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Synthesis of 1*H*-Pyrazolo[3,4-*c*]isoquinolin-1-ones by the Condensation of Cyclohexanone Derivatives with 3-Amino-1-phenyl-1*H*-pyrazol-5(4*H*)-one

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Abstract—The synthesis of 1*H*-pyrazolo[3,4-*c*]isoquinolin-1-ones was carried out by reacting 3-aryl(heteryl)-2,4-diacetyl-5-hydroxy-5-methylcyclohexanones with 3-amino-1-phenyl-1*H*-pyrazol-5(4*H*)-one. The structure of the 7-acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-2-phenyl-6-(fur-2-yl)-1*H*-pyrazolo[3,4-*c*]isoquinolin-1-one obtained was proved by X-ray diffraction analysis.

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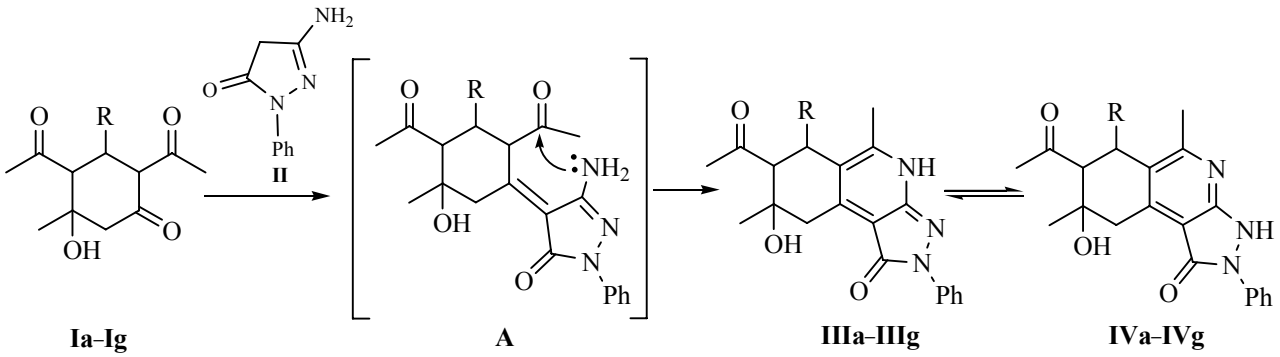
On the basis of tetrahydroisoquinoline a series of compounds used in medicine as drugs has been synthesized [1, 2]. Besides, the isoquinoline framework is a part of many alkaloids exhibiting pharmacological effect [3–5]. In turn, among the pyrazoloizoquinolines some kinase inhibitors were identified, which were taken as the base to develop drugs for the treatment of osteoarthritis, rheumatoid arthritis and asthma [6]. Therefore, the development of the methods of synthesis and production of new compounds of this class is relevant and promising in terms of finding new biologically active substances.

In the present study, we investigated a reaction of 3-aryl(heteryl)-2,4-diacetyl-5-hydroxy-5-methylcyclohexanones (**Ia–Ig**) with 3-amino-1-phenyl-1*H*-pyrazol-5*H*-one (**II**). We found that at reflux in the presence of sodium ethoxide a formation occurs of new derivatives of the tricyclic system 6-aryl(heteryl)-7-acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-2-phenyl-1*H*-pyrazolo[3,4-*c*]isoquinolin-1-ones (**IIIa–IIIg**), apparently as a result of intramolecular cyclization of intermediates (**A**).

Structure of compounds obtained is confirmed by spectral studies (see Experimental). However, unambiguous choice between the prototropic tautomers **III** and **IV** was impossible. Therefore, the structure of 7-acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-2-phenyl-6-(fur-2-yl)-1*H*-pyrazolo[3,4-*c*]isoquinolin-1-one **IIIf** was studied by the X-ray diffraction analysis (see the figure and Tables 1, 2).



Ia–Ig **A** **IIIa–IIIg**

I, III, IV, R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-EtC_6H_4 (**c**), 3-MeOC_6H_4 (**d**), 3-pyridyl (**e**), 2-furyl (**f**), 5-methylfur-2-yl (**g**).

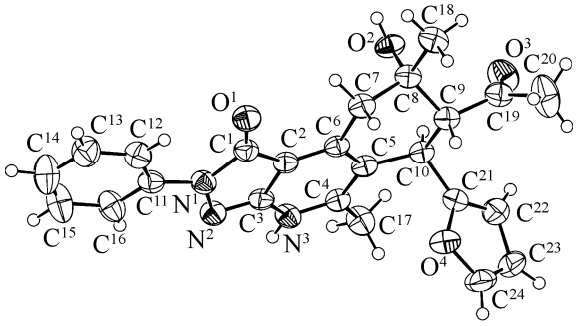
Table 1. Bond lengths (*d*, Å) in structure **IIIf**

Bond	*d*	Bond	*d*
O^1–C^1	1.255(3)	C^6–C^7	1.498(4)
O^2–C^8	1.439(3)	C^7–C^8	1.519(4)
O^3–C^{19}	1.213(4)	C^8–C^{18}	1.520(4)
O^4–C^{21}	1.371(3)	C^8–C^9	1.541(4)
O^4–C^{24}	1.372(4)	C^9–C^{19}	1.524(4)
N^1–C^1	1.402(4)	C^9–C^{10}	1.541(4)
N^1–C^{11}	1.411(4)	C^{10}–C^{21}	1.504(4)
N^1–N^2	1.423(3)	C^{11}–C^{16}	1.383(4)
N^2–C^3	1.311(4)	C^{11}–C^{12}	1.396(4)
N^3–C^4	1.353(4)	C^{12}–C^{13}	1.375(4)
N^3–C^3	1.370(4)	C^{13}–C^{14}	1.370(5)
C^1–C^2	1.437(4)	C^{14}–C^{15}	1.384(5)
C^2–C^6	1.378(4)	C^{15}–C^{16}	1.378(5)
C^2–C^3	1.410(4)	C^{19}–C^{20}	1.500(4)
C^4–C^5	1.401(4)	C^{21}–C^{22}	1.331(4)
C^4–C^{17}	1.498(4)	C^{22}–C^{23}	1.426(5)
C^5–C^6	1.419(4)	C^{23}–C^{24}	1.333(5)
C^5–C^{10}	1.521(4)		

Table 2. Bond angles (ω, deg) in the structure **IIIf**

Angle	ω	Angle	ω
$C^{21}O^4C^{24}$	106.0(3)	$C^7C^8C^{18}$	110.1(2)
$C^1N^1C^{11}$	129.4(3)	$O^2C^8C^9$	106.6(2)
$C^1N^1N^2$	113.0(3)	$C^7C^8C^9$	108.0(3)
$C^{11}N^1N^2$	116.6(3)	$C^{18}C^8C^9$	112.5(3)
$C^3N^2N^1$	102.2(2)	$C^{19}C^9C^8$	113.3(3)
$C^4N^3C^3$	121.3(3)	$C^{19}C^9C^{10}$	110.5(3)
$O^1C^1N^1$	125.1(3)	$C^8C^9C^{10}$	111.9(2)
$O^1C^1C^2$	130.9(3)	$C^{21}C^{10}C^5$	112.2(2)
$N^1C^1C^2$	104.1(3)	$C^{21}C^{10}C^9$	108.6(2)
$C^6C^2C^3$	121.3(3)	$C^5C^{10}C^9$	113.9(2)
$C^6C^2C^1$	134.3(3)	$C^{16}C^{11}C^{12}$	118.9(3)
$C^3C^2C^1$	104.4(3)	$C^{16}C^{11}N^1$	120.0(3)
$N^2C^3N^3$	125.0(3)	$C^{12}C^{11}N^1$	121.1(3)
$N^2C^3C^2$	116.2(3)	$C^{13}C^{12}C^{11}$	119.5(3)
$N^3C^3C^2$	118.7(3)	$C^{14}C^{13}C^{12}$	121.6(4)
$N^3C^4C^5$	121.1(3)	$C^{13}C^{14}C^{15}$	118.8(4)
$N^3C^4C^{17}$	114.3(3)	$C^{16}C^{15}C^{14}$	120.4(4)
$C^5C^4C^{17}$	124.5(3)	$C^{15}C^{16}C^{11}$	120.6(4)
$C^4C^5C^6$	118.8(3)	$O^3C^{19}C^{20}$	120.0(3)
$C^4C^5C^{10}$	119.8(3)	$O^3C^{19}C^9$	121.3(3)
$C^6C^5C^{10}$	121.4(3)	$C^{20}C^{19}C^9$	118.7(3)
$C^2C^6C^5$	118.6(3)	$C^{22}C^{21}O^4$	110.0(3)
$C^2C^6C^7$	120.6(3)	$C^{22}C^{21}C^{10}$	134.3(3)
$C^5C^6C^7$	120.8(3)	$O^4C^{21}C^{10}$	115.6(3)
$C^6C^7C^8$	114.3(2)	$C^{21}C^{22}C^{23}$	107.3(3)
$O^2C^8C^7$	109.3(2)	$C^{24}C^{23}C^{22}$	106.1(3)
$O^2C^8C^{18}$	110.3(2)	$C^{23}C^{24}O^4$	110.6(3)

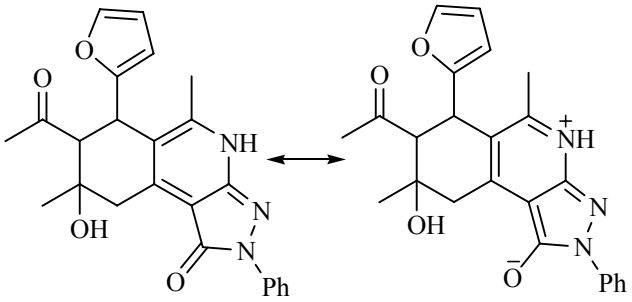
The molecule **IIIf** has three chiral centers, the atoms C^8, C^9 and C^{10}, with relative configuration (*S*,R*,R**). The cyclohexene ring conformation is a distorted *sofa*. The fragment $C^9C^{10}C^5C^6C^7$ is almost flat [the torsion angles $C^9C^{10}C^5C^6$ and $C^{10}C^5C^6C^7$ are 4.0(4)° and 6.2(4)°, respectively], the C^8 atom is deviated from this plane by 0.697(4) Å. Hydroxy group has the axial orientation [the torsion angle $C^6C^7C^8O^2$ is 63.5(3)°], and the methyl group C^{18} and acetyl are in equatorial positions [the torsion angles $C^6C^7C^8C^{18}$ and $C^7C^8C^9C^{19}$ are –175.2(3)° and –171.9(2)°, respectively]. This leads to an appearance of a shortened intramolecular contact $H^{18b}\cdots C^{19}$ 2.66 Å (sum of the van der Waals radii is 2.87 Å [7]). Furyl group is so oriented that the C^{21}–O^4 bond has *ap*-orientation relative to the $C^{10}H^{10}$ (torsion angle $O^4C^{21}C^{10}H^{10}$ is –158°). The nitrogen atom N^1 has a slightly non-planar configuration [the deviation of the N^1 atom from the plane of the atoms bound to it is –0.080(3) Å]. The phenyl substituent is somewhat turned relative to the plane of the bicyclic fragment



Structure of compound **IIIf** by the data of XRD analysis. Thermal ellipsoids of nonhydrogen atoms are shown at 50% probability.

[the torsion angle $C^1N^1C^{11}C^{12}$ is –15.6(5)°]. This orientation of the substituent is stabilized by the formation of an additional intramolecular hydrogen bond $C^{12}–H^{12}\cdots O^1$ (H···O 2.32 Å, C–H···O 122°) and a shotened attractive contact $N^2\cdots H^{16}$ 2.39 Å (the sum of the van der Waals radii is 2.66 Å [7]), which cannot be classified as a hydrogen bond because the $C^{16}–H^{16}\cdots N^2$ angle is too small, 102°.

In the molecule a lengthening of the $C^1–O^1$ bond [1.255(3) Å] is observed to the value characteristic of carboxy groups (1.25 Å [8]) indicating the localization of a significant negative charge on the carbonyl group. The positive charge is apparently delocalized over the pyridine ring, as evidenced by the leveling of the C–C bonds in it (bond lengths are in the range 1.378(4)–1.419(4) Å, while the average values of double and single bond lengths are 1.35 and 1.455 Å, respectively [8]). On this basis, we can assume a significant contribution of zwitterionic resonance structure into the molecular structure of **IIIf**.



Such a redistribution of electron density is stabilized by the formation of intermolecular hydrogen bonds $O^2–H^2\cdots O^{1i}$ [*i*: 1 – *x* , 1 – *y*, –*z*] (H···O 1.93 Å, OH···O 173°) and $N^3–H^3\cdots O^{2ii}$ [*ii*: 1 – *x*, –1/2 + *y*, 1/2 – *z*] (H···O 2.06 Å, NH···O 167°). Due to these hydrogen bonds the molecules in the crystal form layers parallel to the [001] plane. Also, in the crystal a series of weak CH···O, CH···N, and CH···π bonds is formed: $C^{17}–H^{17}\cdots O^{1iii}$ [*iii*: *x*, 1/2–*y*, 1/2+*z*], (H···O 2.54 Å, CH .... O 161°), $C^{24}–H^{24}\cdots O^{3iv}$ [*iv*: *x*, –1+*y*, *z*], (H···O 2.50 Å, CH···O 152°), $C^{10}–H^{10}\cdots N^{2v}$ [*v*: 1 – *x*, 1/2 + *y*, 1/2 – *z*], (H···N 2.50 Å, CH···N 166°), $C^9–H^9\cdots C^{12vi}$ [*vi*: 1 – *x*, –*y*, –*z*] (H···C 2.78 Å, CH···C 170°) and $C^{13}–H^{13}\cdots C^{24vi}$ (H···C 2.83 Å, CH···C 142°).

EXPERIMENTAL

Crystals of compound **IIIf** are monoclinic, $C_{24}H_{23}N_3O_4$, at 298 K *a* = 15.802(3) Å, *b* = 8.1219(10) Å, *c* = 17.147(3) Å, β = 111.761(18), *V* = 2043.9(5) Å^3, M_r = 417.45, *Z* = 4, space group $P2_1/c$, d_{calc} = 1.357 g cm^{-3}, μ(MoK_α) = 0.094 mm^{-1}, *F*(000) = 880. The unit cell parameters and intensities of 19292 reflections (3588 independent, R_{int} = 0.065) were measured on an automatic four-circle diffractometer Xcalibur 3 (MK_α, graphite monochromator, CCD detector, ω-scanning, 2θ max = 50°).

The structure was solved by direct method with a SHELX-97 software [9]. The positions of the hydrogen atoms were calculated geometrically and refined using *rider* model with $U_{iso} = nU_{eq}$ of a carrier atom (*n* = 1.5 for CH_3 and OH groups and *n* = 1.2 for the other hydrogen atoms). The structure was refined with respect to F^2 by a full-matrix least-squares method in the anisotropic approximation for nonhydrogen atoms to wR_2 = 0.182 for 3588 reflections [R_1 = 0.066 for 2109 reflections with $F > 4\sigma(F)$, *S* = 0.99]. The final atomic coordinates are listed in Table 1, bond lengths and angles, in Tables 1 and 2, respectively.

The IR spectra of the synthesized compounds were recorded on a Pelkin Elmer SPECTRUM ONE FTIR-spectrometer from the mulls in mineral oil. The ^{1}H NMR spectra were recorded on a Bruker AVANCE 400 instrument, solvent DMSO-d_6, internal reference TMS. The mass spectra were recorded on a Crommas GC/MS-Hewlett-Packard 5890/5972 spectrometer, column HP-5 MS (70 eV), from a solution in CH_2Cl_2 (compound **IIIg**) and MX-1321 (70 eV) spectrometer with direct inlet of the substance to the ion source (other compounds). Melting points were determined on a Koeffler block. Monitoring the progress of the reaction and the purity of compounds obtained was carried out by TLC on Silufol UV-254 plates, eluent acetone-hexane mixture, 3:5, developers iodine vapor and UV radiation.

3-Aryl(heteryl)-2,4-diacetyl-5-hydroxy-5-methylcyclohexanones **Ia–Ig** were obtained by the known procedure [10].

2,4-Diacetyl-5-hydroxy-5-methyl-3-(3-methoxyphenyl)cyclohexanone (Id). Yield 2.5 g (87%), white powder, mp 107–110°C. IR spectrum, ν, cm^{-1}: 3415 (OH), 1717, 1696 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.17 s (3H, Me), 1.91 s (3H, Me), 1.92 s (3H, Me), 2.33 d (1H, C^6 H, ^2J 13.72 Hz) , 2.91 d (1H, C^6H, ^2J 13.72 Hz), 3.28 d (1H, C^4H, *J* 12.0 Hz), 3.71 s (3H, MeO), 3.95 t (1H, C^3H, *J* 12.0 Hz), 8.4 d (1H, C^2H, *J* 12.0 Hz), 5.21 br.s (1H, OH), 6.73 d (1H, H_{arom}, *J* 8.0 Hz), 6.86 d (1H, H_{arom}, *J* 7.6 Hz), 7.18 m (1H, H_{arom}, *J* 8.0 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 300 (0.6)

$[M - H_2O]^+$, 257 (27.8) $[M - CH_3CO - H_2O]^+$, 215 (22.2), 43 (100) $[CH_3C=O]^+$. Found, %: C 67.79; H 6.83. $C_{18}H_{22}O_5$. Calculated, %: C 67.91; H 6.97.

2,4-Diacetyl-5-hydroxy-5-methyl-3-(4-ethylphenyl)cyclohexanone (Ic). Yield 2.0 g (90%), white powder, mp 135–138°C. IR spectrum, ν, cm^{-1}: 3437 (OH), 1720, 1695 (C=O). ^1H NMR spectrum, δ, ppm: 1.14 m (3H, Me, *J* 7.6 Hz), 1.16 s (3H, Me), 1.88 s (3H, Me), 1.89 s (3H, Me), 2.33 d (1H, C^6 H, ^2J 13.7 Hz), 2.53 q (2H, CH_2, *J* 7.6 Hz), 2.91 d (1H, C^6 H, ^2J 13.7 Hz), 3.26 d (1H, C^4H, *J* 12.0 Hz), 3.91 t (1H, C^3H, *J* 12.0 Hz), 4.4 d (1H, C^2H, *J* 12.0 Hz), 5.20 br.s (1H, OH), 07.09 d (2H, H_{arom}, *J* 7.92 Hz), 7.22 d (2H, H_{arom}, *J* 7.92 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 298 (0.3) $[M - H_2O]^+$, 255 (32.8) $[M - CH_3CO - H_2O]^+$, 213 (22.2), 43 (100) $[CH_3C=O]^+$. Found, %: C 72.01; H 7.55. $C_{19}H_{24}O_4$. Calculated, %: C 72.13; H 7.65.

7-Acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-2,6-diphenyl-1*H*-pyrazolo[3,4-*c*]isoquinolin-1-one (IIIa). To a suspension of 2 g (7 mmol) of cyclohexanone (**Ia**) in 30 ml of anhydrous ethanol was added 1.23 g (7 mmol) of pyrazole **II** and a solution of 0.16 g (7 mmol) of sodium in 5 ml of anhydrous ethanol. The reaction mixture was refluxed for 1 h and then cooled. The resulting precipitate was filtered off and washed with ethanol. Yield 2.55 g (85%), red powder, mp 260°C. IR spectrum, ν, cm^{-1}: 3421 (OH), 3057 (NH), 1714 (C=O), 1673 (NC=O). ^1H NMR spectrum, δ, ppm: 1.25 s (3H, Me), 1.93 s (3H, Me), 2.12 s (3H, Me), 2.93 d (1H, C^7H, *J* 10.4 Hz), 3.18 d (1H, C^9H, ^2J 18.0 Hz), 3.65 d (1H, C^9H, ^2J 18.0 Hz), 4.50 d (1H, C^6H, *J* 10.4 Hz), 4.76 br.s (1H, OH), 7.04 d (2H, H_{arom}, *J* 7.2 Hz), 7.18–7.27 m (4H, H_{arom}), 7.45 t (2H, H_{arom}, *J* 7.6 Hz), 7.96 m (2H, H_{arom}). The NH proton signal is not observed, apparently due to rapid deuterium exchange. Mass spectrum, *m*/*z* (I_{rel}, %): 427 (21.6) $[M]^+$, 366 (100) $[M - CH_3CO - H_2O]^+$, 290 (25.1) 235 (4.2) 178 (3.3), 105 (2.7), 43 (18.7) $[CH_3C=O]^+$. Found, %: C 73.00; H 5.79; N 9.75. $C_{26}H_{25}N_3O_3$. Calculated, %: C 73.05; H 5.89; N 9.83.

7-Acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-6-(*p*-tolyl)-2-phenyl-1*H*-pyrazolo[3,4-*c*]isoquinolin-1-one (IIIb) was prepared analogously to compound **IIIa** using cyclohexanone **Ib**. Yield 2.4 g (78%), red powder, mp 265–270°C. IR spectrum, ν, cm^{-1}: 3372 (OH), 3105 (NH), 1686 (C=O). ^1H NMR spectrum, δ, ppm: 1.24 s (3H, Me), 1.94 s (3H, Me), 2.13 s (3H, Me), 2.24 (3H, Me), 2.90 d (1H, C^7 N, *J* 10.0 Hz), 3.17 d (1H, C^9H, ^2J 17.6 Hz), 3.64 d (1H, C^9H, ^2J 17.6 Hz), 4.45 d (1H, C^6H, *J* 10.0 Hz), 4.75 br.s (1H, OH), 6.92 d (2H, H_{arom}, *J* 7.2 Hz), 6.7 d (2H, H_{arom}, *J* 7.6 Hz), 7.20 d (1H, H_{arom}, *J* 6.8 Hz), 7.46 t (2H , H_{arom}, *J* 7.2 Hz), 7.97 m (2H, H_{arom}), 11.24 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 441 (9.5) $[M]^+$, 380 (100) $[M - CH_3CO - H_2O]^+$, 290 (5.2), 235 (4.4) 193 (3.6), 105 (2.1), 43 (14.6) $[CH_3C=O]^+$. Found, %: C 73.38; H 6.01; N 9.40. $C_{27}H_{27}N_3O_3$. Calculated, %: C 73.45; H 6.16; N 9.52.

7-Acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-2-phenyl-6-(4-ethylphenyl)-1*H*-pyrazolo-[3,4-*c*] isoquinolin-1-one (IIIc) was prepared analogously to compound **IIIa** with an appropriate cyclohexanone derivative **Ic**. Yield 2.8 g (88%), red powder, mp 265–270°C. IR spectrum, ν, cm^{-1}: 3430 (OH), 2921 (NH), 1701 (C=O). ^1H NMR spectrum, δ, ppm: 1.14 m (3H, Me, *J* 7.5 Hz), 1.21 s (3H, Me), 1.84 s (3H, Me), 2.12 s (3H, Me), 2.54 q (2H, CH_2, *J* 7.5 Hz), 2.83 d (1H, C^7H, *J* 9.8 Hz), 3.7 d (1H, C^9H, ^2J 17.7 Hz), 3.60 d (1H, C^9H, ^2J 17.7 Hz), 4.39 d (1H, C^6H, *J* 9.8 Hz), 4.60 br.s (1H, OH), 6.93 d (2H, H_{arom}, *J* 7.6 Hz), 7.7 m (3H, H_{arom}), 7.36–7.40 m (2H, H_{arom}), 8.11 d (2H, H_{arom}, *J* 6.8 Hz). The NH proton signal is not observed, apparently due to rapid deuterium exchange. Mass spectrum, *m*/*z* (I_{rel}, %): 455 (17.5) $[M]^+$, 394 (100) $[M - CH_3CO - H_2O]^+$, 290 (15.4), 206 (8.2) 119 (7.6), 43 (27) $[CH_3C=O]^+$, 31 (76). Found, %: C 73.69; H 6.30; N 9.15. $C_{28}H_{29}N_3O_3$. Calculated, %: C 73.82; H 6.42; N 9.22.

7-Acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-6-(3-methoxyphenyl)-2-phenyl-1*H*-pyrazolo-[3,4-*c*] isoquinolin-1-one (IIId) is obtained similarly to compound **IIIa** with an appropriate cyclohexanone derivative **Id**. Yield 2.7 g (84%), red powder, mp 242–245°C. IR spectrum, ν, cm^{-1}: 3415 (OH), 3235 (NH), 1717, 1655 (C=O). ^1H NMR spectrum, δ, ppm: 1.25 s (3H, Me), 1.97 s (3H, Me), 2.14 s (3H, Me), 2.93 d (1H, C^7H, *J* 10.0 Hz), 3.18 d (1H, C^9H, ^2J 18.1 Hz), 3.64 d (1H, C^9H, ^2J 18.1 Hz), 3.67 s (3H, OMe), 4.47 d (1H, C^6H, *J* 10.0 Hz), 4.74 br.s (1H, OH), 6.60 m (2H, H_{arom}), 6.76 d (1H, H_{arom}, *J* 7.7 Hz), 7.16–7.19 m (2H, H_{arom}), 7.44 t (2H, H_{arom}, *J* 7.2 Hz), 7.97 d (2H, H_{arom}, *J* 6.1 Hz). The NH proton signal is not observed, apparently due to rapid deuterium exchange. Mass spectrum, *m*/*z* (I_{rel}, %): 457 (21) $[M]^+$, 396 (100) $[M - CH_3CO - H_2O]^+$, 326 (12.1), 290 (15.5) 202 (10.0), 133 (8.4), 77 (38.9) $[Ph]^+$, 43 (14.6) $[CH_3C=O]^+$. Found, %: C 70.42; H 5.81; N 9.05. $C_{27}H_{27}N_3O_4$. Calculated, %: C 70.88; H 5.95; N 9.18.

7-Acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-6-(pyridin-3-yl)-2-phenyl-1*H*-pyrazolo[3,4-*c*]-isoquinolin-1-one (IIIe) was prepared analogously to compound **IIIa** with an appropriate cyclohexanone derivative **Ie**. Yield 2.6 g (87%), red powder, mp 245–248°C. IR spectrum, ν, cm^{-1}: 3435 (OH), 2923 (NH), 1707, 1659 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.26 s (3H, Me), 1.94 s (3H, Me), 2.18 s (3H, Me), 2.95 d (1H, C^7 H, *J* 10.0 Hz), 3.24 d (1H, C^9H, ^2J 18.1 Hz), 3.66 d (1H, C^9H, ^2J 18.1 Hz), 4.59 d (1H, C^6H, *J* 10.0 Hz), 4.88 br.s (1H, OH), 7.18–7.29 m (2H, H_{arom}), 7.44–7.48 m (3H, H_{arom}), 7.96 d (2H, H_{arom}, *J* 5.2 Hz), 8.35 s (1H, H_{arom}) , 8.41 d (1H, H_{arom}, *J* 3.6 Hz), 11.49 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 428 (19.7) $[M]^+$, 367 (100) $[M - CH_3CO - H_2O]^+$, 290 (18.5) 248 (11.3) 180 (2.5), 93 (11.1) 43 (70.1) $[CH_3C{=}O]^+$. Found, %: C 79.89; H 5.54; N 12.87. $C_{25}H_{24}N_4O_3$. Calculated, %: C 70.08; H 5.65; N 13.08.

7-Acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-2-phenyl-6-(fur-2-yl)-1*H*-pyrazolo[3,4-*c*]isoquinolin-1-one (IIIf) was prepared analogously to compound **IIIa** with an appropriate cyclohexanone derivative **If**. Yield 2.4 g (82%), red powder, mp. 230–232°C. IR spectrum, ν, cm^{-1}: 3438 (OH), 2927 (NH), 1719, 1661 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.25 s (3H, Me), 2.12 s (3H, Me), 2.20 (3H, Me), 3.08 d (1H, C^7H, *J* 8.4 Hz); 3.15 d (1H, C^9H, ^2J 18.4 Hz), 3.54 d (1H, C^9H, ^2J 18.4 Hz), 4.64 d (1H, C^6H, *J* 8.4 Hz), 4.91 br.s (1H, OH), 6.05 d (1H, furan C^3H, *J* 2.8 Hz), 6.35 d.d (1H, C^4H furan, *J* 2.38 Hz), 7.20 t (1H, H_{Ph}, *J* 7.2 Hz), 7.45 m (2H, H_{Ph}, *J* 7.6 Hz), 7.52 d (1H, C^5H furan, *J* 1.21 Hz), 7.96 d (2H, H_{Ph}, *J* 7.6 Hz), 11.21 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 417 (11.6) $[M]^+$, 356 (100) $[M - CH_3CO - H_2O]^+$, 328 (3.0), 265 (1.7) 209 (1.0), 93 (1.0), 43 (16.3) $[CH_3C{=}O]^+$. Found, %: C 68.89; H 5.44; N 9.87. $C_{24}H_{23}N_3O_4$. Calculated, %: C 69.05; H 5.55; N 10.07.

7-Acetyl-2,4,6,7,8,9-hexahydro-8-hydroxy-5,8-dimethyl-6-(5-methylfur-2-yl)-2-phenyl-1*H*-pyrazolo-[3,4-*c*] isoquinolin-1-one (IIIg) was prepared like the compound **IIIa** with an appropriate cyclohexanone derivative **Ig**. Yield 2.6 g (86%), red powder, mp 230–233°C. IR spectrum, ν, cm^{-1}: 3430 (OH), 2967 (NH), 1725, 1660 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.25 s (3H, Me), 2.16 s (3H, Me), 2.17 s (3H, Me), 2.22 s (3H, Me), 3.08 d (1H, C^7H, *J* 8.1 Hz), 3.11 d (1H, C^9H, ^2J 18.0 Hz), 3.53 d (1H, C^9H, ^2J 18.0 Hz), 4.56 d (1H, C^6 H, *J* 8.1 Hz), 4.88 br.s (1H, OH), 5.87 d (1H, C^4H furan *J* 2.7 Hz), 5.93 d (1H, furan C^3H, *J* 2.7 Hz), 7.19 t (1H, H_{Ph}, *J* 7.3 Hz), 7.45 m (2H, H_{Ph}, *J* 7.7 Hz), 7.96 d (2H , H_{Ph}, *J* 6.6 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 432 $[M + 1]^+$. Found, %: C 69.49; H 5.69; N 9.61. $C_{25}H_{25}N_3O_4$. Calculated, %: C 69.59; H 5.84; N 9.74.

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