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Molecular Design of Pyrazolo[3,4-*d*]pyridazines

V. S. Matiichuk, M. A. Potopnyk, and N. D. Obushak

Ivan Franko Lviv National University, ul. Kirilla i Mefodiya 6, Lviv, 79005 Ukraine
e-mail: obushak@in.lviv.ua

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Abstract—Reactions of arenediazonium chlorides with ethyl 2-methyl- and 2-chloro-4-oxobutanoates gave, respectively, ethyl 2-(arylhydrazono)propanoates and chloro(arylhydrazono)acetates. Ethyl 2-(arylhydrazono)-propanoates reacted with the Vilsmeier–Haak reagent to give ethyl 1-aryl-4-formyl-1*H*-pyrazole-3-carboxylates. Ethyl 1-aryl-4-acetyl-5-methyl-1*H*-pyrazole-3-carboxylates were obtained by reaction of chloro(arylhydrazono)acetates with acetylacetone. Reactions of the obtained pyrazole derivatives with hydrazine and methylhydrazine led to the formation of the corresponding 3,4-R^1_2-6-R^2-2-aryl-2,6-dihydro-7*H*-pyrazolo-[3,4-*d*]pyridazin-7-ones (R^1, R^2 = H, Me) which were subjected to alkylation and sulfurization.

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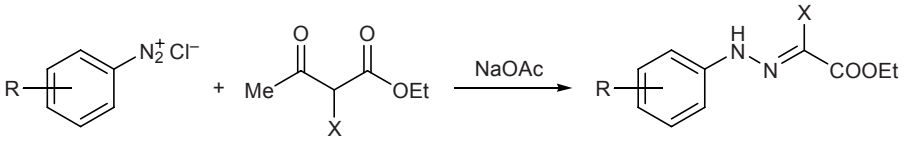
Nitrogen-containing heterocyclic compounds play an important role in organic chemistry and attract strong interest due to diversity of their chemical transformations and broad spectrum of biological activity. A key problem in the design of new heterocyclic systems is search for accessible multipurpose reagents.

In the present article we describe an efficient approach to the design of 2-aryl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one libraries using ethyl 1-aryl-4-formyl- and 1-aryl-4-acetyl-5-methyl-1*H*-pyrazole-3-carboxylates **IVa**–**IVc** and **Va**–**Vi** as initial compounds. It is known that pyrazole-3-carboxylic acid derivatives act as CB_1 cannabinoid receptor antagonists [1–6]; therefore, they are promising as potential biologically active substances.

Pyrazole ring is most frequently built up via reactions of hydrazines with functionalized carbonyl compounds [7–11]. However, this approach is not free from some limitations related to low accessibility of initial hydrazines and their toxicity. On the other hand, the corresponding hydrazones that are formed as intermediate products in the above reactions can be obtained from diazonium salts and compounds having an activated CH group according to Japp–Klingemann. As a rule, products of such reaction contain functional groups, which makes them promising as reagents for the synthesis of fused pyrazole derivatives.

As starting materials we used ethyl 2-(arylhydrazono)propionates **IIIa**–**IIIc** [12] and ethyl (arylhydrazono)chloroacetates **IIId**–**IIIl** [13] which were synthesized from the corresponding arenediazonium chlorides **Ia**–**Ij** and ethyl 2-methyl- and 2-chloro-4-oxobutanoates **IIa** and **IIb** (Scheme 1). The reactions were carried out in aqueous alcohol under mild conditions, and the products were isolated in 61–93% yield. Hydrazones **IIIa**–**IIIl** are colored crystalline substances that are stable on storage. Signals from the NN**H**Ar proton in the ^{1}H NMR spectra of these compounds

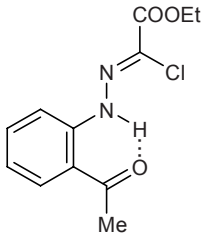
Scheme 1.



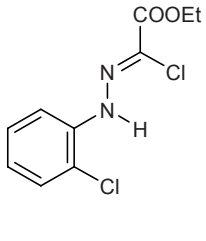
Ia–Ij **IIa**, **IIb** **IIIa–IIIl**

I, R = H (**a**), 4-F (**b**), 2-Cl (**c**), 3-Cl (**d**), 4-Cl (**e**), 3-Me (**f**), 3,4-Me_2 (**g**), 4-MeO (**h**), 3-F_3C (**i**), 2-MeOCO (**j**); **II**, X = Me (**a**), Cl (**b**); **III**, X = Me, R = H (**a**), 3-Me (**b**), 4-Cl (**c**); X = Cl, R = H (**d**), 4-F (**e**), 2-Cl (**f**), 3-Cl (**g**), 4-Cl (**h**), 3,4-Me_2 (**i**), 4-MeO (**j**), 3-F_3C (**k**), 2-MeOCO (**l**).

were observed in the region δ 9.65–9.76 (propionates **IIIa** and **IIIc**) or 10.32–10.64 ppm (chloroacetates **IIId**, **IIIe**, and **IIIg**–**IIIk**). In the spectrum of **IIIl**, the NH signal was displaced downfield, presumably as a result of intramolecular hydrogen bonding, while the corresponding signal in the spectrum of **IIIf** was observed in a stronger field due to shielding by the chlorine atom in the *ortho* position.



IIIl

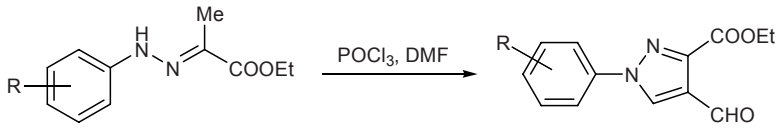


IIIf

A convenient procedure for the synthesis of pyrazole derivatives is based on the Vilsmeier–Haak reaction with methyl ketone arylhydrazones. With a few exceptions [14–17], such reactions involved arylhydrazones derived from aromatic or heteroaromatic ketones [17–23]; therefore, the synthetic potential of this approach was essentially limited. We examined reactions of hydrazones **IIIa**–**IIIc** with $POCl_3$–DMF and obtained 4-formylpyrazole-3-carboxylates **IVa**–**IVc** which may be regarded as promising building blocks for organic synthesis (Scheme 2). 4-Acetyl derivatives **Va**–**Vc** were synthesized by condensation of hydrazones **IIId**–**IIIl** with acetylacetone in the presence of sodium ethoxide [24] (Scheme 3). In the ^{1}H NMR spectra of **IVa**–**IVc**, the aldehyde proton appeared at δ 10.26–10.31 ppm, and proton in position *5* of the pyrazole ring resonated at δ 9.13–9.22 ppm. Pyrazoles **Va**–**Vi** displayed in the ^{1}H NMR spectra signals from the 5-CH_3 group and acetyl protons at δ 2.24–2.43 and 2.46–2.50 ppm, respectively.

Pyrazoles **IV** and **V** were then used to synthesize 2-aryl-1*H*-pyrazolo[3,4-*d*]pyridazin-7-ones **VIa**–**VIk** and **VIIa**–**VIIg** (Scheme 4). Compounds like **VI** and

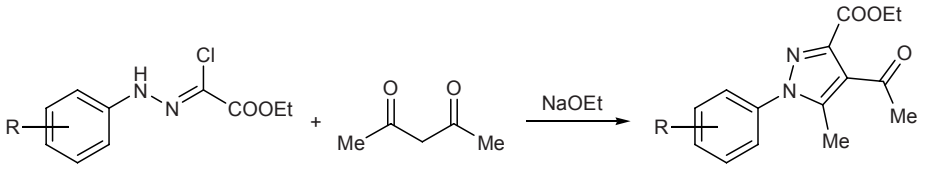
Scheme 2.



IIIa–IIIc **IVa–IVc**

R = H (**a**), 3-Me (**b**), 4-Cl (**c**).

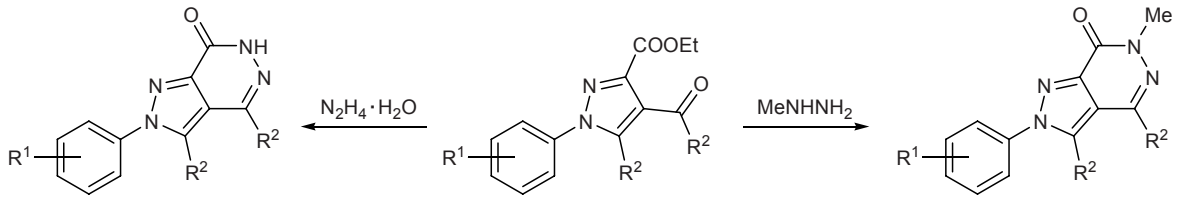
Scheme 3.



IIId–IIIl **Va–Vi**

V, R = H (**a**), 4-F (**b**), 2-Cl (**c**), 3-Cl (**d**), 4-Cl (**e**), 3,4-Me_2 (**f**), 4-MeO (**g**), 3-F_3C (**h**), 2-MeOCO (**i**).

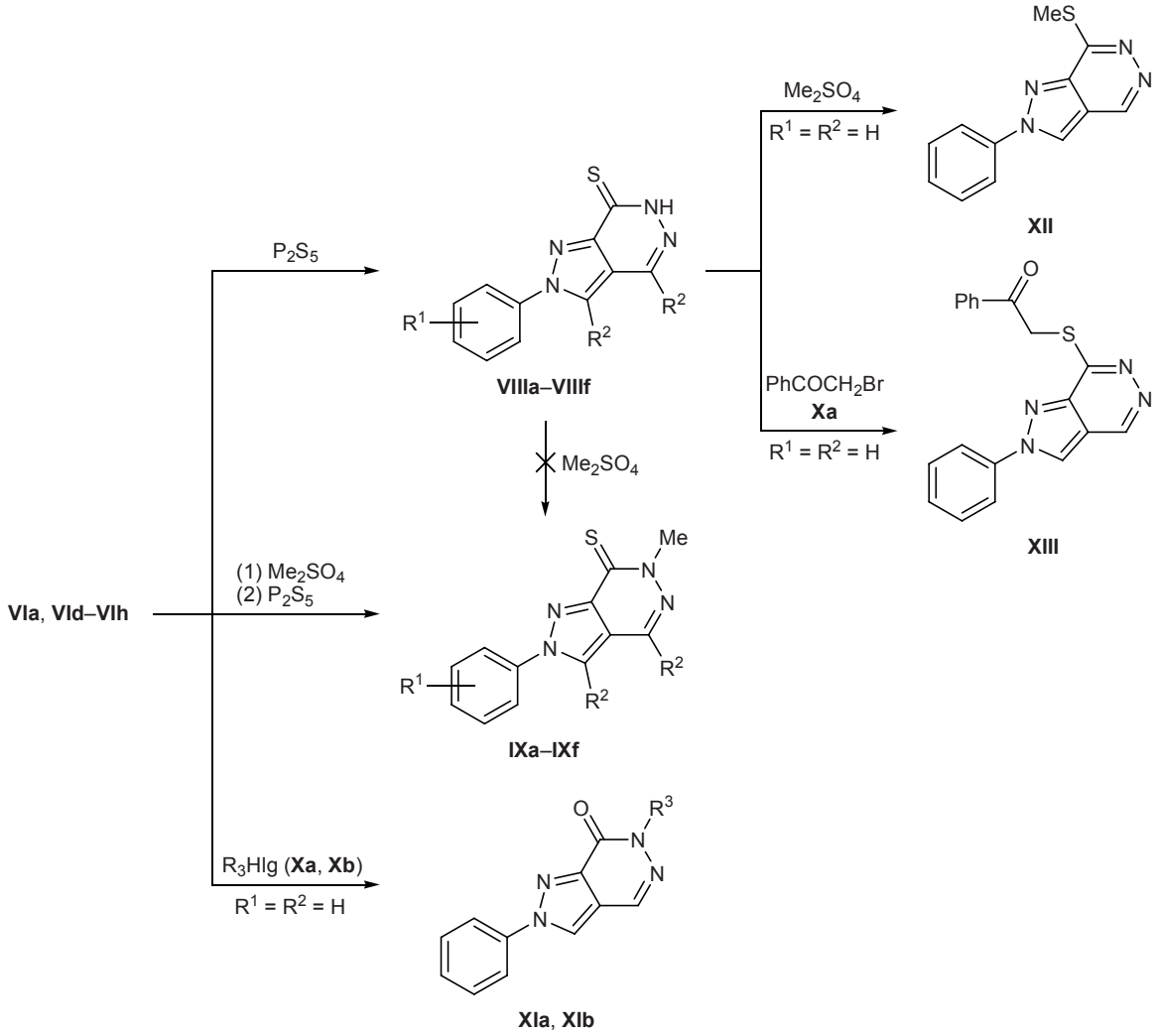
Scheme 4.



VIa–VIk **IVa**, **IVc**, **Va–Vi** **VIIa–VIIg**

VI, $R^1 = R^2$ = H (**a**); R^1 = 4-Cl, R^2 = H (**b**); R^1 = H, R^2 = Me (**c**); R^1 = 4-F, R^2 = Me (**d**); R^1 = 2-Cl, R^2 = Me (**e**); R^1 = 3-Cl, R^2 = Me (**f**); R^1 = 4-Cl, R^2 = Me (**g**); R^1 = 3,4-Me_2, R^2 = Me (**h**); R^1 = 4-MeO, R^2 = Me (**i**); R^1 = 3-F_3C, R^2 = Me (**j**); R^1 = 2-$NH_2NHC(O)$, R^2 = Me (**k**); **VII**, $R^1 = R^2$ = H (**a**); R^1 = 4-Cl, R^2 = H (**b**); R^1 = 4-F, R^2 = Me (**c**); R^1 = 2-Cl, R^2 = Me (**d**); R^1 = 3-Cl, R^2 = Me (**e**); R^1 = 4-Cl, R^2 = Me (**f**); R^1 = 3,4-Me_2, R^2 = Me (**g**).

Scheme 5.

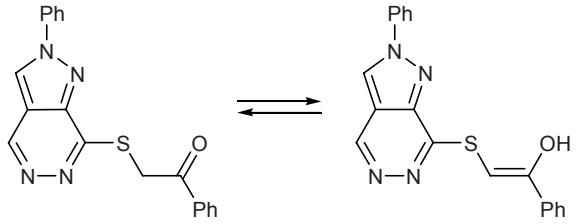


VIII, **IX**, $R^1 = R^2 = H$ (**a**); R^1 = 4-F, R^2 = Me (**b**); R^1 = 2-Cl, R^2 = Me (**c**); R^1 = 3-Cl, R^2 = Me (**d**); R^1 = 4-Cl, R^2 = Me (**e**); R^1 = 3,4-Me_2, R^2 = Me (**f**). **X**, R^3 = $PhC(O)CH_2$, Hlg = Br (**a**); R^3 = 4-$MeC_6H_4NHC(O)CH_2$, Hlg = Cl (**b**); **XI**, R^3 = $PhC(O)CH_2$ (**a**), 4-$MeC_6H_4NHC(O)CH_2$ (**b**).

VII can be obtained by reactions of aldehydo and oxo esters with hydrazine and its derivatives. In the pyrazole series, oxo esters were mostly studied. Among pyrazole derivatives, reactions with oxo esters were mainly reported [24–29]. Compounds **IV** and **V** fairly readily reacted with hydrazine and methylhydrazine to produce pyrazolopyridazines **VIa**–**VIk** and **VIIa**–**VIIg**, respectively, in 57–94% yield. The ^{1}H NMR spectra of the products contained singlets from the 3-H and 4-H protons at δ 8.25–8.26 and 9.10–9.14 ppm, respectively.

Pyrazolopyridazines **VIa**–**VIk** and **VIIa**–**VIIg** turned out to readily undergo further transformations to obtain new compounds containing the pyrazolo[3,4-*d*]pyridazine system. Their reactions with phosphorus pentasulfide gave 2-aryl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thiones **VIIIa**–**VIIIf** and **IXa**–**IXf** (Scheme 5). These reactions required fairly severe conditions, heating in boiling pyridine for 4 h. We also examined regioselectivity in the alkylation of pyrazolopyridazinones **VI** and **VII** and pyrazolopyridazinethione **VIIIa** with dimethyl sulfate, chloroacetanilide (**Xa**), and bromoacetophenone (**Xb**). The alkylation of **VI** and **VIII** was carried out by heating the reactants in boiling dioxane or DMF in the presence of a base. The reactions were selective: compounds **VI** gave rise to the corresponding N-substituted derivatives, while the alkylation of **VIIIa** occurred exclusively at the sulfur atom, and the products were isolated in high yields. By treatment of compounds **VIa** and **VId**–**VIh** with di-

methyl sulfate we obtained pyrazolopyridazines **VIIa** and **VIIc**–**VIIg** which were identical to those synthesized by cyclization of pyrazoles **IV** and **V** with methylhydrazine. Analogous reaction with pyrazolopyridazinethione **VIIIa** gave methylsulfanyl derivative **XII** rather than *N*-methyl isomer **IXa**. N-Alkylation of structurally related compounds was described in [30–32]. The ^{1}H NMR spectrum of pyrazolopyridazine **XIII** obtained by reaction of **VIIIa** with bromoacetophenone lacked signal from methylene protons, but two singlets were present at δ 6.64 and 14.71 ppm; presumably, compound **XIII** in DMSO exists in the enol form.



XIII

To conclude, we have developed convenient procedures for the synthesis of 3,4-R^1_2-6-R^2-2-aryl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-ones and 7-(R^3-sulfanyl)-2-phenyl-2*H*-pyrazolo[3,4-*d*]pyridazines in high yields from accessible starting compounds.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded from solutions in DMSO-d_6 on a Varian Mercury spectrometer (400 MHz) using TMS as internal reference.

Ethyl 2-(arylhydrazono)propionates IIIa–IIIc and ethyl (arylhydrazono)chloroacetates IIId–IIIl (*general procedure*). A solution of 0.02 mol of the corresponding aromatic amine in 8 ml of dilute (1:1) hydrochloric acid was cooled to 0°C, and a solution of 1.52 g (0.022 mol) of sodium nitrite in 10 ml of water was added dropwise under stirring. The resulting solution of diazonium salt **Ia**–**Ij** was added dropwise to a cold solution of 2.88 g (0.02 mol) of ethyl 2-methyl-4-oxobutanoate (**IIa**) or 3.29 g (0.02 mol) of 2-chloro-4-oxobutanoate (**IIb**) and 2.46 g (0.03 mol) of sodium acetate in 60 ml of aqueous ethanol (9:1). The mixture was stirred for 4 h and poured into 500 ml of water, and the precipitate was filtered off, dried, and recrystallized from ethanol.

Ethyl 2-(phenylhydrazono)propionate (IIIa). Yield 88%, mp 118°C. ^{1}H NMR spectrum, δ, ppm: 1.33 t (3H, C**H**$_3$CH$_2$, ^3J = 6.8 Hz), 2.06 s (3H, CH$_3$), 4.20 q (2H, CH$_2$O, ^3J = 6.8 Hz), 6.81–6.85 m (1H, H$_{arom}$), 7.19–7.28 m (4H, H$_{arom}$), 9.65 s (1H, NH). Found, %: C 63.77; H 6.62; N 13.42. $C_{11}H_{14}N_2O_2$. Calculated, %: C 64.06; H 6.84; N 13.58.

Ethyl 2-[(3-methylphenyl)hydrazono]propionate (IIIb). Yield 61%, mp 77°C. Found, %: C 65.22; H 7.24; N 12.84. $C_{12}H_{16}N_2O_2$. Calculated, %: C 65.43; H 7.32; N 12.72.

Ethyl 2-[(4-chlorophenyl)hydrazono]propionate (IIIc). Yield 64%, mp 127–128°C. ^{1}H NMR spectrum, δ, ppm: 1.32 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.05 s (3H, CH$_3$), 4.20 q (2H, CH$_2$O, ^3J = 7.2 Hz), 7.19 d (2H, H$_{arom}$, ^3J = 8.8 Hz), 7.26 d (2H, H$_{arom}$, ^3J = 8.8 Hz), 9.76 s (1H, NH). Found, %: C 54.46; H 5.32; N 11.65. $C_{11}H_{13}ClN_2O_2$. Calculated, %: C 54.89; H 5.44; N 11.64.

Ethyl chloro(phenylhydrazono)acetate (IIId). Yield 65%, mp 77°C. ^{1}H NMR spectrum, δ, ppm: 1.36 t (3H, CH$_3$, ^3J = 7.2 Hz), 4.30 q (2H, CH$_2$, ^3J = 7.2 Hz), 6.94 t (1H, H$_{arom}$, ^3J = 7.6 Hz), 7.26 t (2H, H$_{arom}$, ^3J = 7.6 Hz), 7.37 d (2H, H$_{arom}$, ^3J = 7.6 Hz), 10.32 s (1H, NH). Found, %: C 52.72; H 4.75; N 12.07. $C_{10}H_{11}ClN_2O_2$. Calculated, %: C 52.99; H 4.89; N 12.36.

Ethyl chloro[(4-fluorophenyl)hydrazono]acetate (IIIe). Yield 77%, mp 109°C. ^{1}H NMR spectrum, δ, ppm: 1.36 t (3H, CH$_3$, ^3J = 6.8 Hz), 4.30 q (2H, CH$_2$, ^3J = 6.8 Hz), 7.02 t (2H, H$_{arom}$, ^3J = 8.8 Hz), 7.37 d.d (2H, H$_{arom}$, J_{HH} = 8.8, J_{HF} = 4.8 Hz), 10.37 s (1H, NH). Found, %: C 48.96; H 3.95; N 11.53. $C_{10}H_{10}ClFN_2O_2$. Calculated, %: C 49.09; H 4.12; N 11.45.

Ethyl chloro[(2-chlorophenyl)hydrazono]acetate (IIIf). Yield 89%, mp 90°C. ^{1}H NMR spectrum, δ, ppm: 1.38 t (3H, CH$_3$, ^3J = 7.2 Hz), 4.34 q (2H, CH$_2$, ^3J = 7.2 Hz), 7.03 d.t (1H, H$_{arom}$, ^4J = 1.2, ^3J = 8.0 Hz), 7.33 d.t (1H, H$_{arom}$, ^4J = 1.2, ^3J = 8.0 Hz), 7.40 d.d (1H, H$_{arom}$, ^4J = 1.2, ^3J = 8.0 Hz), 7.55 d.d (1H, H$_{arom}$, ^4J = 1.2, ^3J = 8.0 Hz), 8.86 s (1H, NH). Found, %: C 46.23; H 3.69; N 10.55. $C_{10}H_{10}Cl_2N_2O_2$. Calculated, %: C 46.00; H 3.86; N 10.73.

Ethyl chloro[(3-chlorophenyl)hydrazono]acetate (IIIg). Yield 72%, mp 96°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, CH$_3$, ^3J = 7.2 Hz), 4.31 q (2H, CH$_2$, ^3J = 7.2 Hz), 6.92 d (1H, H$_{arom}$, ^3J = 8.0 Hz), 7.24 t (1H, H$_{arom}$, ^3J = 8.0 Hz), 7.30 d (1H, H$_{arom}$, ^3J = 8.0 Hz), 7.37 s (1H, H$_{arom}$), 10.48 s (1H, NH). Found, %: C 45.77; H 3.84; N 10.59. $C_{10}H_{10}Cl_2N_2O_2$. Calculated, %: C 46.00; H 3.86; N 10.73.

Ethyl chloro[(4-chlorophenyl)hydrazono]acetate (IIIh). Yield 75%, mp 143–145°C. ^{1}H NMR spectrum, δ, ppm: 1.36 t (3H, CH_3, ^3J = 7.2 Hz), 4.30 q (2H, CH_2, ^3J = 7.2 Hz), 7.25 d (2H, H_{arom}, ^3J = 8.4 Hz), 7.36 d (2H, H_{arom}, ^3J = 8.4 Hz), 10.44 s (1H, NH). Found, %: C 45.89; H 3.67; N 10.57. $C_{10}H_{10}Cl_2N_2O_2$. Calculated, %: C 46.00; H 3.86; N 10.73.

Ethyl chloro[(3,4-dimethylphenyl)hydrazono]-acetate (IIIi). Yield 70%, mp 96°C. ^{1}H NMR spectrum, δ, ppm: 1.28 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.17 s (3H, CH_3), 2.19 s (3H, CH_3), 4.27 q (2H, CH_2O, ^3J = 7.2 Hz), 7.06 br.s (2H, H_{arom}), 7.14 s (1H, H_{arom}), 10.36 s (1H, NH). Found, %: C 56.42; H 5.84; N 10.79. $C_{12}H_{15}ClN_2O_2$. Calculated, %: C 56.59; H 5.94; N 11.00.

Ethyl chloro[(4-methoxyphenyl)hydrazono]acetate (IIIj). Yield 72%, mp 94°C. ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 3.71 s (3H, CH_3O), 4.27 q (2H, CH_2O, ^3J = 7.2 Hz), 6.91 d (2H, H_{arom}, ^3J = 7.6 Hz), 7.28 d (2H, H_{arom}, ^3J = 7.6 Hz), 10.40 s (1H, NH). Found, %: C 51.23; H 5.01; N 10.74. $C_{11}H_{13}ClN_2O_3$. Calculated, %: C 51.47; H 5.10; N 10.91.

Ethyl chloro[(3-trifluoromethylphenyl)hydrazono]acetate (IIIk). Yield 80%, mp 131–133°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, CH_3, ^3J = 7.2 Hz), 4.31 q (2H, CH_2, ^3J = 7.2 Hz), 7.21 d (1H, H_{arom}, ^3J = 8.0 Hz), 7.46 t (1H, H_{arom}, ^3J = 8.0 Hz), 7.62 d (1H, H_{arom}, ^3J = 8.0 Hz), 7.66 s (1H, H_{arom}), 10.64 s (1H, NH). Found, %: C 44.51; H 3.38; N 9.37. $C_{11}H_{10}ClF_3N_2O_2$. Calculated, %: C 44.84; H 3.42; N 9.51.

Methyl 2-[2-(1-chloro-2-ethoxy-2-oxoethylidene)-hydrazino]benzoate (IIIl). Yield 93%, mp 105–106°C. ^{1}H NMR spectrum, δ, ppm: 1.38 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 3.93 s (3H, OCH_3), 4.34 q (2H, CH_2O, ^3J = 7.2 Hz), 7.04 t (1H, H_{arom}, ^3J = 8.0 Hz), 7.59 t (1H, H_{arom}, ^3J = 8.0 Hz), 7.70 d (1H, H_{arom}, ^3J = 8.0 Hz), 7.96 d (1H, H_{arom}, ^3J = 8.0 Hz), 11.71 s (1H, NH). Found, %: C 50.75; H 4.49; N 9.64. $C_{12}H_{13}ClN_2O_4$. Calculated, %: C 50.63; H 4.60; N 9.84.

Ethyl 1-aryl-4-formyl-1*H*-pyrazole-3-carboxylates IVa–IVc (*general procedure*). Phosphoryl chloride, 1.8 ml (0.02 mol), was added under stirring to 1.6 ml of dimethylformamide cooled to 0°C. The mixture was stirred for 0.5 h at that temperature, a solution of 0.01 mol ethyl 2-(arylhydrazono)propionate **IIIa**–**IIIc** in 5 ml of DMF was added, and the mixture was stirred for 1 h at 0 to 10°C and for 4 h at 70°C. The mixture was cooled, poured onto 20 g of ice, and neutralized with solid potassium carbonate. The precipitate was filtered off, dried, and recrystallized from ethanol.

Ethyl 4-formyl-1-phenyl-1*H*-pyrazole-3-carboxylate (IVa). Yield 85%, mp 98°C. ^{1}H NMR spectrum, δ, ppm: 1.42 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 4.42 q (2H, CH_2O, ^3J = 7.2 Hz), 7.40 t (1H, H_{arom}, ^3J = 7.8 Hz) 7.51 t (2H, H_{arom}, ^3J = 7.8 Hz), 7.98 d (2H, H_{arom}, ^3J = 7.8 Hz), 9.17 s (1H, 5-H), 10.31 s (1H, CHO). Found, %: C 63.67; H 4.84; N 11.32. $C_{13}H_{12}N_2O_3$. Calculated, %: C 63.93; H 4.95; N 11.47.

Ethyl 4-formyl-1-(3-methylphenyl)-1*H*-pyrazole-3-carboxylate (IVb). Yield 73%, mp 96–97°C. ^{1}H NMR spectrum, δ, ppm: 1.43 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.44 s (3H, CH_3), 4.43 q (2H, CH_2O, ^3J = 7.2 Hz), 7.21 d (1H, H_{arom}, ^3J = 8.0 Hz), 7.38 t (1H, H_{arom}, ^3J = 8.0 Hz), 7.76 d (1H, H_{arom}, ^3J = 8.0 Hz), 7.81 s (1H, H_{arom}), 9.13 s (1H, C^{5}H), 10.31 s (1H, CHO). Found, %: C 64.93; H 5.31; N 10.76. $C_{14}H_{14}N_2O_3$. Calculated, %: C 65.11; H 5.46; N 10.85.

Ethyl 1-(4-chlorophenyl)-4-formyl-1*H*-pyrazole-3-carboxylate (IVc). Yield 68%, mp 127–128°C. ^{1}H NMR spectrum, δ, ppm: 1.34 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 4.39 q (2H, CH_2O, ^3J = 7.2Hz), 7.60 d (2H, H_{arom}, ^3J = 8.0 Hz), 7.98 d (2H, H_{arom}, ^3J = 8.0 Hz), 9.22 s (1H, 5-H), 10.26 s (1H, CHO). Found, %: C 55.89; H 3.83; N 10.11. $C_{13}H_{11}ClN_2O_3$. Calculated, %: C 56.03; H 3.98; N 10.05.

Ethyl 1-aryl-4-acetyl-5-methyl-1*H*-pyrazole-3-carboxylates Va–Vi (*general procedure*). Acetylacetone, 5.2 ml (0.05 mol), was added to a solution of 3.4 g (0.05 mol) of sodium ethoxide in 40 ml of anhydrous ethanol, the mixture was kept for 7 h at room temperature, 0.05 mol of finely powdered ethyl (arylhydrazono)chloroacetate **IIId**–**IIIl** was added, and the mixture was stirred for 4 h, left to stand for 18 h at room temperature, and diluted with 200 ml of water. The precipitate was filtered off, dried, and recrystallized from ethanol.

Ethyl 4-acetyl-5-methyl-1-phenyl-1*H*-pyrazole-3-carboxylate (Va). Oily substance. Yield 65%. Found, %: C 68.35; H 6.01; N 10.20. $C_{15}H_{16}N_2O_3$. Calculated, %: C 66.16; H 5.92; N 10.29.

Ethyl 4-acetyl-1-(4-fluorophenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (Vb). Yield 75%, mp 90–91°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.39 s (3H, CH_3), 2.47 s (3H, CH_3), 4.36 q (2H, CH_2O, ^3J = 7.2 Hz), 7.33 pseudotriplet

(2H, H_{arom}), 7.53–7.59 m (2H, H_{arom}). Found, %: C 61.82; H 5.23; N 9.49. $C_{15}H_{15}FN_2O_3$. Calculated, %: C 62.06; H 5.21; N 9.65.

Ethyl 4-acetyl-1-(2-chlorophenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (Vc). Yield 67%, mp 83–84°C. ^{1}H NMR spectrum, δ, ppm: 1.38 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.24 s (3H, CH_3), 2.50 s (3H, CH_3), 4.36 q (2H, CH_2O, ^3J = 7.2 Hz), 7.55–7.69 m (4H, H_{arom}). Found, %: C 58.56; H 4.85; N 9.02. $C_{15}H_{15}ClN_2O_3$. Calculated, %: C 58.73; H 4.93; N 9.13.

Ethyl 4-acetyl-1-(3-chlorophenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (Vd). Yield 77%, mp 67°C. ^{1}H NMR spectrum, δ, ppm: 1.38 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.43 s (3H, CH_3), 2.47 s (3H, CH_3), 4.36 q (2H, CH_2O, ^3J = 7.2 Hz), 7.49–7.61 m (4H, H_{arom}). Found, %: C 58.69; H 4.86; N 9.01. $C_{15}H_{15}ClN_2O_3$. Calculated, %: C 58.73; H 4.93; N 9.13.

Ethyl 4-acetyl-1-(4-chlorophenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (Ve). Yield 57%, mp 91°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.41 s (3H, CH_3), 2.46 s (3H, CH_3), 4.36 q (2H, CH_2O, ^3J = 7.2 Hz), 7.57 br.s (4H, H_{arom}). Found, %: C 58.51; H 4.80; N 9.05. $C_{15}H_{15}ClN_2O_3$. Calculated, %: C 58.73; H 4.93; N 9.13.

Ethyl 4-acetyl-1-(3,4-dimethylphenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (Vf). Yield 83%, mp 112–114°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.33 s (6H, CH_3), 2.36 s (3H, CH_3), 2.45 s (3H, CH_3), 4.35 q (2H, CH_2O, ^3J = 7.2 Hz), 7.18 d.d (1H, H_{arom}, ^3J = 8.0, ^4J = 2.0 Hz), 7.25 d (1H, H_{arom}, ^4J = 2.0 Hz), 7.30 d (1H, H_{arom}, ^3J = 8.0 Hz). Found, %: C 67.85; H 6.53; N 9.13. $C_{17}H_{20}N_2O_3$. Calculated, %: C 67.98; H 6.71; N 9.33.

Ethyl 4-acetyl-1-(4-methoxyphenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (Vg). Yield 65%, mp 74°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.36 s (3H, CH_3), 2.46 s (3H, CH_3), 3.86 s (3H, CH_3O), 4.35 q (2H, CH_2O, ^3J = 7.2 Hz), 7.06 d (2H, H_{arom}, ^3J = 8.8 Hz), 7.40 d (2H, H_{arom}, ^3J = 8.8 Hz). Found, %: C 63.65; H 5.84; N 9.10. $C_{16}H_{18}N_2O_4$. Calculated, %: C 63.57; H 6.00; N 9.27.

Ethyl 4-acetyl-5-methyl-1-(3-trifluoromethylphenyl)-1*H*-pyrazole-3-carboxylate (Vh). Yield 76%, mp 70°C. ^{1}H NMR spectrum, δ, ppm: 1.39 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.44 s (3H, CH_3), 2.47 s (3H, CH_3), 4.37 q (2H, CH_2, ^3J = 7.2 Hz), 7.78–7.88 m (4H, H_{arom}). Found, %: C 56.74; H 5.38; N 8.16. $C_{16}H_{15}F_3N_2O_3$. Calculated, %: C 56.47; H 4.44; N 8.23.

Ethyl 4-acetyl-1-(2-methoxycarbonylphenyl)-5-methyl-1*H*-pyrazole-3-carboxylate (Vi). Yield 57%, mp 93–95°C. ^{1}H NMR spectrum, δ, ppm: 1.37 t (3H, C**H**$_3$CH$_2$, ^3J = 7.2 Hz), 2.24 s (3H, CH_3), 2.50 s (3H, CH_3), 3.68 s (3H, CH_3O), 4.34 q (2H, CH_2O, ^3J = 7.2 Hz), 7.54 d (1H, H_{arom}, ^3J = 7.6 Hz), 7.71 t (1H, H_{arom}, ^3J = 7.6 Hz), 7.80 t (1H, H_{arom}, ^3J = 7.6 Hz), 8.03 d (1H, H_{arom}, ^3J = 7.6 Hz). Found, %: C 61.88; H 5.22; N 8.45. $C_{17}H_{18}N_2O_5$. Calculated, %: C 61.81; H 5.49; N 8.48.

2-Aryl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-ones VIa–VIk and VIIa–VIIg (*general procedure*). A solution of 0.01 mol of pyrazole **IVa–IVc** or **Va–Vi** in 20 ml of ethanol was mixed with 1.46 ml (0.03 mol) of hydrazine hydrate or 0.80 ml (0.015 mol) of methylhydrazine. The mixture was heated for 5 h under reflux and cooled, and the precipitate was filtered off, dried, and recrystallized from DMF.

2-Phenyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIa). Yield 58%, mp 259–260°C. ^{1}H NMR spectrum, δ, ppm: 7.47 t (1H, H_{arom}, ^3J = 7.6 Hz), 7.58 t (2H, H_{arom}, ^3J = 7.6 Hz), 8.04 d (2H, H_{arom}, ^3J = 7.6 Hz), 8.26 s (1H, 4-H), 9.11 s (1H, 3-H), 12.26 s (1H, NH). Found, %: C 62.32; H 3.68; N 26.26. $C_{11}H_8N_4O$. Calculated, %: C 62.26; H 3.80; N 26.40.

2-(4-Chlorophenyl)-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIb). Yield 67%, mp 351°C. ^{1}H NMR spectrum, δ, ppm: 7.59 d (2H, H_{arom}, ^3J = 8.4 Hz), 8.09 d (2H, H_{arom}, ^3J = 8.4 Hz), 8.25 s (1H, 4-H), 9.14 s (1H, 3-H), 12.27 s (1H, NH). Found, %: C 53.30; H 2.69; N 22.86. $C_{11}H_7ClN_4O$. Calculated, %: C 53.57; H 2.86; N 22.71.

3,4-Dimethyl-2-phenyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIc). Yield 72%, mp >300°C. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 2.63 s (3H, CH_3), 7.55–7.60 m (5H, H_{arom}), 11.87 s (1H, NH). Found, %: C 64.68; H 4.95; N 23.12. $C_{13}H_{12}N_4O$. Calculated, %: C 64.99; H 5.03; N 23.32.

2-(4-Fluorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VId). Yield 90%, mp 318°C. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 2.62 s (3H, CH_3), 7.36 pseudotriplet (2H, H_{arom}), 7.62–7.67 m (2H, H_{arom}), 11.85 s (1H, NH). Found, %: C 60.51; H 4.17; N 21.78. $C_{13}H_{11}FN_4O$. Calculated, %: C 60.46; H 4.29; N 21.69.

2-(2-Chlorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIe). Yield 77%, mp 336–338°C. ^{1}H NMR spectrum, δ, ppm: 2.46 s (3H, CH_3), 2.49 s (3H, CH_3), 7.57–7.73 m (4H,

H_{arom}), 11.92 s (1H, NH). Found, %: C 56.69; H 3.97; N 20.31. $C_{13}H_{11}ClN_4O$. Calculated, %: C 56.84; H 4.04; N 20.39.

2-(3-Chlorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIf). Yield 84%, mp 267–269°C. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 2.66 s (3H, CH_3), 7.56–7.65 m (3H, H_{arom}), 7.69 br.s (1H, H_{arom}), 11.88 s (1H, NH). Found, %: C 56.58; H 3.92; N 20.33. $C_{13}H_{11}ClN_4O$. Calculated, %: C 56.84; H 4.04; N 20.39.

2-(4-Chlorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIg). Yield 79%, mp 295–297°C. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 2.64 s (3H, CH_3), 7.62–7.64 m (4H, H_{arom}), 11.88 s (1H, NH). Found, %: C 56.96; H 3.90; N 20.31. $C_{13}H_{11}ClN_4O$. Calculated, %: C 56.84; H 4.04; N 20.39.

2-(3,4-Dimethylphenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIh). Yield 90%, mp >300°C. ^{1}H NMR spectrum, δ, ppm: 2.36 s (6H, CH_3), 2.50 s (3H, CH_3), 2.62 s (3H, CH_3), 7.24–7.28 m (1H, H_{arom}), 7.32–7.36 m (2H, H_{arom}), 11.86 s (1H, NH). Found, %: C 67.32; H 5.97; N 20.70. $C_{15}H_{16}N_4O$. Calculated, %: C 67.15; H 6.01; N 20.88.

2-(4-Methoxyphenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIi). Yield 89%, mp 292–293°C. ^{1}H NMR spectrum, δ, ppm: 2.50 s (3H, CH_3), 2.61 s (3H, CH_3), 3.88 s (3H, CH_3O), 7.10 d (2H, H_{arom}, ^3J = 8.4 Hz), 7.47 d (2H, H_{arom}, ^3J = 8.4 Hz), 11.83 s (1H, NH). Found, %: C 61.92; H 5.20; N 20.61. $C_{14}H_{14}N_4O_2$. Calculated, %: C 62.21; H 5.22; N 20.73.

3,4-Dimethyl-2-(3-trifluoromethylphenyl)-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIj). Yield 67%, mp 241–242°C. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 2.66 s (3H, CH_3), 7.84–7.95 m (4H, H_{arom}), 11.92 s (1H, NH). Found, %: C 54.74; H 3.46; N 18.11. $C_{14}H_{11}F_3N_4O$. Calculated, %: C 54.55; H 3.60; N 18.17.

2-(3,4-Dimethyl-7-oxo-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyridazin-2-yl)benzohydrazide (VIk). Yield 64%, mp 298–299°C. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 3.12 s (3H, CH_3), 4.21 s (2H, NHN**H**$_2$), 7.46 d (1H, H_{arom}, ^3J = 7.6 Hz), 7.64–7.69 m (3H, H_{arom}), 9.70 s (1H, N**H**NH_2), 11.84 s (1H, NH). Found, %: C 56.21; H 4.62; N 28.02. $C_{14}H_{14}N_6O_2$. Calculated, %: C 56.37; H 4.73; N 28.17.

6-Methyl-2-phenyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIIa). Yield 86%, mp 194–195°C. ^{1}H NMR spectrum, δ, ppm: 3.71 s (3H, CH_3), 7.45 t (1H, H_{arom}, ^3J = 7.6 Hz), 7.56 t (2H, H_{arom}, ^3J = 7.6 Hz), 8.02 d (2H, H_{arom}, ^3J = 7.6 Hz), 8.26 s (1H, 4-H), 9.10 s (1H, 3-H). Found, %: C 63.86; H 4.34; N 24.53. $C_{12}H_{10}N_4O$. Calculated, %: C 63.71; H 4.46; N 24.76.

2-(4-Chlorophenyl)-6-methyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIIb). Yield 70%, mp 293–295°C. ^{1}H NMR spectrum, δ, ppm: 3.72 s (3H, CH_3), 7.58 d (2H, H_{arom}, ^3J = 8.4 Hz), 8.08 d (2H, H_{arom}, ^3J = 8.4 Hz), 8.25 s (1H, 4-H), 9.13 s (1H, 3-H). Found, %: C 55.19; H 3.38; N 21.32. $C_{12}H_9ClN_4O$. Calculated, %: C 55.29; H 3.48; N 21.49.

2-(4-Fluorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIIc). Yield 73%, mp 225–227°C. ^{1}H NMR spectrum, δ, ppm: 2.49 s (3H, CH_3), 2.61 s (3H, CH_3), 3.62 s (3H, CH_3N), 7.36 pseudotriplet (2H, H_{arom}), 7.61–7.66 m (2H, H_{arom}). Found, %: C 61.81; H 4.69; N 20.41. $C_{14}H_{13}FN_4O$. Calculated, %: C 61.76; H 4.81; N 20.58.

2-(2-Chlorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIId). Yield 57%, mp 255–257°C. ^{1}H NMR spectrum, δ, ppm: 2.47 s (3H, CH_3), 2.52 s (3H, CH_3), 3.64 s (3H, CH_3N), 7.58–7.75 m (4H, H_{arom}). Found, %: C 58.35; H 4.48; N 19.19. $C_{14}H_{13}ClN_4O$. Calculated, %: C 58.24; H 4.54; N 19.40.

2-(3-Chlorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIIe). Yield 64%, mp 275–277°C. ^{1}H NMR spectrum, δ, ppm: 2.52 s (3H, CH_3), 2.67 s (3H, CH_3), 3.64 s (3H, CH_3N), 7.56–7.65 m (3H, H_{arom}), 7.68 br.s (1H, H_{arom}). Found, %: C 57.98; H 4.43; N 19.45. $C_{14}H_{13}ClN_4O$. Calculated, %: C 58.24; H 4.54; N 19.40.

2-(4-Chlorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIIf). Yield 94%, mp 268–270°C. ^{1}H NMR spectrum, δ, ppm: 2.50 s (3H, CH_3), 2.64 s (3H, CH_3), 3.63 s (3H, CH_3N), 7.62 br.s (4H, H_{arom}). Found, %: C 58.41; H 4.43; N 19.24. $C_{14}H_{13}ClN_4O$. Calculated, %: C 58.24; H 4.54; N 19.40.

2-(3,4-Dimethylphenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (VIIg). Yield 88%, mp 224–225°C. ^{1}H NMR spectrum, δ, ppm: 2.35 s (6H, CH_3), 2.49 s (3H, CH_3), 2.61 s (3H, CH_3), 3.63 s (3H, CH_3N), 7.22–7.26 m (1H, H_{arom}), 7.30–7.33 m (2H, H_{arom}). Found, %: C 67.82; H 6.31; N 19.56. $C_{16}H_{18}N_4O$. Calculated, %: C 68.06; H 6.43; N 19.84.

2-Aryl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thiones VIIIa–VIIIf and IXa–IXf (*general procedure*). A mixture of 0.007 mol of compound **VIa**, **VId–VIh**, **VIIa**, or **VIIc–VIIg**, 4.66 g (0.021 mol) of P_2S_5, and 30 ml of pyridine was heated for 4 h. The mixture was cooled and diluted with 200 ml of water, and the precipitate was filtered off, dried, and recrystallized from DMF.

2-Phenyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (VIIIa). Yield 80%, mp 255–256°C. ^{1}H NMR spectrum, δ, ppm: 7.49 t (1H, H_{arom}, ^3J = 8.0 Hz), 7.58 t (2H, H_{arom}, ^3J = 8.0 Hz), 8.08 d (2H, H_{arom}, ^3J = 8.0 Hz), 8.66 s (1H, 4-H), 9.23 s (1H, 3-H), 13.89 s (1H, NH). Found, %: C 57.75; H 3.45; N 24.31; S 14.19. $C_{11}H_8N_4S$. Calculated, %: C 57.88; H 3.53; N 24.54; S 14.05.

2-(4-Fluorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (VIIIb). Yield 69%, mp >350°C. ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 2.67 s (3H, CH_3), 7.37–7.42 m (2H, H_{arom}), 7.67–7.70 m (2H, H_{arom}), 13.61 s (1H, NH). Found, %: C 56.75; H 3.98; N 20.20; S 11.80. $C_{13}H_{11}FN_4S$. Calculated, %: C 56.92; H 4.04; N 20.42; S 11.69.

2-(2-Chlorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (VIIIc). Yield 82%, mp >350°C. ^{1}H NMR spectrum, δ, ppm: 2.52 s (3H, CH_3), 2.60 s (3H, CH_3), 7.60–7.75 m (4H, H_{arom}), 13.64 s (1H, NH). Found, %: C 53.81; H 3.68; N 19.04; S 11.12. $C_{13}H_{11}ClN_4S$. Calculated, %: C 53.70; H 3.81; N 19.27; S 11.03.

2-(3-Chlorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (VIIId). Yield 84%, mp 315°C. ^{1}H NMR spectrum, δ, ppm: 2.77 s (3H, CH_3), 2.93 s (3H, CH_3), 7.59–7.65 m (2H, H_{arom}), 7.72 br.s (1H, H_{arom}), 7.91 s (1H, H_{arom}), 13.65 s (1H, NH). Found, %: C 53.95; H 3.72; N 19.06; S 11.25. $C_{13}H_{11}ClN_4S$. Calculated, %: C 53.70; H 3.81; N 19.27; S 11.03.

2-(4-Chlorophenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (VIIIe). Yield 89%, mp >350°C. ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 2.69 s (3H, CH_3), 7.64 d (2H, H_{arom}, ^3J = 8.6 Hz), 7.68 d (2H, H_{arom}, ^3J = 8.6 Hz), 13.63 s (1H, NH). Found, %: C 53.84; H 3.69; N 19.10; S 11.21. $C_{13}H_{11}ClN_4S$. Calculated, %: C 53.70; H 3.81; N 19.27; S 11.03.

2-(3,4-Dimethylphenyl)-3,4-dimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (VIIIf). Yield 84%, mp 337–338°C. ^{1}H NMR spectrum, δ, ppm: 2.36 s (6H, CH_3), 2.57 s (3H, CH_3), 2.65 s (3H, CH_3), 7.29–7.35 m (3H, H_{arom}), 13.57 s (1H, NH). Found, %: C 63.42; H 5.52; N 19.58; S 11.39. $C_{15}H_{16}N_4S$. Calculated, %: C 63.35; H 5.67; N 19.70; S 11.28.

6-Methyl-2-phenyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (IXa). Yield 76%, mp 186°C. ^{1}H NMR spectrum, δ, ppm: 4.15 s (3H, CH_3), 7.48 t (1H, H_{arom}, ^3J = 7.2 Hz), 7.58 t (2H, H_{arom}, ^3J = 7.2 Hz), 8.08 d (2H, H_{arom}, ^3J = 7.2 Hz), 8.66 s (1H, 4-H), 9.22 s (1H, 3-H). Found, %: C 59.58; H 4.05; N 22.84; S 13.07. $C_{12}H_{10}N_4S$. Calculated, %: C 59.48; H 4.16; N 23.12; S 13.23.

2-(4-Fluorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (IXb). Yield 71%, mp 222–223°C. ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 2.66 s (3H, CH_3), 4.08 s (3H, CH_3N), 7.37 pseudotriplet (2H, H_{arom}), 7.66 d.d (2H, H_{arom}, J_{HH} = 8.4, J_{HF} = 4.8 Hz). Found, %: C 58.43; H 4.41; N 19.22; S 10.98. $C_{14}H_{13}FN_4S$. Calculated, %: C 58.32; H 4.54; N 19.43; S 11.12.

2-(2-Chlorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (IXc). Yield 85%, mp 246–248°C. ^{1}H NMR spectrum, δ, ppm: 2.51 s (3H, CH_3), 2.61 s (3H, CH_3), 4.09 s (3H, CH_3N), 7.62–7.73 m (4H, H_{arom}). Found, %: C 55.02; H 4.18; N 18.16; S 10.35. $C_{14}H_{13}ClN_4S$. Calculated, %: C 55.17; H 4.30; N 18.38; S 10.52.

2-(4-Chlorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (IXd). Yield 72%, mp 245–247°C. ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 2.69 s (3H, CH_3), 4.08 s (3H, CH_3N), 7.59–7.69 m (4H, H_{arom}). Found, %: C 55.21; H 4.20; N 18.08; S 10.39. $C_{14}H_{13}ClN_4S$. Calculated, %: C 55.17; H 4.30; N 18.38; S 10.52.

2-(4-Chlorophenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (IXe). Yield 87%, mp 263–265°C. ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 2.68 s (3H, CH_3), 4.08 s (3H, CH_3N), 7.60 d (2H, H_{arom}, ^3J = 8.4 Hz), 7.64 d (2H, H_{arom}, ^3J = 8.4 Hz). Found, %: C 54.94; H 4.21; N 18.15; S 10.40. $C_{14}H_{13}ClN_4S$. Calculated, %: C 55.17; H 4.30; N 18.38; S 10.52.

2-(3,4-Dimethylphenyl)-3,4,6-trimethyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazine-7-thione (IXf). Yield 86%, mp 216–217°C. ^{1}H NMR spectrum, δ, ppm: 2.35 s (6H, CH_3), 2.59 s (3H, CH_3), 2.65 s (3H, CH_3), 4.08 s (3H, CH_3N), 7.28–7.33 m (3H, H_{arom}).

Found, %: C 64.23; H 5.95; N 18.62; S 10.51. $C_{16}H_{18}N_4S$. Calculated, %: C 64.40; H 6.08; N 18.77; S 10.74.

2-Aryl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-ones VIIa, VIIc–VIIg, XIa, and XIb (*general procedure*). *a*. A mixture of 3.5 mmol of pyrazolopyridazine **VIa** or **VId–VIh**, 0.4 ml (4.2 mmol) of dimethyl sulfate, 0.14 g (3.5 mmol) of NaOH dissolved in 1 ml of water, and 10 ml of dioxane was stirred for 4 h at 100°C. The mixture was cooled and poured into 50 ml of water, and the precipitate was filtered off, dried, and recrystallized from DMF. Compounds **VIIa** and **VIIc–VIIg** thus obtained were identical to samples prepared as described above in the ^{1}H NMR data and melting points; their elemental analyses were consistent with the calculated values.

b. A mixture of 1 g (4.7 mmol) of pyrazolopyridazine **VIa**, 4.7 mmol of halogen derivative **Xa** or **Xb**, 0.65 g (4.7 mmol) of potassium carbonate, and 40 ml of anhydrous DMF or dioxane was stirred for 4 h at 100°C. The mixture was cooled and poured into 200 ml of water, and the precipitate was filtered off, dried, and recrystallized from DMF.

6-(2-Oxo-2-phenylethyl)-2-phenyl-2,6-dihydro-7*H*-pyrazolo[3,4-*d*]pyridazin-7-one (XIa). Yield 54%, mp 222–224°C. ^{1}H NMR spectrum, δ, ppm: 5.65 s (2H, CH_2), 7.48 t (1H, H_{arom}, ^3J = 7.2 Hz), 7.55 t (2H, H_{arom}, ^3J = 7.6 Hz), 7.59 t (2H, H_{arom}, ^3J = 8.0 Hz), 7.67 t (1H, H_{arom}, ^3J = 7.2 Hz), 8.05 d (2H, H_{arom}, ^3J = 8.0 Hz), 8.08 d (2H, H_{arom}, ^3J = 7.6 Hz), 8.36 s (1H, 4-H), 9.18 s (1H, 3-H). Found, %: C 68.93; H 4.15; N 16.75. $C_{19}H_{14}N_4O_2$. Calculated, %: C 69.08; H 4.27; N 16.96.

***N*-(4-Methylphenyl)-2-(7-oxo-2-phenyl-2,7-dihydro-6*H*-pyrazolo[3,4-*d*]pyridazin-6-yl)acetamide (XIb).** Yield 60%, mp >320°C. ^{1}H NMR spectrum, δ, ppm: 2.29 s (3H, CH_3), 4.89 s (2H, CH_2), 7.07 br.s (2H, H_{arom}), 7.46 br.s (3H, H_{arom}), 7.60 br.s (2H, H_{arom}), 8.04–8.06 m (2H, H_{arom}), 8.34 s (1H, 4-H), 9.16 s (1H, 3-H), 10.02 s (1H, NH). Found, %: C 66.68; H 4.69; N 19.32. $C_{20}H_{17}N_5O_2$. Calculated, %: C 66.84; H 4.77; N 19.49.

7-Methylsulfanyl-2-phenyl-*2H*-pyrazolo[3,4-*d*]-pyridazine (XII). A mixture of 0.80 g (3.5 mmol) of compound **VIIIa**, 0.4 ml (4.2 mmol) of dimethyl sulfate, 0.14 g (3.5 mmol) of sodium hydroxide dissolved in 1 ml of water, and 10 ml of dioxane was heated for 4 h under reflux with stirring. The mixture was cooled and poured into 50 ml of water, and the precipitate was filtered off, dried, and recrystallized from DMF. Yield 63%, mp 206–208°C. ^{1}H NMR spectrum, δ, ppm: 2.74 s (3H, CH_3), 7.50 t (1H, H_{arom}, ^3J = 8.0 Hz), 7.60 t (2H, H_{arom}, ^3J = 8.0 Hz), 8.10 d (2H, H_{arom}, ^3J = 8.0 Hz), 9.28 s (1H, 4-H), 9.34 s (1H, 3-H). Found, %: C 59.62; H 4.04; N 23.02; S 13.32. $C_{12}H_{10}N_4S$. Calculated, %: C 59.48; H 4.16; N 23.12; S 13.23.

1-Phenyl-2-(2-phenyl-2*H*-pyrazolo[3,4-*d*]pyridazin-7-ylsulfanyl)ethanone (XIII). A solution of 1 g (4.4 mmol) of compound **VIIIa** in 10 ml of DMF was mixed with 0.25 g (4.4 mmol) of potassium hydroxide, the mixture was stirred for 30 min at 100°C, 0.88 g (4.4 mmol) of phenacyl bromide (**Xa**) was added, and the mixture was stirred for an additional 2 h. The mixture was cooled and poured into 50 ml of water, and the precipitate was filtered off, dried, and recrystallized from DMF. Yield 48%, mp 236–238°C. ^{1}H NMR spectrum, δ, ppm: 6.64 s (1H, CH=), 7.48 br.s (4H, H_{arom}), 7.60 t (2H, H_{arom}, ^3J = 7.6 Hz), 7.99 d (2H, H_{arom}, ^3J = 6.4 Hz), 8.09 d (2H, H_{arom}, ^3J = 7.6 Hz), 8.48 s (1H, 4-H), 9.18 s (1H, 3-H), 14.71 s (1H, OH). Found, %: C 65.60; H 3.94; N 16.02; S 9.41. $C_{19}H_{14}N_4OS$. Calculated, %: C 65.88; H 4.07; N 16.17; S 9.26.

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