ammonium acetate afforded indazole **IIId**. The formation of indazole ring in this case is accompanied with the cleavage of cyanoacetyl group due to the high thermodynamic stability of *N*-unsubstituted indazole moiety, which has been observed earlier in other similar reactions [6].

Compounds **Ia–Ir** and **IIId** were tested for antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus* strains. Minimum inhibitory concentration (MIC) varied in the range from 250 to 1000 mg mL^{-1} are presented in the table. Compounds **Ia**, **Ij**, **Im**, and **IIId** showed the best results.

EXPERIMENTAL

IR spectra were recorded on a SPECORD-M80 spectrophotometer as mulls in mineral oil. ^{1}H NMR spectra of the solutions in DMSO-d_6 were taken on a Bruker DRX 500 and Bruker PLUS 300 spectrometers operating at 500.13 and 300.055 MHz, respectively, internal reference tetramethylsilane. Mass spectra were obtained on a Finnigan MAT INCOS-50 instrument (EI, 70 eV). Elemental analysis was performed on a Perkin Elmer 2400 instrument. Melting points were determined on a Melting Point M-565 apparatus.

6-Hydroxy-6-methyl-4-oxo-*N*,*N*'-diphenyl-2-(4-ethylphenyl)cyclohexane-1,3-dicarboxamide (Ia). To a solution of 0.02 mol of *N*-arylacetoacetamide in 25 mL of ethanol were added 0.01 mol of aromatic aldehyde and 2 mL of piperidine. The mixture was kept at room temperature for 1–3 days. The formed precipitate was filtered off and recrystallized from ethanol or 2-propanol. Yield 4.14 g (88%), mp 232–

233°C. IR spectrum, ν, cm^{-1}: 1668 (CONHAr), 1720 (CO), 3304 (NH), 3400 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.04 t (3H, 4-$CH_3CH_2C_6H_4$, *J* 7.5), 1.30 s (3H, CH_3), 2.45 d (1H, $C^5H_AH_B$, *J* 14.0), 2.46 q (2H, 4-CH_3CH_2 C_6H_4, *J* 7.5), 2.81 d (1H, $C^5H_AH_B$, *J* 14.0), 3.20 d (1H, C^1H, *J* 12.0), 3.90 d (1H, C^3H, *J* 12.0), 4.08 t (1H, C^2H, *J* 12.0), 5.10 s (1H, OH), 6.95–7.41 m (14H, C_6H_5, C_6H_4), 9.67 s (1H, C^1CONH), 9.69 s (1H, C^3CONH). Found, %: C 74.12; H 6.45; N 5.85. $C_{29}H_{30}N_2O_4$. Calculated, %: C 74.02; H 6.43; N 5.95.

Compound **Ib–Ir**, **IIa–IIc** were prepared similarly.

6-Hydroxy-6-methyl-4-oxo-2-(4-*tert*-butylphenyl)-*N,N'*-diphenylcyclohexane-1,3-dicarboxamide (Ib). Yield 4.43 g (89%), mp 229–230°C. IR spectrum, ν, cm^{-1}: 1672 (CONHAr), 1720 (CO), 3312 (NH), 3420 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.14 s [9H, 4-$(CH_3)_3CC_6H_4$], 1.31 s (3H, CH_3), 2.46 d (1H, $C^5H_AH_B$, *J* 14.0), 2.79 d (1H, $C^5H_AH_B$, *J* 14.0), 3.15 d (1H, C^1H, *J* 12.0), 3.94 d (1H, C^3H, *J* 12.0), 4.06 t (1H, C^2H, *J* 12.0), 5.10 s (1H, OH), 6.95–7.25 m (14H, $2C_6H_5$, C_6H_4), 9.50 s (1H, C^1CONH), 9.70 s (1H, C^3CONH). Found, %: C 74.54; H 6.85; N 5.66. $C_{31}H_{34}N_2O_4$. Calculated, %: C 74.67; H 6.87; N 5.62.

6-Hydroxy-6-methyl-2-(2-methoxyphenyl)-4-oxo-*N,N'*-diphenylcyclohexane-1,3-dicarboxamide (Ic). Yield 3.54 g (75%), mp 222–224°C. IR spectrum, ν, cm^{-1}: 1676 (CONHAr), 1696 (CO), 3312 (NH), 3416 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.32 s (3H, CH_3), 2.47 d (1H, $C^5H_AH_B$, *J* 14.0), 2.69 d (1H, $C^5H_AH_B$, *J* 14.0), 3.32 d (1H, C^1H, *J* 12.0), 3.89 s (3H, 2-$CH_3OC_6H_4$), 4.10 t (1H, C^2H, *J* 12.0), 4.47 d (1H, C^3H, *J* 12.0), 5.12 s (1H, OH), 6.67–7.42 m (14H, C_6H_5, C_6H_4), 9.57 s (1H, C^1CONH), 9.71 s (1H, C^3CONH). Found, %: C 71.35; H 5.99; N 5.88. $C_{28}H_{28}N_2O_5$. Calculated, %: C 71.17; H 5.97; N 5.93.

6-Hydroxy-6-methyl-2-(2,4-dimethoxyphenyl)-4-oxo-*N,N'*-diphenylcyclohexane-1,3-dicarboxamide (Id). Yield 3.62 g (72%), mp 201–202°C. IR spectrum, ν, cm^{-1}: 1672 (CONHAr), 1724 (CO), 3288 (NH), 3400 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.31 s (3H, CH_3), 2.45 d (1H, $C^5H_AH_B$, *J* 14.0), 2.66 d (1H, $C^5H_AH_B$, *J* 14.0), 3.16 d (1H, C^1H, *J* 12.0), 3.61 s (3H, 4-$CH_3OC_6H_4$), 3.88 s (3H, 2-$CH_3OC_6H_4$), 4.03 t (1H, C^2H, *J* 12.0), 4.42 d (1H, C^3H, *J* 12.0), 5.10 s (1H, OH), 6.25–7.44 m (13H, C_6H_5, C_6H_3), 9.57 s (1H, C^1CONH), 9.70 s (1H, C^3CONH). Found, %: C 69.50; H 6.00; N 5.64. $C_{29}H_{30}N_2O_6$. Calculated, %: C 69.31; H 6.02; N 5.57.

6-Hydroxy-6-methyl-2-(4-dimethylaminophenyl)-4-oxo-*N,N'*-diphenylcyclohexane-1,3-dicarboxamide (Ie). Yield 4.37 (90%), mp 207–208°C. IR spectrum, ν, cm^{-1}: 1656 (CONHAr), 1716 (CO), 3288 (NH), 3400 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.29 s (3H, CH_3), 2.44 d (1H, $C^5H_AH_B$, *J* 14.0), 2.76 s (6H, 4-$(CH_3)_2NC_6H_4$), 2.74 d (1H, $C^5H_AH_B$, *J* 14.0), 3.15 d (1H, C^1H, *J* 12.0), 3.84 d (1H, C^3H, *J* 12.0), 4.00 t (1H, C^2H, *J* 12.0), 5.05 s (1H, OH), 6.95–7.45 m (14H, C_6H_5, C_6H_4), 9.60 s (1H, C^1CONH), 9.65 s (1H, C^3CONH). Found, %: C 71.57; H 6.39; N 8.72. $C_{29}H_{31}N_3O_4$. Calculated, %: C 71.73; H 6.43; N 8.65.

6-Hydroxy-6-methyl-2-(3-nitrophenyl)-4-oxo-*N,N'*-diphenylcyclohexane-1,3-dicarboxamide (If). Yield 2.90 g (60%), mp 216–217°C. IR spectrum, ν, cm^{-1}: 1620 (CONHAr), 1720 (CO), 3280 (NH), 3416 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.35 s (3H, CH_3), 2.51 d (1H, $C^5H_AH_B$, *J* 14.0), 2.93 d (1H, $C^5H_AH_B$, *J* 14.0), 3.37 d (1H, C^1H, *J* 12.0), 4.04 d (1H, C^3H, *J* 12.0), 4.31 t (1H, C^2H, *J* 12.0), 5.10 s (1H, OH), 6.53–8.37 m (14H, C_6H_5, C_6H_4), 9.70 s (1H, C^1CONH), 9.80 s (1H, C^3CONH). Found, %: C 66.64; H 5.15; N 8.67. $C_{27}H_{25}N_3O_6$. Calculated, %: C 66.52; H 5.17; N 8.62.

6-Hydroxy-6-methyl-4-oxo-*N,N'*-diphenyl-2-(4-fluorophenyl)cyclohexane-1,3-dicarboxamide (Ig). Yield 2.72 g (60%), mp 232–234°C. IR spectrum, ν, cm^{-1}: 1632 (CONHAr), 1700 (CO), 3336 (NH), 3384 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.31 s (3H, CH_3), 2.48 d (1H, $C^5H_AH_B$, *J* 14.0), 2.82 d (1H, $C^5H_AH_B$, *J* 14.0), 3.22 d (1H, C^1H, *J* 12.0), 3.89 d (1H, C^3H, *J* 12.0), 4.14 t (1H, C^2H, *J* 12.0), 5.10 s (1H, OH), 6.95–7.41 m (14H, C_6H_5, C_6H_4), 9.64 s (1H, C^1CONH), 9.71 s (1H, C^3CONH). Found, %: C 70.58; H 5.49; N 6.12. $C_{27}H_{25}FN_2O_4$. Calculated, %: C 70.42; H 5.47; N 6.08.

6-Hydroxy-6-methyl-4-oxo-2-(2-thienyl)-*N,N'*-diphenylcyclohexane-1,3-dicarboxamide (Ih). Yield 2.70 g (61%), mp 209–210°C. IR spectrum, ν, cm^{-1}: 1664 (CONHAr), 1716 (CO), 3300 (NH), 3400 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.32 s (3H, CH_3), 2.47 d (1H, $C^5H_AH_B$, *J* 14.0), 2.78 d (1H, $C^5H_AH_B$, *J* 14.0), 3.19 d (1H, C^1H, *J* 12.0), 3.86 d (1H, C^3H, *J* 12.0), 4.46 t (1H, C^2H, *J* 12.0), 5.02 s (1H, OH), 6.79–7.48 m (13H, C_6H_5, thienyl), 9.83 s (1H, C^1CONH), 10.02 s (1H, C^3CONH). Found, %: C 66.85; H 5.34; N 6.38. $C_{25}H_{24}N_2O_4S$. Calculated, %: C 66.95; H 5.39; N 6.25.

6-Hydroxy-6-methyl-4-oxo-2-(3-pyridyl)-*N,N'*-diphenylcyclohexane-1,3-dicarboxamide (Ii). Yield

3.86 g (87%), mp 198–199°C. IR spectrum, ν, cm^{-1}: 1660 (CONHAr), 1700 (CO), 3320 (NH), 3420 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.33 s (3H, CH_3), 2.49 d (1H, $C^5H_AH_B$, *J* 14.0), 2.86 d (1H, $C^5H_AH_B$, *J* 14.0), 3.31 d (1H, C^1H, *J* 12.0), 3.96 d (1H, C^3H, *J* 12.0), 4.18 t (1H, C^2H, *J* 12.0), 5.20 s (1H, OH), 6.96–8.55 m (14H, C_6H_5, pyridyl), 9.20 s (1H, C^1CONH), 9.76 s (1H, C^3CONH). Found, %: C 70.58; H 5.66; N 9.52. $C_{26}H_{25}N_3O_4$. Calculated, %: C 70.41; H 5.68; N 9.47.

6-Hydroxy-6-methyl-*N*,*N*'-di-(2-methoxyphenyl)-4-oxo-2-phenylcyclohexane-1,3-dicarboxamide (Ij). Yield 4.50 g (89%), mp 218–220°C. IR spectrum, ν, cm^{-1}: 1672 (CONHAr), 1700 (CO), 3352 (NH), 3434 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.32 s (3H, CH_3), 2.48 d (1H, $C^5H_AH_B$, *J* 14.0), 2.72 d (1H, $C^5H_AH_B$, *J* 14.0), 3.28 d (1H, C^1H, *J* 12.0), 3.70 s (3H, 3-$CH_3OC_6H_3OH$), 3.75 s (3H, $CH_3OC_6H_4$), 3.91 t (1H, C^2H, *J* 12.0), 4.32 d (1H, C^3H, *J* 12.0), 5.60 s (1H, OH), 6.65–7.46 m (13H, C_6H_4, C_6H_5), 8.87 s (1H, C^1CONH), 9.22 s (1H, C^3CONH). Found, %: C 69.19; H 6.06; N 5.51. $C_{29}H_{30}N_2O_6$. Calculated, %: C 69.31; H 6.02; N 5.57.

6-Hydroxy-6-methyl-2-(4-dimethylaminophenyl)-*N*,*N*'-di(2-methoxyphenyl)-4-oxocyclohexane-1,3-dicarboxamide (Ik). Yield 4.98 (91%), mp 235–236°C. IR spectrum, ν, cm^{-1}: 1670 (CONHAr), 1720 (CO), 3312 (NH), 3400 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.29 s (3H, CH_3), 2.44 d (1H, $C^5H_AH_B$, *J* 14.0), 2.76 s [6H, 4-$(CH_3)_2NC_6H_4$], 2.74 d (1H, $C^5H_AH_B$, *J* 14.0), 3.15 d (1H, C^1H, *J* 12.0), 3.84 d (1H, C^3H, *J* 12.0), 4.00 t (1H, C^2H, *J* 12.0), 5.05 s (1H, OH), 6.95–7.45 m (14H, C_6H_5, C_6H_4), 9.60 s (1H, C^1CONH), 9.65 s (1H, C^3CONH). Found, %: C 68.37; H 6.51; N 7.74. $C_{31}H_{35}N_3O_6$. Calculated, %: C 68.24; H 6.47; N 7.70.

6-Hydroxy-6-methyl-*N*,*N*'-di-(2-methoxyphenyl)-4-oxo-2-(2-chlorophenyl)cyclohexane-1,3-dicarboxamide (Il). Yield 4.20 g (78%), mp 216–218°C. IR spectrum, ν, cm^{-1}: 1664 (CONHAr), 1716 (CO), 3280 (NH), 3420 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.34 s (3H, CH_3), 2.88 d (1H, $C^5H_AH_B$, *J* 14.0), 3.18 d (1H, C^1H, *J* 12.0), 3.19 d (1H, $C^5H_AH_B$, *J* 14.0), 3.75 s (3H, $CH_3OC_6H_4$), 3.81 s (3H, $CH_3OC_6H_4$), 4.35 d (1H, C^3H, *J* 12.0), 4.65 t (1H, C^2H, *J* 12.0), 5.05 s (1H, OH), 6.75–7.88 m (12H, C_6H_4), 8.80 s (1H, C^1CONH), 9.45 s (1H, C^3CONH). Found, %: C 64.71; H 5.48; N 5.18. $C_{29}H_{29}ClN_2O_6$. Calculated, %: C 64.86; H 5.44; N 5.22.

6-Hydroxy-6-methyl-*N*,*N*'-di-(2-methoxyphenyl)-4-oxo-2-(2-thienyl)cyclohexane-1,3-dicarboxamide (Im). Yield 4.23 g (82%), mp 219–220°C. IR spectrum, ν, cm^{-1}: 1660 (CONHAr), 1700 (CO), 3320 (NH), 3440 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.33 s (3H, CH_3), 2.45 d (1H, $C^5H_AH_B$, *J* 14.0), 2.79 d (1H, $C^5H_AH_B$, *J* 14.0), 3.22 d (1H, C^1H, *J* 12.0), 3.79 s (3H, $CH_3OC_6H_4$), 3.82 s (3H, $CH_3OC_6H_4$), 4.26 t (1H, C^2H, *J* 12.0), 4.31 d (1H, C^3H, *J* 12.0), 5.60 s (1H, OH), 6.81–8.00 m (11H, C_6H_4, thienyl), 9.06 s (1H, C^1CONH), 9.37 s (1H, C^3CONH). Found, %: C 63.88; H 5.59; N 5.58. $C_{27}H_{28}N_2O_6S$. Calculated, %: C 63.76; H 5.55; N 5.51.

6-Hydroxy-6-methyl-*N*,*N*'-di-(2-methoxyphenyl)-4-oxo-2-(3-pyridyl)cyclohexane-1,3-dicarboxamide (In). Yield 4.43 g (87%), mp 209-210°C. IR spectrum, ν, cm^{-1}: 1656 (CONHAr), 1720 (CO), 3320 (NH), 3420 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.35 s (3H, CH_3), 2.48 d (1H, $C^5H_AH_B$, *J* 14.0), 2.84 d (1H, $C^5H_AH_B$, *J* 14.0), 3.36 d (1H, C^1H, *J*12.0), 3.75 s (3H, $CH_3OC_6H_4$), 3.81 s (3H, $CH_3OC_6H_4$), 3.98 t (1H, C^2H, *J* 12.0), 4.38 d (1H, C^3H, *J* 12.0), 5.70 s (1H, OH), 6.93–8.50 m (12H, C_6H_4, pyridyl), 9.04 s (1H, C^1CONH), 9.41 s (1H, C^3CONH). Found, %: C 66.63; H 5.76; N 8.42. $C_{28}H_{29}N_3O_6$. Calculated, %: C 66.79; H 5.80; N 8.34.

6-Hydroxy-6-methyl-*N*,*N*'-di-(2-methylphenyl)-2-(4-dimethylaminophenyl)-4-oxocyclohexane-1,3-dicarboxamide (Io). Yield 4.17 g (81%), mp 208–209°C. IR spectrum, ν, cm^{-1}: 1664 (CONHAr), 1716 (CO), 3300 (NH), 3400 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.37 s (3H, CH_3), 1.83 s (3H, $CH_3C_6H_4$), 1.84 s (3H, $CH_3C_6H_4$), 2.46 d (1H, $C^5H_AH_B$, *J* 14.0), 2.79 d (1H, $C^5H_AH_B$, *J* 14.0), 2.82 s [6H, 4-$(CH_3)_2$·NC_6H_4], 3.22 d (1H, C^1H, *J* 12.0), 3.90 t (1H, C^2H, *J* 12.0), 3.97 d (1H, C^3H, *J* 12.0), 5.20 s (1H, OH), 6.60–7.20 m (12H, C_6H_4), 9.00 s (1H, C^1CONH), 9.24 s (1H, C^3CONH). Found, %: C 72.35; H 6.84; N 8.24. $C_{31}H_{35}N_3O_4$. Calculated, %: C 72.49; H 6.87; N 8.18.

6-Hydroxy-6-methyl-*N*,*N*'-di-(2-methylphenyl)-4-oxo-2-(4-diethyl aminophenyl)cyclohexane-1,3-dicarboxamide (Ip). Yield 4.55 (84%), mp 205–206°C. IR spectrum, ν, cm^{-1}: 1672 (CONHAr), 1720 (CO), 3320 (NH), 3420 (OH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.03 t (3H, 4-$CH_3CH_2NC_6H_4$, *J* 7.0), 1.36 s (3H, CH_3), 1.82 s (3H, $CH_3C_6H_4$), 1.84 s (3H, $CH_3C_6H_4$), 2.45 d (1H, $C^5H_AH_B$, *J* 14.0), 2.77 d (1H, $C^5H_AH_B$, *J* 14.0), 3.20 d (1H, C^1H, *J* 12.0), 3.27 q (2H, 4-$CH_3CH_2NC_6H_4$, *J* 7.0), 3.86 t (1H, C^2H, *J* 12.0), 3.94 d (1H, C^3H, *J* 12.0), 5.10 s (1H, OH), 6.50–7.20 m (12H, C_6H_4), 9.03 s (1H, C^1CONH), 9.26 s (1H, C^3CONH).

Found, %: C 73.26; H 7.30; N 7.83. $C_{33}H_{39}N_3O_4$. Calculated, %: C 73.17; H 7.26; N 7.76.

6-Hydroxy-6-methyl-*N,N'*-di-(2-methylphenyl)-4-oxo-2-(3-pyridyl)cyclohexane-1,3-dicarboxamide (Iq). Yield 3.73 g (79%), mp 226–227°C. IR spectrum, ν, cm^{-1}: 1672 (CONHAr), 1720 (CO), 3340 (NH), 3420 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.40 s (3H, CH_3), 1.78 s (3H, $CH_3C_6H_4$), 1.79 s (3H, $CH_3C_6H_4$), 2.53 d (1H, $C^5H_AH_B$, *J* 14.0), 2.88 d (1H, $C^5H_AH_B$, *J* 14.0), 3.39 d (1H, C^1H, *J* 12.0), 4.05 d (1H, C^3H, *J* 12.0), 4.08 t (1H, C^2H, *J* 12.0), 5.30 s (1H, OH), 6.80–8.67 m (12H, C_6H_4, pyridyl), 9.17 s (1H, C^1CONH), 9.38 s (1H, C^3CONH). Found, %: C 71.18; H 6.23; N 8.79. $C_{28}H_{29}N_3O_4$. Calculated, %: C 71.32; H 6.20; N 8.91.

6-Hydroxy-6-methyl-4-oxo-2-(3-pyridyl)-*N,N'*-di-(2-chlorophenyl) cyclohexane-1,3-dicarboxamide (Ir). Yield 4.61 (90%), mp 196–197°C. IR spectrum, ν, cm^{-1}: 1660 (CONHAr), 1716 (CO), 3304 (NH), 3440 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.37 s (3H, CH_3), 2.46 d (1H, $C^5H_AH_B$, *J* 14.0), 2.81 s [6H, 4-$(CH_3)_2$·NC_6H_4], 2.85 d (1H, $C^5H_AH_B$, *J* 14.0), 3.23 d (1H, C^1H, *J* 12.0), 3.89 t (1H, C^2H, *J* 12.0), 4.22 d (1H, C^3H, *J* 12.0), 5.20 s (1H, OH), 6.56–7.20 m (12H, C_6H_4), 9.21 s (1H, C^1CONH), 9.52 s (1H, C^3CONH). Found, %: C 63.52; H 4.78; N 5.41. $C_{27}H_{24}Cl_2N_2O_4$. Calculated, %: C 63.41; H 4.73; N 5.48.

6-Methyl-2-(3-nitrophenyl)-4-oxo-*N,N'*-diphenyl-5-cyclohexene-1.3-dicarboximide (IIa). Yield 1.20 g (26%), mp 216–217°C. IR spectrum, ν, cm^{-1}: 1636 (CONHAr), 1716 (CO), 3280 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.01 s (3H, CH_3), 3.20 d (1H, C^1H, *J* 12.0), 3.73 d (1H, C^3H, *J* 12.0), 4.23 t (1H, C^2H, *J* 12.0), 6.18 s (1H, =CH), 6.53–8.37 m (14H, C_6H_5, C_6H_4), 10.00 s (1H, C^1CONH), 10.10 s (1H, C^3CONH). Found, %: C 69.21; H 4.98; N 8.89. $C_{27}H_{23}N_3O_5$. Calculated, %: C 69.07; H 4.94; N 8.95.

6-Methyl-4-oxo-*N,N'*-diphenyl-2-(4-fluorophenyl)-5-cyclohexene-1.3-dicarboximide (IIb). Yield 1.12 g (25%), mp 230–231°C. IR spectrum, ν, cm^{-1}: 1632 (CONHAr), 1716 (CO), 3384 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.98 s (3H, CH_3), 3.22 d (1H, C^1H, *J* 12.0), 3.82 d (1H, C^3H, *J* 12.0), 4.10 t (1H, C^2H, *J* 12.0), 6.13 s (1H, =CH), 6.95–7.41 m (14H, C_6H_5, C_6H_4), 9.89 s (1H, C^1CONH), 10.01 s (1H, C^3CONH). Found, %: C 73.14; H 5.27; N 6.40. $C_{27}H_{23}FN_2O_3$. Calculated, %: C 73.29; H 5.24; N 6.33.

6-Methyl-4-oxo-2-(2-thienyl)-*N,N'*-diphenyl-5-cyclohexen-1,3-dicarboxamide (IIc). Yield 1.06 g (24%), mp 209–210°C. IR spectrum, ν, cm^{-1}: 1664 (CONHAr), 1720 (CO), 3320 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.98 s (3H, CH_3), 3.15 d (1H, C^1H, *J* 12.0), 4.11 d (1H, C^3H, *J* 12.0), 4.34 t (1H, C^2H, *J* 12.0), 6.13 s (1H, =CH), 6.79–7.48 m (13H, C_6H_5, thienyl), 10.19 s (1H, C^1CONH), 10.28 s (1H, C^3CONH). Found, %: C 69.93; H 5.21; N 6.44. $C_{25}H_{22}N_2O_3S$. Calculated, %: C 69.75; H 5.15; N 6.51.

6-Methyl-*N,N'*-di-(2-methoxyphenyl)-4-oxo-2-phenyl-5-cyclohexene-1.3-dicarboximide (IId). A mixture of 0.005 mol ***N,N'*-2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamide and 0.005 mol of *p*-toluidine in 30 mL of acetic acid was refluxed for 3 h, and then cooled. The formed crystals were filtered off and washed with ethanol. Yield 1.36 g (56%), mp 193–194°C. IR spectrum, ν, cm^{-1}: 1672 (CONHAr), 1700 (CO), 3352 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.00 s (3H, CH_3), 3.32 d (1H, C^1H, *J* 12.0), 3.69 s (3H, $CH_3OC_6H_4$), 3.76 s (3H, $CH_3OC_6H_4$), 3.96 t (1H, C^2H, *J* 12.0), 4.13 d (1H, C^3H, *J* 12.0), 6.08 s (1H, =CH), 6.76–7.80 m (13H, C_6H_4, C_6H_5), 9.09 s (1H, C^1CONH), 9.26 s (1H, C^3CONH). Found, %: C 71.71; H 5.86; N 5.69. $C_{29}H_{28}N_2O_5$. Calculated, %: C 71.88; H 5.82; N 5.78.

6-Methyl-2-(4-dimethylaminophenyl)-*N,N'*-di-(2-methoxyphenyl)-4-oxo-5-cyclohexene-1,3-dicarboxamide (IIe) was prepared similarly. Yield 1.61 g (61%), mp 213–214°C. IR spectrum, ν, cm^{-1}: 1676 (CONHAr), 1720 (CO), 3320 (NH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.98 s (3H, CH_3), 2.78 s [6H, 4-$(CH_3)_2NC_6H_4$], 3.32 d (1H, C^1H, *J* 12.0), 3.69 s (3H, $CH_3OC_6H_4$), 3.77 s (3H, $CH_3OC_6H_4$), 3.86 t (1H, C^2H, *J* 12.0), 4.05 d (1H, C^3H, *J* 12.0), 6.05 s (1H, =CH), 6.54–7.89 m (12H, $3C_6H_4$), 9.03 s (1H, C^1CONH), 9.21 s (1H, C^3CONH). Found, %: C 70.41; H 6.26; N 8.02. $C_{31}H_{33}N_3O_5$. Calculated, %: C 70.57; H 6.30; N 7.96.

3,6-Dihydroxy-6-methyl-*N*-phenyl-4-(4-ethylphenyl)-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxamide (IIIa). A 20–40% excess of hydrazine hydrate was added dropwise to a solution of 0.005 mol of ***N,N'*-2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamide in 25 mL of ethanol. The reaction mixture was refluxed for 2 h, and then cooled. The formed crystals were filtered off and recrystallized from ethanol. Yield 1.46 g (74%), mp 252–254°C. IR spectrum, ν, cm^{-1}: 1660 (CONHAr), 3260 (NH), 3400 (=COH), 3575 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.11 t (3H, 4-$CH_3CH_2C_6H_4$, *J* 7.5), 1.25 s (3H,

CH_3), 2.52 q (2H, 4-$CH_3\underline{CH_2}C_6H_4$, *J* 7.5), 2.54 d (1H, C^5H, *J* 10.0), 2.59 d (1H, $C^7\underline{H_A}H_B$, *J* 16.0), 2.66 d (1H, $C^7H_A\underline{H_B}$, *J* 16.0), 4.11 d (1H, C^4H, *J* 10.0), 4.50 s (1H, OH), 7.00–7.42 m (9H, C_6H_5, C_6H_4), 9.56 s (1H, C^1CONH), 10.20–11.50 br.s (2H, NH, OH). Found, %: C 70.39; H 6.48; N 10.66. $C_{23}H_{25}N_3O_3$. Calculated, %: C 70.57; H 6.44; N 10.73.

Compound **IIIb**, **IIIc** were prepared similarly.

3,6-Dihydroxy-6-methyl-4-(4-dimethylaminophenyl)-*N*-phenyl-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxamide (IIIb). Yield 1.46 g (72%), mp 214–216°C. IR spectrum, ν, cm^{-1}: 1675 (CONHAr), 3330 (NH), 3436 (=COH), 3525 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 s (3H, CH_3), 2.52 d (1H, C^5H, *J* 10.0), 2.57 d (1H, $C^7\underline{H_A}H_B$, *J* 16.0), 2.65 d (1H, $C^7H_A\underline{H_B}$, *J* 16.0), 2.80 s [6H, 4-$(\underline{CH_3})_2NC_6H_4$], 4.03 d (1H, C^4H, *J* 10.0), 4.45 s (1H, OH), 6.92–7.45 m (9H, C_6H_5, C_6H_4), 9.58 s (1H, C^1CONH), 10.20–11.50 br.s (2H, NH, OH). Found, %: C 67.79; H 6.40; N 13.86. $C_{23}H_{26}N_4O_3$. Calculated, %: C 67.96; H 6.45; N 13.78.

3,6-Dihydroxy-6-methyl-4-(3-pyridyl)-*N*-phenyl-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxamide (IIIc). Yield 1.26 g (69%), mp 304–305°C. IR spectrum, ν, cm^{-1}: 1660 (CONHAr), 3300 (NH), 3425 (=COH), 3620 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.33 s (3H, CH_3), 2.60 d (1H, C^5H, *J* 10.5), 2.62 d (1H, $C^7\underline{H_A}H_B$, *J* 16.0), 2.71 d (1H, $C^7H_A\underline{H_B}$, *J* 16.0), 4.18 d (1H, C^4H, *J* 10.5), 4.63 s (1H, OH), 6.99–8.34 m (9H, C_6H_5, pyridyl), 9.63 s (1H, C^1CONH), 10.00–11.00 br.s (2H, NH, OH). Found, %: C 65.76; H 5.59; N 15.27. $C_{20}H_{20}N_4O_3$. Calculated, %: C 65.92; H 5.53; N 15.37.

3,6-Dihydroxy-6-methyl-4-(4-*tert*-butylphenyl)-*N*-phenyl-4,5,6,7-tetrahydro-2*H*-indazole-5-carboxamide (IIId). A mixture of 0.005 mol of *N*,*N*′-2-triaryl-6-hydroxy-6-methyl-4-oxocyclohexane-1,3-dicarboxamide, 0.005 mol of cyanoacetic acid hydrazide, and 0.005 mol of ammonium acetate was heated at 210–220°C until gas evolution completed. The resulting gummy product was treated with ethanol. The precipitated crystals were filtered off and washed with a mixture EtOH–EtOAc (3 : 1). Yield 0.92 g (44%), mp 178–180°C. IR spectrum, ν, cm^{-1}: 1644 (CONHAr), 2968 (NH), 3300 (=COH), 3648 (OH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.21 s [9H, 4-$(\underline{CH_3})_3CC_6H_4$), 1.26 s (3H, CH_3), 2.52 d (1H, C^5H, *J* 10.0), 2.59 d (1H, $C^7\underline{H_A}H_B$, *J* 16.0), 2.65 d (1H, $C^7H_A\underline{H_B}$, *J* 16.0), 4.11 d (1H, C^4H, *J* 10.0), 4.51 s (1H, OH), 7.01–7.39 m (14H, C_6H_5, C_6H_4), 9.52 s (1H, C^1CONH), 10.00–11.50 br.s (2H, NH, OH). Found, %: C 71.72; H 6.91; N 10.10. $C_{25}H_{29}N_3O_3$. Calculated, %: C 71.58; H 6.97; N 10.02.

Testing for antimicrobial activity was performed by the method of successive serial dilutions of meat-peptone broth at bacterial load of 250 000 microbial units per 1 mL of the solution. Minimum inhibitory concentration (MIC) was taken as an acting dose. Dioxidine and furacilin were used as references.

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