ISSN 1070-4280, Russian Journal of Organic Chemistry, 2006, Vol. 42, No. 7, pp. 1015–1021. © Pleiades Publishing, Inc., 2006.
Original Russian Text © V.V. Lipson, M.G. Shirobokova, O.V. Shishkin, S.V. Shishkina, 2006, published in Zhurnal Organicheskoi Khimii, 2006, Vol. 42, No. 7, pp. 1034–1039.

Synthesis of Partially Hydrogenated Pyrazolo[3,4-*b*]quinolinones by Condensation of 3-Amino-5-methylpyrazole with Aromatic Aldehydes and Dimedone

V. V. Lipson[a], M. G. Shirobokova[a], O. V. Shishkin[b], and S. V. Shishkina[b]

[a] *Danilevskii Institute of Endocrinic Pathology Problems, Academy of Medical Sciences of Ukraine, ul. Artema 10, Kharkiv, 61002 Ukraine*
e-mail: lipson@ukr.net

[b] *State Scientific Enterprise Research and Technology Association "Institute of Single Crystals," National Academy of Sciences of Ukraine*

Received September 7, 2005

Abstract—Cyclocondensation of 3-amino-5-methylpyrazole with 2-arylmethylidene-5,5-dimethylcyclohexane-1,3-diones or 9-aryl-3,3,6,6-tetramethyl-2,3,4,5,6,7,8,9-octahydro-1*H*-xanthene-1,8-diones, as well as with synthetic precursors of the latter (*para*-substituted benzaldehydes and dimedone), in dimethylformamide or methanol gives the corresponding 4-aryl-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-ones. The structure of 4-(4-methoxyphenyl)-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one was proved by the X-ray diffraction data.

DOI: 10.1134/S1070428006070141

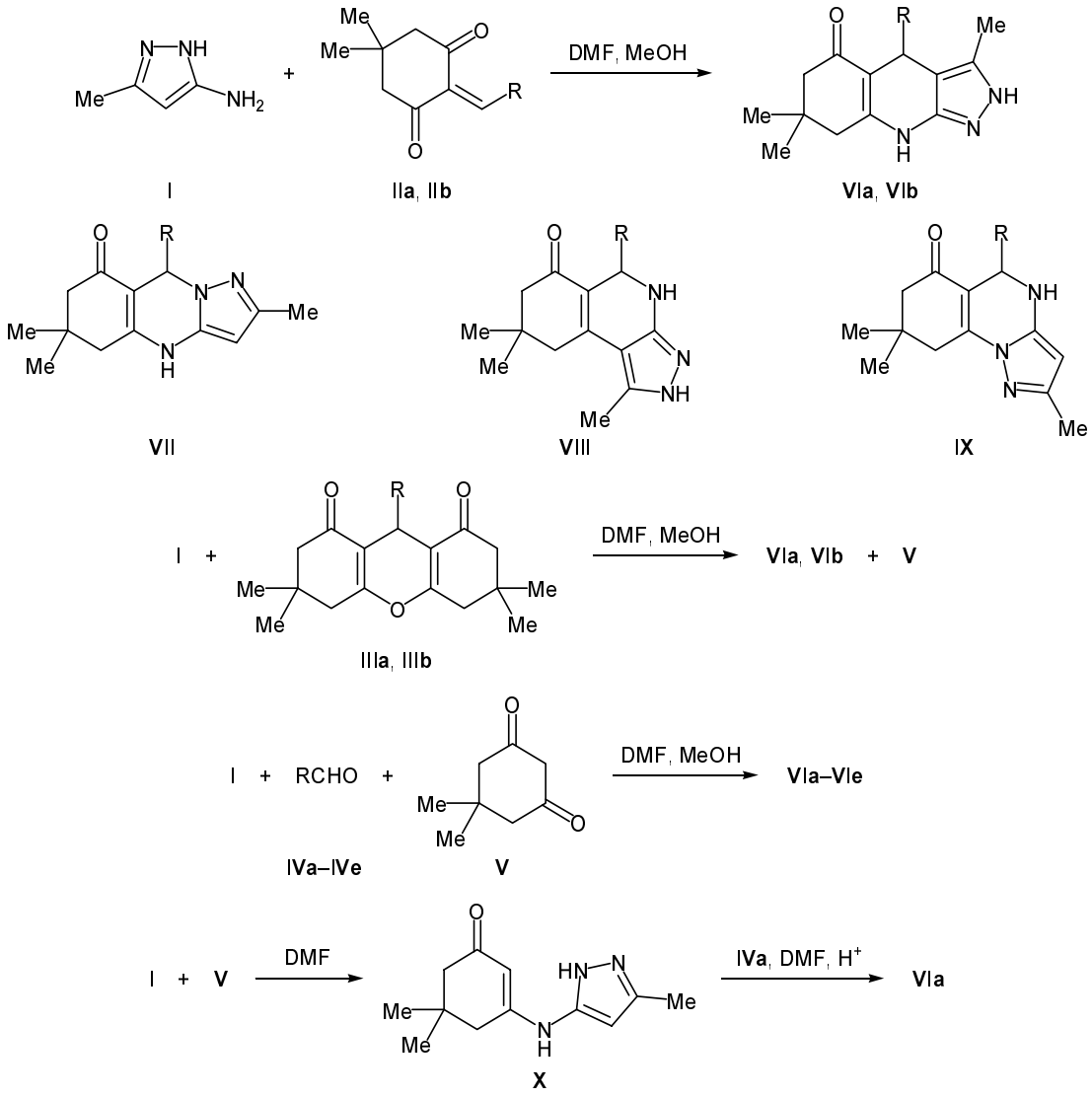
Fused heterocyclic systems containing a 1,4-dihydropyridine or pyrimidine fragment attract interest due to their structural analogy to the known calcium channel modulators which have been used over the last two decades in medical practice as effective vasodilators and antihypertensive agents [1, 2]. Partially hydrogenated azolopyrimidines and quinazolines synthesized by cyclocondensation of 3-amino-1,2,4-triazoles [3–10], 2-aminobenzimidazole [11–14], and 5-substituted 3-aminopyrazoles [15–19] with α,β-unsaturated ketones, their synthetic precursors and equivalents [20], Mannich base hydrochlorides [21, 22], and derivatives of oxo [23–28] and unsaturated aromatic acids [29–34] were reported previously. Some of the cyclocondensation products were shown to exhibit cardiovascular [23, 24], neurotropic [12], analgetic [7, 34], and antiphlogistic [34] activity.

The goal of the present work was to determine the reaction direction of 3-amino-5-methylpyrazole (**I**) with 2-arylmethylidene-5,5-dimethylcyclohexane-1,3-diones **IIa** and **IIb**, 9-aryl-3,3,6,6-tetramethyl-2,3,4,5,6,7,8,9-octahydro-1*H*-xanthene-1,8-diones **IIIa** and **IIIb**, and synthetic precursors of the latter, *para*-substituted benzaldehydes **IVa**–**IVe** and dimedone (**V**), under different conditions.

By heating equimolar amounts of amine **I** and arylmethylidene derivatives **IIa** and **IIb** in DMF for 15–20 min or in methanol for 1 h we obtained 4-aryl-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]-quinolin-5-ones **VIa** and **VIb**, respectively, in high yield (Scheme 1). According to the TLC data, compounds **VIa**–**VIe** were the only products formed in the three-component condensations of amine **I** with *para*-substituted benzaldehydes **IVa**–**IVe** and dimedone (**V**). Likewise, the reaction of enaminoketone **X** with benzaldehyde **IVa** in the presence of a catalytic amount of an acid gave compound **VIa**. In the condensation of 3-amino-5-methylpyrazole (**I**) with xanthenediones **IIIa** and **IIIb** as bielectrophile component we isolated the corresponding pyrazoloquinolinones **VIa** and **VIb** together with dimedone (**V**). Taking into account nonequivalence of the endocyclic reaction centers (N^2 and C^4) in the aminopyrazole molecule and different electrophilic properties of unsaturated carbonyl compounds **IIa**, **IIb** and **IIIa**, **IIIb**, the reactions under study could give rise to four isomeric products **VI**–**IX**. Nevertheless, no alternative products **VII**–**IX** were detected.

Compounds **VIa**–**VIe** were identified by spectral and analytical methods, and the structure of pyrazolo-

Scheme 1.



II–IV, **VI**, R = Ph (**a**), 4-ClC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-$Me_2NC_6H_4$ (**d**), 4-$O_2NC_6H_4$ (**e**).

quinolinone **VIc** was proved by the X-ray diffraction data (Tables 1, 2; see figure). The IR spectra of **VIa**–**VIe** contained carbonyl absorption bands in the region 1580–1588 cm^{-1} and a broad band at 2650–3400 cm^{-1}, the latter originating from superposition of bands belonging to stretching vibrations of the N–H and methylene and methyl C–H bonds. However, the IR data did not allow us to distinguish between possible isomers **VI**–**IX**. Derivatives of the quinoline (**VI**, **VIII**) and quinazoline series (**VII**, **IX**) may be identified by analysis of the ^1H NMR spectra. The isolated products showed in the ^1H NMR spectra signals from aromatic protons, *AB* systems from two methylene fragments, and singlets from CH_3 protons. The presence of a singlet from 4-H and signals from two NH protons and the absence of signal from pyrazole CH proton may be regarded as evidences in favor of structures **VI** and **VIII**. The choice between the latter was made on the basis of the results of NOE experiment for compound **VIa**. Irradiation at a frequency corresponding to resonance of the 3-CH_3 protons (δ 1.89 ppm) gave a response on the NH proton in the pyrazole ring (δ 11.70 ppm), *ortho*-protons in the benzene ring, and CH proton in the dihydropyridine ring (δ 4.89 ppm), which appear spatially close to the 3-CH_3 group in structure **VI**. Therefore, compound **VIa** was assigned the structure of pyrazolo[3,4-*b*]quinolin-5-one existing in DMSO as N^2H tautomer.

Unambiguous proofs for the product structure were obtained by X-ray analysis of a single crystal of com-

pound **VIc** (see figure; Tables 1, 2). The 1,4-dihydropyridine ring in pyrazolo[3,4-*b*]quinolin-5-one **VIc** adopts a *sofa* conformation with the following puckering parameters: $S = 0.28$, $\theta = 62.2$, $\psi = 3.9°$ [35]. The C^6 atom deviates by –0.29 Å from the mean-square plane formed by the other atoms of the dihydropyridine ring. The cyclohexene ring also has a *sofa* conformation (puckering parameters: $S = 0.70$, $\theta = 38.9$, $\psi = 0.6°$) with the C^2 atom deviating by –0.65 Å from the mean-square plane passing through the other ring atoms. One methyl group at C^2 occupies axial position, and the other is equatorial: the torsion angles $C^{10}C^1C^2C^{12}$ and $C^{10}C^1C^2C^{11}$ are equal to 69.3(2) and –170.9(2)°, respectively. The methoxyphenyl substituent on C^6 is disordered by two positions (*A* and *B*) with a population ratio of 60:40. These positions are characterized by different torsion angles $C^{10}C^5C^6C^{14}$ [–98.1(3) (*A*) and 115.4(5)° (*B*)] and $C^5C^6C^{14}C^{15}$ [–52.2(7) (*A*) and –44.0(1)° (*B*)].

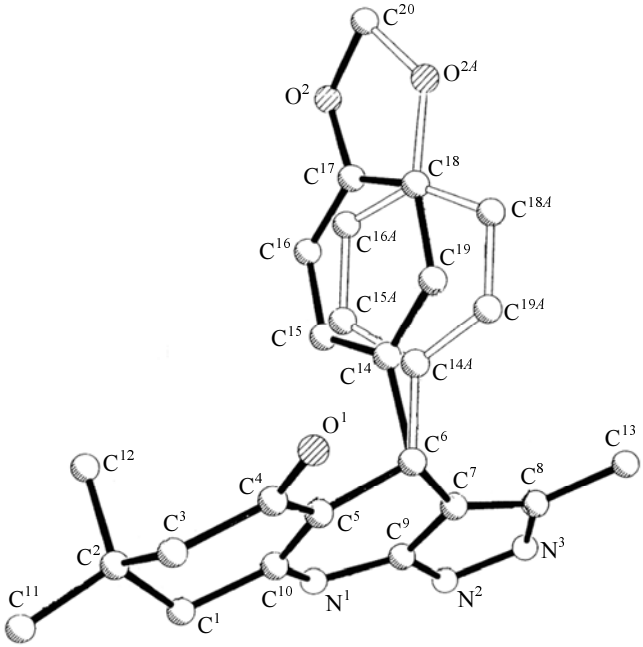
Shortened intramolecular contacts $H^{13A}\cdots C^{19B}$ 2.77, $H^{12C}\cdots C^4$ 2.76, $H^{12C}\cdots C^5$ 2.84, and $H^{12C}\cdots C^{10}$ 2.80 Å (the sum of the corresponding van der Waals radii is 2.87 Å [36]) were found in molecule **VIc**. Molecules **VIc** in crystal give rise to pleated layers via intermolecular hydrogen bonds $N^3–H^{3N}\cdots O^{1'}$ ($-x - 0.5$, $y + 0.5$, $-z + 0.5$), (H···O 2.01 Å, ∠NHO 165.0°) and $N^1–H^{1N}\cdots N^{2'}$ ($-x - 1$, $-y + 1$, $-z$), (H···N 2.10 Å, ∠NHN 153.6°). As a result, the $O^1–C^4$ bond extends to 1.238(2) Å against standard value 1.210 Å [37], the $C^5–C^{10}$ bond extends to 1.369(3) Å, (1.330), and $C^5–C^6$, to 1.528(3) Å (1.507).

The structure of compounds **VIa**–**VIe** implies that amine **I** reacts with compounds **II** and **III** in a way different from that observed by us previously in its reactions with α,β-unsaturated ketones [16, 17] and arylmethylidenecycloalkanones [6]. In the latter cases, electrophilic attack by the β-carbon atom of unsaturated ketone was directed at the endocyclic nitrogen atom in molecule **I** to form dihydropyrimidine rather than dihydropiridine ring. The formation of quinolinones **VI** in the reaction of **I** with arylmethylidenecyclohexanediones **IIa** and **IIb** involves attack by the β-carbon atom in **II** on C^4, and the carbonyl carbon atom reacts with the amino group of **I**.

It is known that dimedone (**V**) reacts with benzaldehydes to give arylmethylidene derivatives **II** together with xanthenediones **III** [38, 39]. The latter may undergo retro condensation. Taking into account that the above reactions give identical products, one could presume that these processes are not independent but include intermediate formation of α,β-unsaturated diketones **II**. In fact, TLC analysis of the reaction mixture obtained from benzaldehyde (**IVa**) and dimedone (**V**) in DMF revealed the presence of both benzylidene

Table 1. Bond lengths in the molecule of 4-(4-methoxyphenyl)-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo-[3,4-*b*]quinolin-5-one (**VIc**)

Bond	*d*, Å	Bond	*d*, Å
$N^1–C^{10}$	1.367(2)	$N^1–C^9$	1.392(2)
$N^2–C^9$	1.329(2)	$N^2–N^3$	1.370(2)
$C^1–C^{10}$	1.509(3)	$C^1–C^2$	1.530(3)
$C^2–C^3$	1.532(3)	$C^2–C^{11}$	1.536(3)
$C^2–C^{12}$	1.538(3)	$C^3–C^4$	1.510(3)
$C^4–C^5$	1.448(3)	$C^5–C^{10}$	1.370(3)
$C^5–C^6$	1.528(3)	$C^6–C^{14B}$	1.502(5)
$C^6–C^7$	1.517(3)	$C^6–C^{14A}$	1.530(4)
$C^7–C^8$	1.380(3)	$C^7–C^9$	1.400(3)
$C^8–C^{13}$	1.495(3)	$O^{2A}–C^{20}$	1.356(4)
$O^{2A}–C^{17A}$	1.372(5)	$C^{14A}–C^{15A}$	1.434(7)
$C^{14A}–C^{19A}$	1.442(6)	$C^{15A}–C^{16A}$	1.375(5)
$C^{16A}–C^{17A}$	1.413(5)	$C^{17A}–C^{18A}$	1.347(5)
$C^{18A}–C^{19A}$	1.455(3)	$O^{2B}–C^{20}$	1.406(6)
$C^{14B}–C^{15B}$	1.320(1)	$C^{14B}–C^{19B}$	1.330(1)
$C^{15B}–C^{16B}$	1.440(1)	$C^{18B}–C^{19B}$	1.370(8)



Structure of the molecule of 4-(4-methoxyphenyl)-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one (**VIc**) according to the X-ray diffraction data.

Table 2. Bond angles in the molecule of 4-(4-methoxyphenyl)-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one (**VIc**)

Angle	ω, deg	Angle	ω, deg
$C^{10}N^1C^9$	118.1(2)	$C^9N^2N^3$	102.7(2)
$C^8N^3N^2$	112.9(2)	$C^{10}C^1C^2$	113.4(2)
$C^1C^2C^3$	107.2(2)	$C^1C^2C^{11}$	108.9(2)
$C^3C^2C^{11}$	111.4(2)	$C^1C^2C^{12}$	110.9(2)
$C^3C^2C^{12}$	109.6(2)	$C^{11}C^2C^{12}$	108.8(2)
$O^1C^4C^3$	119.3(2)	$C^5C^4C^3$	118.8(2)
$C^{10}C^5C^4$	119.4(2)	$C^{10}C^6C^6$	123.5(2)
$C^4C^5C^6$	117.1(2)	$C^{14B}C^6C^7$	115.1(5)
$C^{14B}C^6C^5$	120.6(5)	$C^7C^6C^5$	107.7(1)
$C^7C^6C^{14A}$	108.7(3)	$C^{19A}C^{14A}C^6$	123.4(5)
$C^5C^6C^{14A}$	108.6(3)	$C^8C^7C^9$	103.8(2)
$C^8C^7C^6$	134.5(2)	$C^9C^7C^6$	103.8(2)
$C^{12}C^7C^8$	118.5(2)	$C^{12}C^7C^3$	118.8(2)
$N^3C^8C^7$	106.9(2)	$N^3C^8C^{13}$	121.4(2)
$C^7C^8C^{13}$	131.7(2)	$N^2C^9N^1$	123.6(2)
$N^2C^9C^7$	113.7(2)	$N^1C^9C^7$	122.7(2)
$N^1C^{10}C^5$	122.5(2)	$N^1C^{10}C^1$	114.6(2)
$C^5C^{10}C^1$	122.9(2)	$C^{20}O^{2A}C^{17A}$	116.1(3)
$C^{15A}C^{14A}C^{19A}$	111.1(4)	$C^{15A}C^{14A}C^6$	125.5(4)
$C^{15A}C^{16A}C^{17A}$	121.0(4)	$C^{18A}C^{17A}C^{16A}$	121.8(4)
$C^{17A}C^{18A}C^{19A}$	115.6(3)	$C^{14B}C^{19B}C^{18B}$	120.0(7)
$C^{15B}C^{14B}C^{19B}$	125.6(6)	$C^{15B}C^{14B}C^6$	113.6(7)
$C^{19B}C^{14B}C^6$	120.8(7)	$C^{14B}C^{15B}C^{16B}$	116.0(7)

derivative **IIa** and xanthenedione **IIIa**. On the other hand, no new compounds were formed on prolonged heating of **IIIa** in DMF. These data suggest that the reaction of aminopyrazole **I** with xanthenediones **III** occurs directly, i.e., without preliminary decomposition of compound **III** into unsaturated diketones **II** and dimedone (**V**).

Presumably, the first stage in the heterocyclization with xanthenediones **III** is attack by the exocyclic amino group of aminoazole **I** on one electrophilic center in the α-position with respect to the bridging oxygen atom in **III**. As a result, the pyran ring is opened, and dimedone molecule is released. Closure of the dihydropyridine ring occurs via interaction between C^4 in **I** and electrophilic carbon atom in the β-position, leading to pyrazoloquinolinones **VI**. Three-component condensations of aminopyrazole **I** with aldehydes **IV** and diketone **V** may follow both mechanisms, as indicated by the presence of the enone and xanthenedione simultaneously in the reaction mixture. However, we cannot rule out alternative heterocyclization paths, e.g., through initial formation of enaminoketone **X** and its subsequent reaction with aldehyde.

To check the possibility for the latter path, we synthesized compound **X** by heating dimedone (**V**) with amine **I** in boiling DMF. The structure of **X** was confirmed by spectral data. Its IR spectrum characteristically contained absorption bands due to stretching vibrations of the carbonyl and associated NH groups. In the ^{1}H NMR spectrum of **X**, signals from the methyl and methylene protons, singlets from two NH groups, and signals from the CH= protons in the pyrazole ring and enone fragments were present, in keeping with the assumed structure.

Enaminoketone **X** was heated with benzaldehyde (**IVa**) in boiling DMF in the absence and in the presence of a catalytic amount of hydrochloric acid. Pyrazoloquinolinone **VIa** was isolated only from the reaction mixture containing HCl. According to the TLC data ($CHCl_3$–MeOH, 10 : 1), compound **X** in DMF in the presence of acid undergoes decomposition into initial amine **I** and dimedone (**V**). Provided that benzaldehyde (**IVa**) is present in the reaction mixture, its condensation with dimedone gives arylmethylidene derivative **IIa** or xanthenedione **IIIa**, and the process then follows one of the mechanisms described above. Thus our experimental data indicate that the formation of pyrazoloquinolinones **VI** through intermediate enaminoketone **X** is improbable.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Specord M-82 spectrometer. The ^{1}H NMR spectra were measured from solutions in DMSO-d_6 on a Bruker DRX-500 instrument using TMS as internal reference. Thin-layer chromatography was performed on Kieselgel 60 F_{254} plates (Merck). The melting points were determined on a Kofler melting point apparatus.

2-Arylmethylidene-5,5-dimethylcyclohexane-1,3-diones **IIa** and **IIb** were synthesized by the procedure described in [38]. 9-Aryl-3,3,6,6-tetramethyl-2,3,4,5,-6,7,8,9-octahydro-1*H*-xanthene-1,8-diones **IIIa** and **IIIb** were reported in [39].

4-Aryl-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-ones VIa–VIe (*general procedure*). *a.* A mixture of 1 mmol of 3-amino-5-methylpyrazole (**I**) and 1 mmol of 2-arylmethylidene-5,5-dimethylcyclohexane-1,3-dione **IIa** or **IIb** in 1 ml of

DMF was heated for 15–20 min under reflux. The mixture was cooled and diluted with 5–7 ml of propan-2-ol, and the precipitate was filtered off and recrystallized from DMF–propan-2-ol, 1:2.

3,7,7-Trimethyl-4-phenyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one (VIa). Yield 61%, mp 295–296°C. IR spectrum, ν, cm^{-1}: 3350–2650 (NH), 1584 (CO), 1556 (C=N). ^1H NMR spectrum, δ, ppm: 0.94 s and 1.00 s (3H each, 7- CH_3), 1.89 s (3H, 3-CH_3), 1.94 d and 2.12 d (1H each, 6-H_A, 8-H_A, J_{AB} = –16.5 Hz), 2.40 d (2H, 6-H_B, 8-H_B, J_{AB} = –11.1 Hz),* 4.92 s (1H, 4-H), 7.02–7.10 m (5H, H_{arom}), 9.70 s (1H, 9-H), 11.70 s (1H, 2-H). Found, %: C 74.36; H 6.90; N 13.72. $C_{19}H_{21}N_3O$. Calculated, %: C 74.27; H 6.84; N 13.68.

4-(4-Chlorophenyl)-3,7,7-trimethyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one (VIb). Yield 59%, mp >300°C. IR spectrum, ν, cm^{-1}: 3400–2800 (NH), 1580 (CO), 1556 (C=N). ^1H NMR spectrum, δ, ppm: 0.93 s and 1.00 s (3H each, 7-CH_3), 1.89 s (3H, 3-CH_3), 1.94 d and 2.12 d (1H each, 6-H_A and 8-H_A, J_{AB} = –16.5 Hz), 2.42 d (2H, 6-H_B, 7-H_B, J_{AB} = –7.8 Hz),* 4.94 s (1H, 4-H), 7.10–7.21 d (4H, H_{arom}, J = 7.8 Hz), 9.71 s (1H, 9-H), 11.81 s (1H, 2-H). Found, %: C 66.74; H 5.91; Cl 10.39; N 12.35. $C_{19}H_{20}ClN_3O$. Calculated, %: C 66.76; H 5.86; Cl 10.40; N 12.30.

b. A mixture of 1 mmol of amine **I** and 1 mmol of compound **IIIa** or **IIIb** in 1 ml of DMF was heated for 20 min under reflux. The products were isolated as described above in *a*. The yields of pyrazoloquinolinones **VIa** and **VIb** were 47 and 53%, respectively. Dimedone (**V**) was extracted from the filtrate into chloroform. The solvent was removed from the extract under reduced pressure, and the oily residue was crystallized from methanol; mp 149–151°C; published data [40]: mp 148–150°C.

c. A mixture of 1 mmol of amine **I**, 1 mmol of dimedone (**V**), and 1 mmol of substituted benzaldehyde **IVa**–**IVe** in 5 ml of methanol was heated for 1 h under reflux until a solid precipitated. The precipitate was filtered off and recrystallized from DMF–MeOH (1:2). The yields of pyrazoloquinolinones **VIa** and **VIb** were 60 and 62%, respectively.

4-(4-Methoxy-phenyl)-3,7,7-trimethyl-2,4,6,7,-8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one (VIc). Yield 67%, mp 290–292°C. IR spectrum, ν, cm^{-1}: 3228–2924 (NH), 1588 (CO), 1556 (C=N). ^1H NMR spectrum, δ, ppm: 0.94 s and 1.00 s (3H each, 7- CH_3), 1.90 s (3H, 3-CH_3), 1.94 d and 2.10 d (1H each, 6-H_A, 8-H_A, J_{AB} = –17.7 Hz), 2.41 d (2H, 6-H_B, 8-H_B, J_{AB} = –9.0 Hz),* 3.70 s (3H, OCH_3), 4.89 s (1H, 4-H), 6.74–7.12 d.d (4H, C_6H_4, J = 8.0 Hz), 9.71 s (1H, 9-H), 11.72 s (1H, 2-H). Found, %: C 71.29; H 6.89; N 12.44. $C_{20}H_{23}N_3O_2$. Calculated, %: C 71.22; H 6.82; N 12.46.

4-(4-Dimethylaminophenyl)-3,7,7-trimethyl-4-phenyl-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one (VId). Yield 73%, mp >300°C. IR spectrum, ν, cm^{-1}: 3192–2956 (NH), 1584 (CO), 157 (C=N). ^1H NMR spectrum, δ, ppm: 0.94 s and 1.03 s (3H each, 7-H), 1.90 s (3H, 3-CH_3), 2.00 d and 2.11 d (1H each, 6-H_A, 8-H_A, J_{AB} = –15.6 Hz), 2.40 d (2H, 6-H_B, 8-H_B, J_{AB} = –8.4 Hz),* 2.79 s [6H, $N(CH_3)_2$], 4.81 s (1H, 4-H), 6.53–6.94 d.d (4H, C_6H_4, J = 8.2 Hz), 9.62 s (1H, 9-H), 11.69 s (1H, 2-H). Found, %: C 72.06; H 7.33; N 15.97. $C_{21}H_{26}N_4O$. Calculated, %: C 72.00; H 7.39; N 16.00.

3,7,7-Trimethyl-4-(4-nitrophenyl)-2,4,6,7,8,9-hexahydropyrazolo[3,4-*b*]quinolin-5-one (VIe). Yield 68%, mp >300°C. IR spectrum, ν, cm^{-1}: 3260–2952 (NH), 1588 (CO), 1540 (C=N), 1340 (NO_2). ^1H NMR spectrum, δ, ppm: 0.94 s and 1.01 s (3H each, 7-CH_3), 1.88 s (3H, 3-CH_3), 1.96 d and 2.13 d (1H each, 6-H_A, 8-H_A, J_{AB} = –11.4 Hz), 2.45 d (2H, 6-H_B, 8-H_B, J_{AB} = –7.3 Hz),* 5.10 s (1H, 4-H), 7.41–8.10 d.d (4H, C_6H_4, J = 8.2 Hz), 9.90 s (1H, 9-H), 11.90 s (1H, 2-H). Found, %: C 64.85; H 5.74; N 15.96. $C_{19}H_{20}N_4O_3$. Calculated, %: C 64.77; H 5.68; N 15.91.

d. A mixture of 1 mmol of enaminoketone **X** and 1 mmol of benzaldehyde (**IVa**) in 1 ml of DMF containing a catalytic amount of hydrochloric acid was heated for 30 min under reflux. The product was isolated as described above. Yield of **VIa** 53%.

5,5-Dimethyl-3-(5-methyl-2*H*-pyrazol-3-ylamino)cyclohex-2-en-1-one (X). A solution of 3 mmol of amine **I** and 3 mmol of dimedone (**V**) in 2 ml of DMF was heated for 1.5 h under reflux. The mixture was cooled and diluted with 7 ml of propan-2-ol, and the precipitate was filtered off. Yield 62%, mp 251–253°C. IR spectrum, ν, cm^{-1}: 3400–2800 (NH), 1588 (CO), 1540 (C=N). ^1H NMR spectrum, δ, ppm: 1.00 s (6H, 5-CH_3), 2.19 s (3H, 5'-CH_3), 2.02 s (2H, CH_2), 2.34 s (2H, CH_2), 5.72 s (1H), 5.96 s (1H), 8.91 s (1H, NH), 12.11 s (1H, NH). Found, %: C 65.72; H 7.73; N 19.15. $C_{12}H_{17}N_3O$. Calculated, %: C 65.75; H 7.76; N 19.18.

X-Ray analysis of a single crystal of compound (VIc). Monoclinic crystals; $C_{20}H_{23}N_3O_2$; unit cell pa-

* Partially overlapped by the signal from residual protons in the deuterated solvent.

rameters (20°C): a = 8.742(3), b = 14.848(6), c = 14.623(6) Å; β = 106.32(3)°; V = 1821.6(12) Å^3; M_R = 337.41; Z = 4; space group $P2(1)/n$; d_{calc} = 1.230 g × cm^{-3}; μ(MoK_α) = 0.081 mm^{-1}; $F(000)$ = 720. The unit cell parameters and intensities of 3187 reflections (2989 of which were independent with R_{int} = 0.07) were measured on a Siemens P3/PC automatic four-circle diffractometer (MoK_α irradiation, graphite monochromator, 2θ/θ scanning to $2\theta_{max}$ = 50°). The structure was solved by the direct method using SHELX97 software [41]. The positions of hydrogen atoms (except for those in the disordered fragment) were determined by the difference synthesis of electron density; the positions of hydrogen atoms in the disordered fragment were calculated from the geometry considerations. The positions of all hydrogen atoms were refined by the rider model assuming $U_{iso} = nU_{eq}$ for a non-hydrogen atom linked to a given hydrogen atom (n = 1.5 for CH_3 group, n = 1.2 for the other hydrogen atoms). In the structure refinement, the bond lengths in the disordered fragment were limited to 1.51(1) (C_{sp^3}–C_{arom}) and 1.40(1) Å (C_{arom}–C_{arom}). The structure was refined with respect to F^2 by the full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms; the final divergence factors were wR_2 = 0.172 (from 2989 reflections) and R_1 = 0.59 [from 2373 reflections with $F > 4\sigma(F)$, S = 1.077].

This study was performed under financial support by the Foundation for Basic Research of Ukraine (project no. 0307/00154).

REFERENCES

1. Bossert, F. and Vater, W., *Med. Res. Rev*., 1989, vol. 9, p. 291.
2. Alajarin, R., Alvarez-Builla, J., Vaquero, J.J., Sunkel, C., Fau de Casa-Juanna, M., Statkow, P.R., and Sanz-Aparicio, J., *Tetrahedron: Asymmetry*, 1993, vol. 4, p. 617.
3. Orlov, V.D., Desenko, S.M., Potekhin, K.A., and Struchkov, Yu.T., *Khim. Geterotsikl. Soedin*., 1988, p. 229.
4. Desenko, S.M., Orlov, V.D., and Estrada, Kh., *Khim. Geterotsikl. Soedin*., 1990, p. 999.
5. Desenko, S.M., Orlov, V.D., Estrada, Kh., and Ponomarev, O.A., *Khim. Geterotsikl. Soedin*., 1991, p. 105.
6. Desenko, S.M., Orlov, V.D., and Estrada, Kh., *Khim. Geterotsikl. Soedin*., 1991, p. 694.
7. Desenko, S.M., Orlov, V.D., Lipson, V.V., Ryndina, E.N., Chuvurin, A.V., Kirichenko, A.A., and Gorbenko, N.I., *Khim.-Farm. Zh*., 1994, no. 3, p. 19.
8. Lipson, V.V., Desenko, S.M., Shirobokova, M.G., and Borodina, V.V., *Khim. Geterotsikl. Soedin*., 2003, p. 1383.
9. Lipson, V.V., Ignatenko, I.V., Desenko, S.M., Shishkina, S.V., Shishkin, O.V., Komykhov, S.A., Logvinenko, N.V., Orlov, V.D., and Meier, H., *J. Heterocycl. Chem*., 2003, vol. 40, p. 1081.
10. Lipson, V.V., Desenko, S.M., Borodina, V.V., Shirobokova, M.G., and Musatov, V.I., *Russ. J. Org. Chem*., 2005, vol. 41, p. 114.
11. Desenko, S.M., Orlov, V.D., Lipson, V.V., and Estrada, Kh., *Khim. Geterotsikl. Soedin*., 1991, p. 1215.
12. Lipson, V.V., Desenko, S.M., Orlov, V.D., Ryndina, E.N., Chuvurin, A.V., Gorbenko, N.I., and Kirichenko, A.A., *Khim.-Farm. Zh*., 1994, no. 2, p. 14.
13. El Ella, D.A., Gnitzer, E., and Wendelin, W., *J. Heterocycl. Chem*., 1996, vol. 33, p. 373.
14. Lipson, V.V. Desenko, S.M., Shishkina, S.V., Shirobokova, M.G., Shishkin, O.V., and Orlov, V.D., *Khim. Geterotsikl. Soedin*., 2003, p. 1194.
15. Orlov, V.D., Kolos, N.N., Quiroga, J., and Desenko, S.M., *Khim. Geterotsikl. Soedin*., 1988, p. 962.
16. Desenko, S.M., Orlov, V.D., Lipson, V.V., Shishkin, O.V., Potekhin, K.A., and Struchkov, Yu.T., *Khim. Geterotsikl. Soedin*., 1993, p. 109.
17. Lindeman, S.V., Strychkov, Yu.T., Shishkin, O.V., Desenko, S.M., Lipson, V.V., and Orlov, V.D., *Acta Crystallogr., Sect. C*, 1993, vol. 49, p. 896.
18. Bellec, C. and Lhommet, G., *J. Heterocycl. Chem*., 1995, vol. 32, p. 1793.
19. Quiroga, J., Hormaza, A., Insuasty, B., Saitz, C., Jullian, C., and Canete, A., *J. Heterocycl. Chem*., 1998, vol. 35, p. 61.
20. Desenko, S.M., Orlov, V.D., Shishkin, O.V., Getmanskii, N.V., Lipson, V.V., Lindeman, S.V., and Struchkov, Yu.T., *Khim. Geterotsikl. Soedin*., 1993, p. 481.
21. Quiroga, J., Insuasty, B., Hormaza, A., Gamenara, D., Dominguez, L., and Saldana, J., *J. Heterocycl. Chem*., 1999, vol. 36, p. 11.
22. Desenko, S.M., Orlov, V.D., Lipson, V.V., Lindeman, S.V., and Struchkov, Yu.T., *Khim. Geterotsikl. Soedin*., 1991, p. 1539.
23. Tsuda, Y.N., Mishina, T., Obata, M., Araki, K., Inui, A., and Nakamura, T., JPN Patent Appl. no. 61-227584, 1986; *Chem. Abstr*., 1987, vol. 106, no. 176416m.
24. Tsuda, Y.N., Mishina, T., Obata, M., Araki, K., Inui, A., and Nakamura, T., JPN Patent Appl. no. 63-101383, 1988; *Chem. Abstr*., 1988, vol. 109, no. 128988g.
25. Reiter, J. and Esses-Reiter, K., *J. Heterocycl. Chem*., 1991, vol. 28, p. 561.
26. Reiter, J., Berecz, G., and Pallagi, I., *J. Heterocycl. Chem*., 1991, vol. 28, p. 721.
27. Rivo, E. and Reiter, J., *J. Heterocycl. Chem*., 1992, vol. 29, p. 1189.
28. Berecz, G., Reiter, J., and Csaszar, J., *J. Heterocycl. Chem*., 1999, vol. 36, p. 1199.

29. Desenko, S.M., Lipson, V.V., Shishkin, O.V., Komykhov, S.A., Orlov, V.D., Lakin, E.E., Kuznetsov, V.P., and Meier, H., *J. Heterocycl, Chem*., 1999, vol. 36, p. 205.
30. Lipson, V.V., Orlov, V.D., Desenko, S.M., Karnozhitskaya, T.M., and Shirobokova, M.G., *Khim. Geterotsikl. Soedin*., 1999, p. 664.
31. Lipson, V.V., Orlov, V.D., Desenko, S.M., Shishkina, S.V., Shishkin, O.V., and Shirobokova, M.G., *Khim. Geterotsikl. Soedin*., 2000, p. 1190.
32. Lipson, V.V., Orlov, V.D., Desenko, S.M., Shishkin, O.V., Shirobokova, M.G., Chernenko, V.N., and Zinov'eva, L.I., *Khim. Geterotsikl. Soedin*., 2000, p. 1542.
33. Lipson, V.V., Desenko, S.M., Borodina, V.V., Shirobokova, M.G., Karnozhitskaya, T.M., Musatov, V.I., and Kravchenko, S.V., *Khim. Geterotsikl. Soedin*., 2005, p. 246.
34. Lipson, V.V., Borodina, V.V., Bozhko, T.S., Ladogubets, E.V., and Rozhovetskaya, I.A., Ukrainian Patent no. 68302A, 2004; *Ukr. Pat. Byul*., 2004, p. 7.
35. Zefirov, N.S., Palyulin, V.A., and Dashevskaya, E.E., *J. Phys. Org. Chem*., 1990, vol. 3, p. 147.
36. Zefirov, Yu.V. and Zorkii, P.M., *Usp. Khim*., 1989, vol. 58, p. 713.
37. Burgi, H.-B. and Dunitz, J.D., *Structure Correlation*, Weinheim: VCH, 1994, vol. 2, p. 741.
38. Margaretha, P. and Polansky, O.E., *Monatsh. Chem*., 1970, vol. 101, p. 824.
39. Zitsmanie, A.Kh., Klyavin'sh, M.K., and Roska, A.S., *Izv. Akad. Nauk Latv. SSR*, 1988, no. 1, p. 91.
40. *Handbook of Chemistry and Physics*, Lide, D.R., Ed., London: CRC, 1994, pp. 3–122.
41. Sheldrick, G.M., *SHELX97. PC Version. Rev. 2*, 1998.