ISSN 1070-4280, Russian Journal of Organic Chemistry, 2016, Vol. 52, No. 4, pp. 546–552. © Pleiades Publishing, Ltd., 2016.
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Reaction of Methyl 3-Aroyl-1-aryl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates with Arylhydrazines. Synthesis of Isomeric 5-Arylcarbamoyl-4-aroyl- and 5-Aryl-4-aryloxamoyl-1*H*-pyrazoles

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Received September 23, 2015

Abstract—Methyl 3-aroyl-1-aryl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates reacted with arylhydrazines to give methyl 3-aroyl-1-aryl-2-(2-arylhydrazinyl)-4-hydroxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxylates which underwent thermal recyclization into isomeric methyl 1-aryl-5-(arylcarbamoyl)-4-aroyl-1*H*-pyrazole-3-carboxylates and methyl 1,5-diaryl-4-[2-oxo-2-(arylamino)acetyl]-1*H*-pyrazole-3-carboxylates.

DOI: 10.1134/S1070428016040126

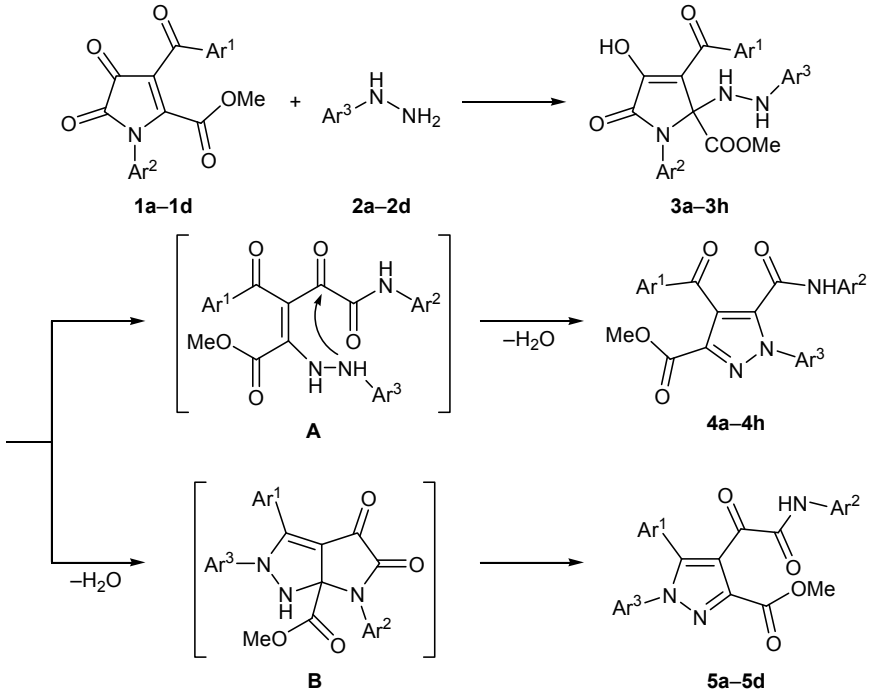
Recyclizations and heterocyclizations of 1*H*-pyrrole-2,3-diones by the action of binucleophiles provide convenient synthetic approaches to five-, six-, and seven-membered nitrogen heterocycles and various fused, bridged and spirocyclic systems [1–4]. The reaction direction depends on the binucleophile nature (distance between the nucleophilic centers and their nucleophilicity) and functional groups in positions *4* and *5* of the pyrrole ring.

Pyrrolediones containing no electron-withdrawing functional groups were reported to react with arylhydrazines via attack by the primary amino of arylhydrazine group on the C^3=O carbonyl group of pyrroledione with formation of the corresponding hydrazones [5–8]. By contrast, 4-acyl-substituted pyrrolediones initially take up substituted hydrazine at C^5 of the pyrrole ring, and next follows cyclization involving the second nitrogen atom of the hydrazine and C^3=O carbonyl group [9, 10] or carbonyl group of the acyl substituent on C^4 [11–13].

In the present work we studied the reaction of methyl 3-aroyl-1-aryl-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates **1a**–**1d** with arylhydrazines **2a**–**2d** containing electron-donating and electron-withdrawing substituents in the aromatic ring with the goal of estimating their effect on the reaction course. The reactions were carried out with equimolar amounts of the reactants by carefully adding a solution of arylhydrazine **2a**–**2d** in anhydrous toluene to a solution of pyrroledione **1a**–**1d** in the same solvent. The red color typical of initial compounds **1** disappeared almost instantaneously, and the corresponding products, methyl 3-aroyl-1-aryl-2-(2-arylhydrazinyl)-4-hydroxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxylates **3a**–**3h** resulting from addition of the primary amino group of **2** to C^2 of **1**, were formed in high yields (Scheme 1). Attempted recrystallization of **3a**–**3h** from ethanol on heating for a short time led to their recyclization to give isomeric methyl 1-aryl-5-(arylcarbamoyl)-4-aroyl-1*H*-pyrazole-3-carboxylates **4a**–**4h** and methyl 1,5-diaryl-4-[2-oxo-2-(arylamino)acetyl]-1*H*-pyrazole-3-carboxylates **5a**–**5d** whose structure was confirmed by X-ray analysis of compounds **4a** and **5a**. Compound **4h** was synthesized by heating a mixture of **1d** and **2b** in boiling chloroform for 30 min.

Compounds **3a**–**3h** are colorless or light yellow crystalline substances which melt with decomposition. They are readily soluble in DMSO and DMF, poorly soluble in ethyl acetate and aromatic and chlorinated hydrocarbons, and insoluble in alkanes and water. Compounds **3a**–**3h** showed a positive color test (cherry color) for enolic hydroxy group on treatment with an alcoholic solution of iron(III) chloride. The IR spectra of **3a**–**3h** contained absorption bands due to stretching vibrations of NH (3273–3567 cm^{-1}), enolic hydroxy (3251–3314 cm^{-1}, broad band), and ester

Scheme 1.



1, Ar^1 = Ph, Ar^2 = 4-$MeOC_6H_4$ (**a**), 4-BrC_6H_4 (**b**), Ph (**c**); Ar^1 = 4-$MeOC_6H_4$, Ar^2 = Ph (**d**); **2**, Ar^3 = Ph (**a**), 4-$O_2NC_6H_4$ (**b**), 2,4-$(O_2N)_2C_6H_3$ (**c**), 4-MeC_6H_4 (**d**); **3**, Ar^1 = Ph, Ar^2 = 4-$MeOC_6H_4$, Ar^3 = Ph (**a**); Ar^2 = 4-$MeOC_6H_4$, Ar^3 = 4-$O_2NC_6H_4$ (**b**); Ar^2 = 4-$MeOC_6H_4$, Ar^3 = 2,4-$(O_2N)_2C_6H_3$ (**c**); Ar^2 = 4-BrC_6H_4, Ar^3 = Ph (**d**); Ar^2 = 4-BrC_6H_4, Ar^3 = 4-$O_2NC_6H_4$ (**e**); Ar^2 = 4-BrC_6H_4, Ar^3 = 4-MeC_6H_4 (**f**); Ar^2 = Ph, Ar^3 = Ph (**g**); Ar^2 = Ph, Ar^3 = 4-$O_2NC_6H_4$ (**h**); **4**, Ar^1 = Ph, Ar^2 = 4-$MeOC_6H_4$, Ar^3 = Ph (**a**); Ar^2 = 4-$MeOC_6H_4$, Ar^3 = 4-$O_2NC_6H_4$ (**b**); Ar^2 = 4-BrC_6H_4, Ar^3 = Ph (**c**); Ar^2 = 4-BrC_6H_4, Ar^3 = 4-$O_2NC_6H_4$ (**d**); Ar^2 = 4-BrC_6H_4, Ar^3 = 4-MeC_6H_4 (**e**); Ar^2 = Ph, Ar^3 = Ph (**f**); Ar^2 = Ph, Ar^3 = 4-$O_2NC_6H_4$ (**g**); Ar^1 = 4-$MeOC_6H_4$, Ar^2 = Ph, Ar^3 = 4-$O_2NC_6H_4$ (**h**); **5**, Ar^1 = Ph, Ar^2 = 4-$MeOC_6H_4$, Ar^3 = Ph (**a**); Ar^2 = 4-BrC_6H_4, Ar^3 = Ph (**b**); Ar^2 = 4-BrC_6H_4, Ar^3 = 4-MeC_6H_4 (**c**); Ar^2 = Ph, Ar^3 = Ph (**d**).

(1744–1755 cm^{-1}), lactam (1709–1728 cm^{-1}) and ketone carbonyl groups (1662–1687 cm^{-1}). In the ^1H NMR spectra of **3a**–**3h** we observed signals from aromatic protons and substituents in the aromatic rings, a three-proton singlet at δ 3.68–3.84 ppm from the ester methoxy group, singlets from two NH protons at δ 5.42–6.46 (**3a**, **3d**, **3f**, **3g**) or 6.03–6.28 and 8.19–9.07 ppm (**3b**, **3c**, **3e**, **3h**), and a broadened OH singlet at δ 11.48–12.62 ppm.

Pyrazoles **4a**–**4h** and **5a**–**5d** were isolated as high-melting colorless or yellow crystalline substances readily soluble in DMSO, DMF, ethyl acetate, and aromatic and chlorinated hydrocarbons and insoluble in alkanes and water. Unlike addition products **3a**–**3h**, pyrazoles **4a**–**4h** and **5a**–**5d** showed a negative color test for enolic hydroxy group with alcoholic iron(III) chloride. Compounds **4a**–**4h** showed in the IR spectra absorption bands at 3186–3324 (NH), 1729–1751 (C=O, ester), 1674–1701 (C=O, amide), and 1634–1681 cm^{-1} (4-C=O). The IR spectra of **5a**–**5d** displayed NH (3235–3330 cm^{-1}), ester carbonyl (1738–1749 cm^{-1}), and oxamoyl ketone (1681–1686 cm^{-1}) and amide carbonyl stretching vibration bands (1665–1677 cm^{-1}).

Methoxy protons resonated in the ^1H NMR spectra of **4a**–**4h** and **5a**–**5d** as a three-proton singlet at δ 3.62–3.69 and 3.74–3.75 ppm, respectively, and the NH singlet was located at δ 10.60–10.99 ppm. The downfield region of the ^{13}C NMR spectra of **4a**–**4h** and **5a**–**5d** contained signals at δ_C 156.00–156.82 and 160.64–161.66 ppm due to carbonyl carbon atoms of the amide and ester groups, respectively; the 4-C=O signal of **4a**–**4h** was observed at δ_C 188.49–188.76 ppm; and the signal at δ_C 184.27–185.68 ppm in the spectra of **5a**–**5d** was assigned to the oxamoyl ketone carbonyl. The observed differences in the ^1H and ^{13}C NMR spectra allowed us to assign compounds **4a**–**4h** and **5a**–**5d** to different series. Furthermore, the ^1H–^{13}C HMBC spectra of **4a**–**4h** revealed a correlation between the *ortho*-protons of the benzoyl group and carbonyl carbon atom of that group (e.g., δ/δ_C 7.80/188.73 and 7.84/188.73 ppm for **4a**).

According to the X-ray diffraction data (Fig. 1), compound **4a** crystallized in a centrosymmetric space

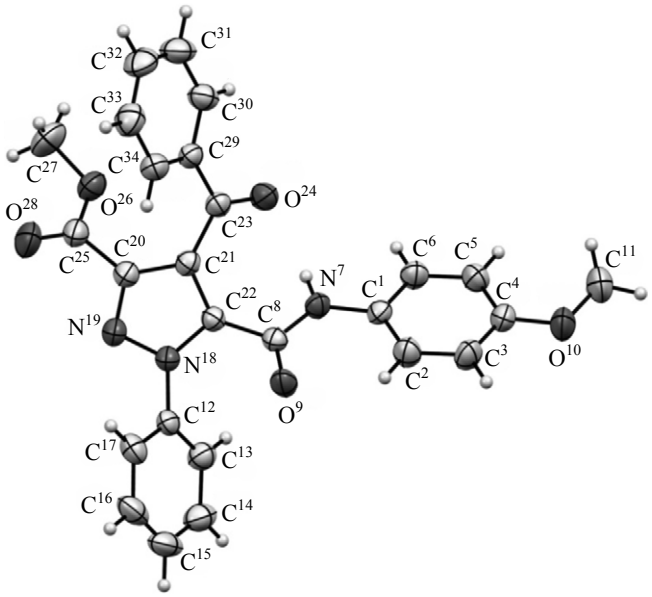


Fig. 1. Structure of the molecule of methyl 4-benzoyl-5-[(4-methoxyphenyl)carbamoyl]-1-phenyl-1*H*-pyrazole-3-carboxylate (**4a**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

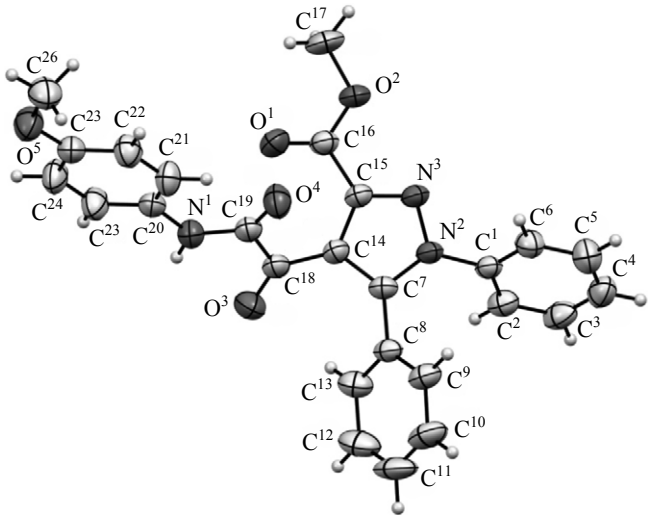


Fig. 2. Structure of the molecule of methyl 4-{2-[(4-methoxyphenyl)amino]-2-oxoacetyl}-1,5-diphenyl-1*H*-pyrazole-3-carboxylate (**5a**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

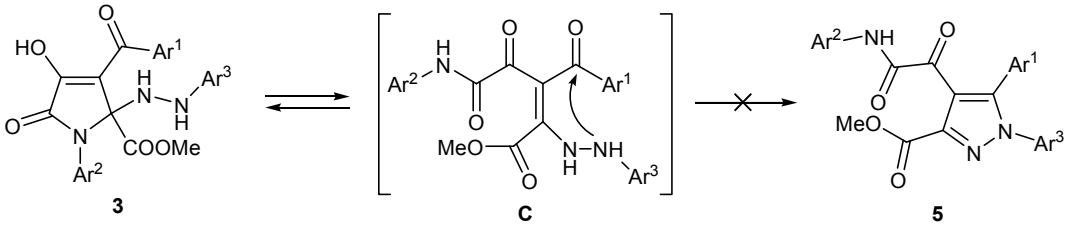
group belonging to the triclinic crystal system. The pyrazole ring is planar with delocalized bonds typical of heteroaromatic systems. Because of steric crowding, all substituents in the pyrazole ring are non-coplanar with the latter, which hampers conjugation of π-systems. The orientation of substituents is determined by the torsion angles $N^{19}C^{20}C^{25}O^{28}$ 34.7(3), $C^{22}C^{21}C^{23}O^{24}$ 44.3(3), $O^{9}C^{8}C^{22}N^{18}$ –28.0(3), and $C^{13}C^{12}N^{18}C^{22}$ –54.9(3)°. The benzoyl fragment is not planar [torsion angle $C^{30}C^{29}C^{23}O^{24}$ 25.2(3)°]. The arylcarbamoyl substituent is planar within 0.11 Å due to intramolecular hydrogen bond N^{7}–$H^{7}\cdots O^{24}$ [N^{7}–H^{7} 0.85(1), O^{24}–H^{7} 2.03(2), $O^{24}\cdots N^{7}$ 2.774(2) Å]. Molecules **4a** in crystal are linked to centrosymmetric dimers via $CH\cdots O$ contacts [$O^{9}\cdots H^{34}$ 2.40, $O^{9}\cdots C^{34}$ 3.288(2) Å, $\angle O^{9}H^{34}C^{34}$ 159°, O^{9} $(1-x, -y, 1-z)$].

Compound **5a** crystallizes in a centrosymmetric space group belonging to the monoclinic crystal system; its unit cell includes two crystallographically independent molecules with fairly similar geometric parameters (Fig. 2; only one independent molecule is shown). On the whole, the molecular structures of **5a** and **4a** are similar: in both cases, the four substituents are turned with respect to the aromatic pyrazole ring plane. The orientation of the aryloxamoyl fragment is determined by mutual repulsion of the amide and ester carbonyl groups. The crystal packing of **5a** is stabilized by conventional van der Waals interactions.

Presumably, pyrazoles **4a**–**4h** are formed via ring–chain isomerization of primary adducts **3a**–**3h**, followed by attack by the secondary amino group of the arylhydrazine residue in intermediate **A** on the ketone carbonyl carbon atom of the aryloxamoyl fragment with closure of five-membered ring. Analogous reaction path is typical of pyrrolediones **1** and some 1,3-nitrogen binucleophiles, e.g., 5-aminopyrazole [14]. Alternatively, the attack by the secondary amino group of the arylhydrazine residue on the ketone carbonyl carbon atom of the aroyl substituent on C^{3} in **3a**–**3h** gives intermediate pyrrolo[2,3-*c*]pyrazole **B** which undergoes opening of the pyrrole ring at the N^{6}–C^{6a} bond. Cleavage of the latter is facilitated by steric strains in the fused pyrrolopyrazole system; furthermore, the ease of C–N bond cleavage in geminal diamines is well known. Analogous transformations (but not including pyrrole ring opening) were observed previously in the reactions of pyrrolediones **1** with 1,4-binucleophiles, *o*-phenylenediamine [15] and *o*-aminobenzenethiol [16].

The positive charge on the $Ar^{3}NHCO\mathbf{C}O$ carbon atom in acyclic intermediate *Z*-**A** is higher than that on the $Ar^{1}\mathbf{C}O$ carbon atom in cyclic isomer **3** and acyclic intermediate *E*-**C**. Presumably, this is essential for the cyclization of adducts derived from arylhydrazines containing electron-withdrawing substituents such as nitro group. The nucleophilicity of the secondary amino group in 4-nitrophenylhydrazine is strongly

Scheme 2.



$Ar^3 = 4\text{-}O_2NC_6H_4$.

reduced, so that substituted 5-carbamoylpyrazoles **4b**, **4d**, **4f**, and **4h** are formed as the only product. Compound **3c** obtained by addition of 2,4-dinitrophenylhydrazine to pyrroledione **1a** did not undergo recyclization at all because of very low nucleophilicity of the secondary amino group therein.

The described transformation is an example of recyclization of pyrrolediones with arylhydrazines, leading to difficultly accessible functionalized di- and triacylpyrazoles. Acyl-substituted pyrazoles are of great practical interest due to their biological activity. For example, 1*H*-pyrazole-3,5-dicarboxylic acid shows antimicrobial activity [17], 1-methyl-1*H*-pyrazole-3,4-dicarboxylic acid is an NDMA antagonist [18], and 1,5-dimethyl-4-methoxycarbonyl-1*H*-pyrazole-3-carboxylic acid inhibits the growth of phytopathogenic fungi [19].

EXPERIMENTAL

The IR spectra were recorded on a Perkin Elmer Spectrum Two spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were recorded on a Bruker DRX 400 spectrometer at 400 MHz using tetramethylsilane as internal standard. The ^{13}C NMR spectra were measured on a Bruker Avance III HD 400 instrument at 100 MHz from solutions in $CDCl_3$. The elemental analyses were obtained on a Vario MICRO cube analyzer. The purity of the isolated compounds was checked by TLC on Silufol plates using chloroform as eluent; spots were visualized by treatment with iodine vapor.

Methyl 3-benzoyl-4-hydroxy-1-(4-methoxyphenyl)-5-oxo-2-(2-phenylhydrazinyl)-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3a). A solution of 3 mmol of phenylhydrazine (**2a**) in 5 mL of anhydrous toluene was slowly added under stirring to a solution of 3 mmol of pyrroledione **1a** in 10 mL of anhydrous toluene. The mixture was cooled to 0°C, and the colorless solid was filtered off. Yield 95%, mp 115–117°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3343, 3331 (NH), 3264 br (OH), 1748 (C=O, ester), 1709 (C^5=O), 1687 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.69 s (3H, OMe), 3.80 s (3H, OMe), 5.42 s (1H, NH), 6.40 s (1H, NH), 6.85–7.54 m (14H, H_{arom}), 12.07 br.s (1H, OH). Found, %: C 65.74; H 4.72; N 8.89. $C_{26}H_{23}N_3O_6$. Calculated, %: C 65.95; H 4.90; N 8.87.

Compounds **3b**–**3h** were synthesized in a similar way.

Methyl 3-benzoyl-4-hydroxy-1-(4-methoxyphenyl)-2-[2-(4-nitrophenyl)hydrazinyl]-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3b). Yield 87%, mp 136–138°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3455, 3427 (NH), 3305 br (OH), 1754 (C=O, ester), 1722 (C^5=O), 1673 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.69 s (3H, OMe), 3.80 s (3H, OMe), 6.03 s (1H, NH), 6.80–7.66 m (13H, H_{arom}), 8.45 s (1H, NH), 12.09 br.s (1H, OH). Found, %: C 60.01; H 4.13; N 10.73. $C_{26}H_{22}N_4O_8$. Calculated, %: C 60.23; H 4.28; N 10.81.

Methyl 3-benzoyl-4-hydroxy-1-(4-methoxyphenyl)-2-[2-(2,4-dinitrophenyl)hydrazinyl]-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3c). Yield 92%, mp 180–182°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3431, 3426 (NH), 3273 br (OH), 1748 (C=O, ester), 1723 (C^5=O), 1681 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.80 s (3H, OMe), 3.84 s (3H, OMe), 7.02–7.61 m (12H, H_{arom}), 8.73 s (1H, NH), 9.07 s (1H, NH), 12.06 br.s (1H, OH). Found, %: C 55.34; H 3.67; N 12.55. $C_{26}H_{21}N_5O_{10}$. Calculated, %: C 55.42; H 3.76; N 12.43.

Methyl 3-benzoyl-1-(4-bromophenyl)-4-hydroxy-5-oxo-2-(2-phenylhydrazinyl)-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3d). Yield 89%, mp 122–124°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3374, 3330 (NH), 3251 br (OH), 1747 (C=O, ester), 1718 (C^5=O), 1662 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.69 s (3H, OMe), 5.63 s (1H, NH), 6.46 s (1H, NH), 6.67–7.79 m (14H, H_{arom}), 12.62 br.s (1H, OH). Found, %: C 57.61; H 3.81;

Br 15.24; N 7.97. $C_{25}H_{20}BrN_3O_5$. Calculated, %: C 57.48; H 3.86; Br 15.30; N 8.04.

Methyl 3-benzoyl-1-(4-bromophenyl)-4-hydroxy-2-[2-(4-nitrophenyl)hydrazinyl]-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3e). Yield 80%, mp 124–125°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3567, 3479 (NH), 3314 br (OH), 1731 (C=O, ester), 1710 (C^5=O), 1675 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.71 s (3H, OMe), 6.28 s (1H, NH), 6.75–7.71 m (13H, H_{arom}), 8.19 s (1H, NH), 11.48 br.s (1H, OH). Found, %: C 52.79; H 3.32; Br 14.18; N 9.94. $C_{25}H_{19}BrN_4O_7$. Calculated, %: C 52.93; H 3.38; Br 14.08; N 9.88.

Methyl 3-benzoyl-1-(4-bromophenyl)-4-hydroxy-5-oxo-2-[2-(4-methylphenyl)hydrazinyl]-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3f). Yield 82%, mp 128–130°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3475, 3415 (NH), 3253 br (OH), 1748 (C=O, ester), 1717 (C^5=O), 1673 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.01 s (3H, Me), 3.68 s (3H, OMe), 5.53 s (1H, NH), 6.31 s (1H, NH), 7.02–7.61 m (13H, H_{arom}), 12.12 br.s (1H, OH). Found, %: C 58.03; H 4.00; Br 14.26; N 7.89. $C_{26}H_{22}BrN_3O_5$. Calculated, %: C 58.22; N 4.13; Br 14.90; N 7.83.

Methyl 3-benzoyl-4-hydroxy-5-oxo-1-phenyl-2-(2-phenylhydrazinyl)-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3g). Yield 78%, mp 128–129°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3321, 3307 (NH), 3283 br (OH), 1748 (C=O, ester), 1717 (C^5=O), 1662 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.70 s (3H, OMe), 5.53 s (1H, NH), 6.41 t (1H, NH), 6.61–7.52 m (15H, H_{arom}), 12.19 br.s (1H, OH). Found, %: C 67.58; H 4.72; N 9.44. $C_{25}H_{21}N_3O_5$. Calculated, %: C 67.71; H 4.77; N 9.41.

Methyl 3-benzoyl-4-hydroxy-2-[2-(4-nitrophenyl)hydrazinyl]-5-oxo-1-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxylate (3h). Yield 89%, mp 155–157°C (decomp., from toluene). IR spectrum, ν, cm^{-1}: 3340, 3309 (NH), 3223 br (OH), 1755 (C=O, ester), 1728 (C^5=O), 1676 (3-C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.70 s (3H, OMe), 6.26 s (1H, NH), 6.80–7.66 m (14H, H_{arom}), 8.21 s (1H, NH), 11.52 br.s (1H, OH). Found, %: C 67.38; H 4.06; N 11.52. $C_{25}H_{20}N_4O_7$. Calculated, %: C 61.47; H 4.13; N 11.47.

Methyl 4-benzoyl-5-[(4-methoxyphenyl)carbamoyl]-1-phenyl-1*H*-pyrazole-3-carboxylate (4a) and methyl 4-{2-[(4-methoxyphenyl)amino]-2-oxoacetyl}-1,5-diphenyl-1*H*-pyrazole-3-carboxylate (5a). A solution of 2 mmol of compound **3a** in 15 mL of ethanol was refluxed for 1 h. The mixture was evaporated, and the dry residue was subjected to column chromatography on Al_2O_3 (40–250 μm) using benzene–ethyl acetate (10:1) as eluent to isolate compounds **5a** (first yellow fraction) and **4a** (colorless second fraction); the separation process was monitored by TLC.

Compound **5a**. Yield 21%, mp 155–157°C (from EtOH). IR spectrum, ν, cm^{-1}: 3330 (NH), 1739 (C=O, ester), 1699 (4-C=O), 1668 (CONH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.74 br.s (6H, OMe), 6.95–7.69 m (14H, H_{arom}), 10.63 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.11 (COO**Me**), 55.12 (MeO), 113.94–141.86 (C_{arom}), 156.00 (CONH), 160.82 (**C**OOMe), 185.68 (4-C=O). Found, %: C 68.51; H 4.62; N 9.26. $C_{26}H_{21}N_3O_5$. Calculated, %: C 68.56; H 4.65; N 9.23.

Compound **4a**. Yield 72%, mp 172–174°C (from EtOH). IR spectrum, ν, cm^{-1}: 3302 (NH), 1729 (C=O, ester), 1674 (CONH), 1640 (4-C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.63 s (3H, OMe), 3.69 s (3H, OMe), 6.82–7.83 m (14H, H_{arom}), 10.60 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.40 (COO**Me**), 55.34 (OMe), 114.05–146.37 (C_{arom}), 156.00 (CONH), 161.58 (**C**OOMe), 188.73 (4-C=O). Found, %: C 68.48; H 4.43; N 9.28. $C_{26}H_{21}N_3O_5$. Calculated, %: C 68.56; H 4.65; N 9.23.

X-Ray analysis of 4a and 5a. The X-ray diffraction data for compounds **4a** and **5a** were acquired at 295(2) K on an XcaliburR automated four-circle diffractometer with a CCD detector (monochromatized MoK_α radiation, ω–2θ-scanning). A correction for absorption was applied empirically using SCALE3 ABSPACK algorithm [20]. The structures were solved by the direct statistical method and refined by the full-matrix least squares method in anisotropic approximation for all non-hydrogen atoms. Hydrogen atoms of the NH groups were localized and refined independently in isotropic approximation, while the other hydrogens were placed into geomtrically calculated positions and refined according to the riding model with dependent thermal parameters. All calculations were performed using SHELX97 [21].

The data for compound **4a** ($C_{26}H_{21}N_3O_5$) were obtained from a 0.40×0.20×0.08-mm colorless single crystal. The reflection data set was converted into the HKLF 5 format file for a two-component twin. Triclinic crystal system, space group *P*-1; unit cell parameters: a = 8.3723(15), b = 11.989(2), c = 12.553(2) Å; α = 71.939(16), β = 74.225(16), γ = 73.100(16)°; V = 1123.1(4) $Å^3$; d_{calc} = 1.347 g/cm^3; Z = 2. Intensities of 7644 independent reflections, including 5106 reflec-

tions with $I > 2\sigma(I)$, were measured in the range $2.82 < \theta < 29.29°$. Final divergence factors: $R_1 = 0.0463$, $wR_2 = 0.1086$ [for reflections with $I > 2\sigma(I)$], $R_1 = 0.0691$, $wR_2 = 0.1159$ (for all reflections); goodness of fit $S = 0.930$; twin component ratio 0.570(1):0.430(1).

The data for compound **5a** ($C_{26}H_{21}N_3O_5$) were obtained from a 0.60×0.40×0.35-mm yellow single crystal. Monoclinic crystal system, space group $P2_1/c$; unit cell parameters: $a = 11.3866(16)$, $b = 40.584(11)$, $c = 10.2378(17)$ Å; $\beta = 103.269(15)°$; $V = 4604.8(16)$ Å^3; $d_{calc} = 1.314$ g/cm^3; $Z = 8$. Intensities of 10447 independent reflections, including 7972 reflections with $I > 2\sigma(I)$, were measured in the range $3.01 < \theta < 28.74°$. Final divergence factors: $R_1 = 0.0617$, $wR_2 = 0.1340$ [for reflections with $I > 2\sigma(I)$], $R_1 = 0.0829$, $wR_2 = 0.1469$ (for all reflections); goodness of fit $S = 1.080$.

The X-ray diffraction data were deposited to the Cambridge crystallographic Data Centre [entry nos. CCDC 1472481 (**4a**), 1472482 (**5a**)] and are available at *www.ccdc.cam.ac.uk*.

Compounds **4b**–**4g** and **5b**–**5d** were synthesized in a similar way.

Methyl 4-benzoyl-5-(4-methoxyphenyl)carbamoyl)-1-(4-nitrophenyl)-1*H*-pyrazole-3-carboxylate (4b). Yield 82%, mp 211–212°C (from EtOH). IR spectrum, ν, cm^{-1}: 3186 (NH), 1751 (C=O, ester), 1697 (CONH), 1651 (4-C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.65 s (3H, OMe), 3.69 s (3H, OMe), 6.84–8.43 m (13H, H_{arom}), 10.67 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.39 (COO**Me**), 55.33 (OMe), 114.05–147.25 (C_{arom}), 156.44 (CONH), 160.73 (**C**OOMe), 188.51 (4-C=O). Found, %: C 62.28; H 3.94; N 11.21. $C_{26}H_{20}N_4O_7$. Calculated, %: C 62.40; H 4.03; N 11.20.

Methyl 4-benzoyl-5-[(4-bromophenyl)carbamoyl]-1-phenyl-1*H*-pyrazole-3-carboxylate (4c). Yield 52%, mp 155–157°C (from EtOH). IR spectrum, ν, cm^{-1}: 3194 (NH), 1739 (C=O, ester), 1692 (CONH), 1635 (4-C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.63 s (3H, OMe), 7.27–7.82 m (14H, H_{arom}), 10.91 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.19 (COO**Me**), 116.50–141.94 (C_{arom}), 156.73 (CONH), 161.13 (**C**OOMe), 188.65 (4-C=O). Found, %: C 59.39; H 4.13; Br 15.89; N 8.33. $C_{25}H_{18}BrN_3O_4$. Calculated, %: C 59.54; H 4.13; Br 15.84; N 8.26.

Methyl 4-{2-[(4-bromophenyl)amino]-2-oxoacetyl}-1,5-diphenyl-1*H*-pyrazole-3-carboxylate (5b). Yield 34%, mp 155–157°C (from EtOH). IR spectrum, ν, cm^{-1}: 3266 (NH), 1738 (C=O, ester), 1686 (4-C=O), 1672 (CONH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.75 s (3H, OMe), 6.89–7.84 m (14H, H_{arom}), 10.99 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.15 (COO**Me**), 114.21–141.17 (C_{arom}), 156.26 (CONH), 161.02 (**C**OOMe), 184.27 (4-C=O). Found, %: C 59.41; H 4.18; Br 15.90; N 8.22. $C_{25}H_{18}BrN_3O_4$. Calculated, %: C 59.54; H 4.13; Br 15.84; N 8.26.

Methyl 4-benzoyl-5-[(4-bromophenyl)carbamoyl]-1-(4-nitrophenyl)-1*H*-pyrazole-3-carboxylate (4d). Yield 82%, mp 168–170°C (from EtOH). IR spectrum, ν, cm^{-1}: 3310 (NH), 1731 (C=O, ester), 1699 (CONH), 1681 (4-C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.66 s (3H, OMe), 7.11–8.44 m (13H, H_{arom}), 10.86 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.35 (COO**Me**), 120.08–147.29 (C_{arom}), 156.27 (CONH), 160.90 (**C**OOMe), 188.53 (4-C=O). Found, %: C 59.61; H 3.07; Br 14.60; N 10.27. $C_{25}H_{18}BrN_3O_4$. Calculated, %: C 54.66; H 3.12; Br 14.55; N 10.20.

Methyl 4-benzoyl-5-[(4-bromophenyl)carbamoyl]-1-(4-methylphenyl)-1*H*-pyrazole-3-carboxylate (4e). Yield 43%, mp 184–186°C (from EtOH). IR spectrum, ν, cm^{-1}: 3191 (NH), 1739 (C=O, ester), 1690 (CONH), 1634 (4-C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.36 s (3H, Me), 3.62 s (3H, OMe), 7.23–7.82 m (13H, H_{arom}), 10.75 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 39.46 (Me), 52.27 (OMe), 116.50–141.94 (C_{arom}), 156.82 (CONH), 161.10 (**C**OOMe), 188.72 (4-C=O). Found, %: C 60.13; H 3.82; Br 15.52; N 8.09. $C_{26}H_{20}BrN_3O_4$. Calculated, %: C 60.24; H 3.89; Br 15.41; N 8.11.

Methyl 4-{2-[(4-bromophenyl)amino]-2-oxoacetyl}-1-(4-methylphenyl)-5-phenyl-1*H*-pyrazole-3-carboxylate (5c). Yield 25%, mp 168–170°C (from EtOH). IR spectrum, ν, cm^{-1}: 3235 (NH), 1736 (C=O, ester), 1686 (4-C=O), 1677 (CONH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.31 s (3H, Me), 3.74 s (3H, OMe), 7.20–7.85 m (13H, H_{arom}), 10.95 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 39.54 (Me), 52.30 (OMe), 116.46–146.59 (C_{arom}), 156.80 (CONH), 161.66 (**C**OOMe), 185.17 (4-C=O). Found, %: C 59.47; H 4.15; Br 15.82; N 8.24. $C_{25}H_{18}BrN_3O_4$. Calculated, %: C 59.54; H 4.13; Br 15.84; N 8.26.

Methyl 4-benzoyl-1-phenyl-5-(phenylcarbamoyl)-1*H*-pyrazole-3-carboxylate (4f). Yield 46%, mp 203–204°C (from EtOH). IR spectrum, ν, cm^{-1}: 3303 (NH), 1729 (C=O, ester), 1677 (CONH), 1642 (4-C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.63 s (3H, OMe), 7.15–7.84 m (15H, Ph), 10.77 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.30 (OMe), 116.39–141.76 (C_{arom}), 156.67 (CONH), 161.65 (**C**OOMe),

188.76 (4-C=O). Found, %: C 70.50; H 4.43; N 9.91. $C_{25}H_{19}N_3O_4$. Calculated, %: C 70.58; H 4.50; N 9.88.

Methyl 4-{2-[(4-bromophenyl)amino]-2-oxoacetyl}-1,5-diphenyl-1*H*-pyrazole-3-carboxylate (5d). Yield 35%, mp 182–183°C (from EtOH). IR spectrum, ν, cm^{-1}: 3258 (NH), 1749 (C=O, ester), 1681 (4-C=O), 1665 (CONH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.75 s (3H, OMe), 7.11–7.89 m (14H, H_{arom}), 10.76 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.28 (OMe), 118.26–146.59 (C_{arom}), 156.36 (CONH), 160.64 (**C**OOMe), 185.18 (4-C=O). Found, %: C 70.48; H 4.56; N 9.93. $C_{25}H_{19}N_3O_4$. Calculated, %: C 70.58; H 4.50; N 9.88.

Methyl 4-benzoyl-1-(4-nitrophenyl)-5-(phenylcarbamoyl)-1*H*-pyrazole-3-carboxylate (4g). Yield 71%, mp 213–214°C (from EtOH). IR spectrum, ν, cm^{-1}: 3324 (NH), 1751 (C=O, ester), 1694 (CONH), 1672 (4-C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.66 s (3H, OMe), 7.28–8.45 m (14H, H_{arom}), 10.99 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 52.55 (OMe), 116.84–147.30 (C_{arom}), 156.47 (CONH), 160.69 (**C**OOMe), 188.49 (4-C=O). Found, %: C 63.73; H 3.79; N 11.95. $C_{25}H_{18}N_4O_6$. Calculated, %: C 63.83; H 3.86; N 11.91.

Methyl 4-(4-methoxybenzoyl)-1-(4-nitrophenyl)-5-(phenylcarbamoyl)-1*H*-pyrazole-3-carboxylate (4h). A solution of 1 mmol of pyrroledione **1d** and 1 mmol of 4-nitrophenylhydrazine (**2b**) in 5 mL of anhydrous chloroform was refluxed for 1 h and evaporated to dryness. Yield 65%, mp 203–204°C (from EtOH). IR spectrum, ν, cm^{-1}: 3306 (NH), 1738 (C=O, ester), 1701 (CONH), 1679 (4-C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.65 s (3H, OMe), 3.87 s (3H, OMe), 6.96–8.06 m (13H, H_{arom}), 10.92 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 55.14 (MeO), 52.56 (COO**Me**), 116.86–145.31 (C_{arom}), 156.52 (CONH), 160.84 (**C**OOMe), 188.52 (4-C=O). Found, %: C 62.28; H 3.89; N 11.34. $C_{26}H_{20}N_4O_7$. Calculated, %: C 62.40; H 4.03; N 11.20.

This study was performed under financial support by the Ministry of Education and Science of the Russian Federation (project no. 965), by the Ministry of Education of Perm Krai (International Research Teams competition), and by the Russian Foundation for Basic Research (project no. 16-43-590613).

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