ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 5, pp. 716–721. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © I.M. Sakhautdinov, O.R. Tukhvatullin, A.A. Fatykhov, F.Z. Galin, 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 5, pp. 723–727.

Synthesis of Pyridazinedione Derivatives Starting from Anhydrides of 2,3-Pyridine- and 2,3-Quinolinedicarboxylic Acids

I. M. Sakhautdinov[a], O. R. Tukhvatullin[a], A. A. Fatykhov[a], and F. Z. Galin[a,b]

[a]*Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences, Ufa, 450054, Russia; ε-mail: ims@anrb.ru*
[b]*Bashkir State University, Ufa, Russa*

Received June 2, 2009

Abstract—A method was developed of preparation of heterocyclic compounds with pyridopyridazinoisoquinalinedione and isoquinopyridazinoquinalinedione structures formed regioselectively by intramolecular cyclization of phosphorus ylides containing pyridopyridazinedione and pyridazinoquinolinedione fragments.

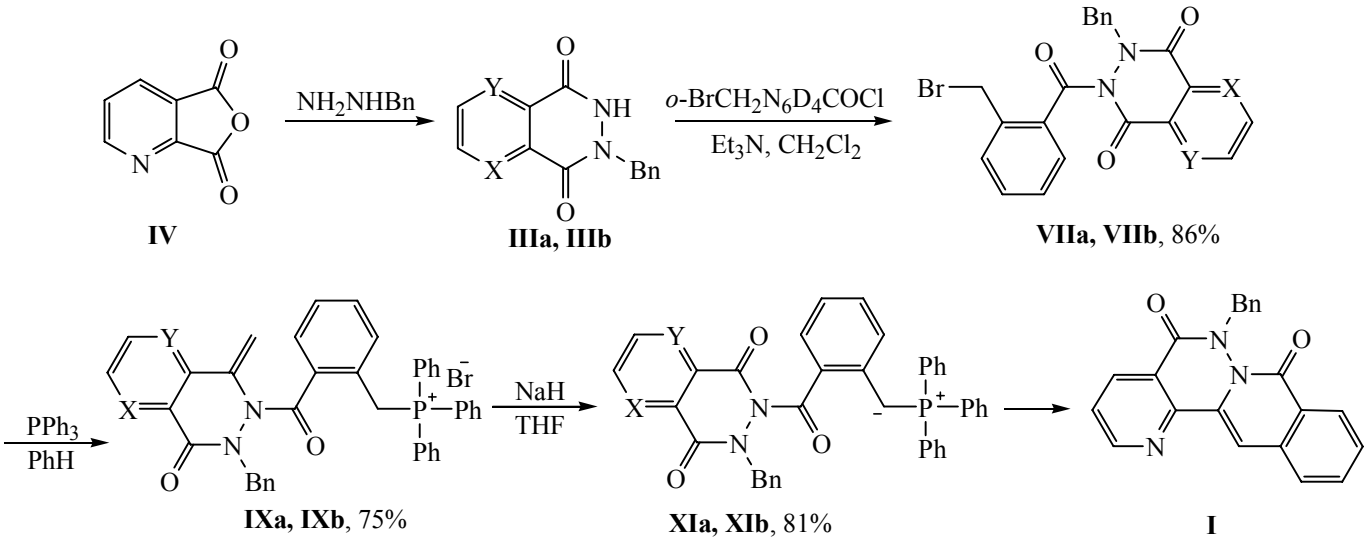
DOI: 10.1134/S1070428010050210

Pyridazine derivatives are extremely rare in the natural objects [1, 2]. Some among them exhibit high biological action, for instance, Galavit is an immuno-modulator of the new generation and is successfully used in the treatment of acute infectious and chronic inflam-matory diseases [3–5]. The extension of the application field of pyridazinedione derivatives for the synthesis of new heterocyclic compounds is very promising.

It was shown formerly [6–9] thet keto-stabilized phosphonium ylides prepared from the N-protected α- and β-amino acids underwent the intramolecular cyclization. We performed through phosphorus ylides the preparation of products **I, II** with a pyridazinedione fragment starting from 2,3-pyridine- and 2,3-quinolinedicarboxylic acids anhydrides.

The synthesis of compound with the pyridopyridazino-

Scheme 1.



IV **IIIa, IIIb** **VIIa, VIIb**, 86%

IXa, IXb, 75% **XIa, XIb**, 81% **I**

X = N, Y = CH (**a**); Y = N, X = CH (**b**); **a** : **b** = 2 : 1.

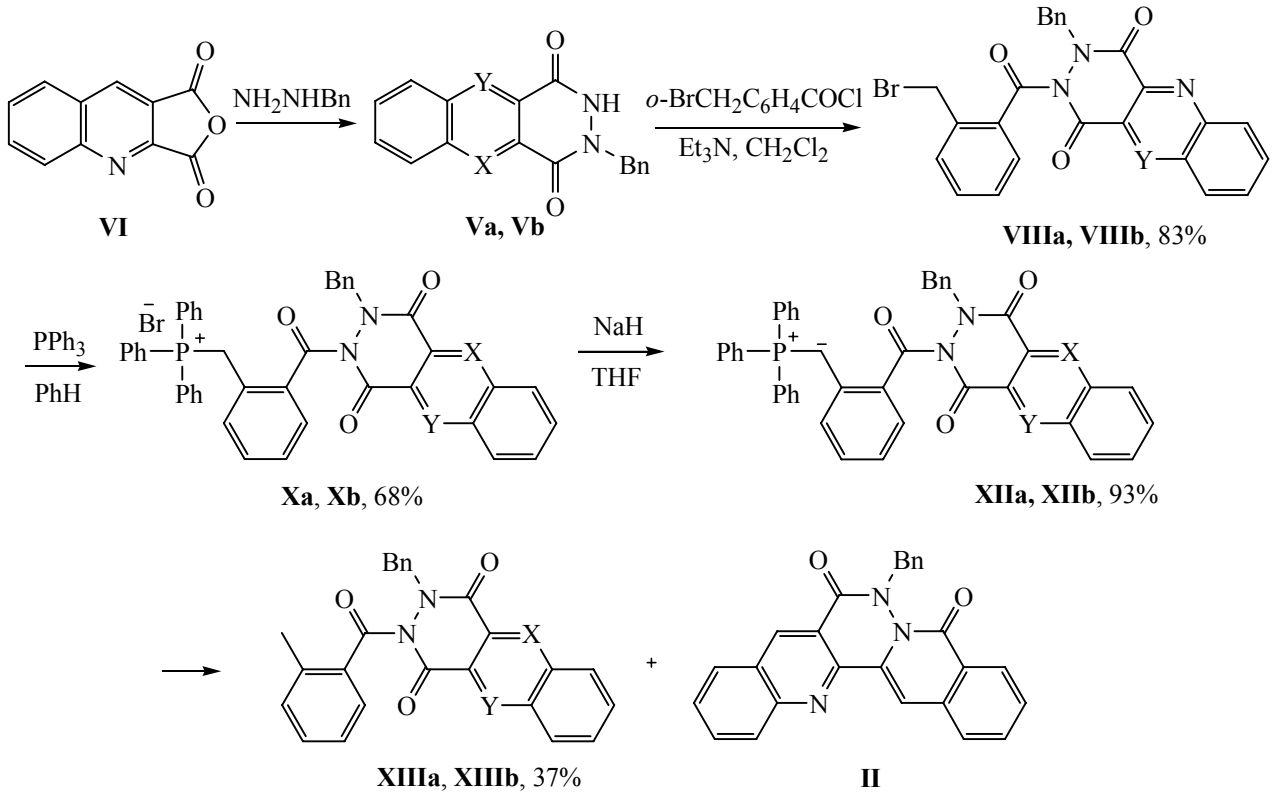
isoquinolidinedione structure **I** was carried out using the mixture of benzyl-substituted 2,3-dihydropyrido[2,3-*d*]-pyridazine-5,8-diones (**IIIa, IIIb**) obtained by direct melting of benzylhydrazine with 2,3-pyridinedicarboxylic acid anhydride (**IV**) (Scheme 1).

The synthesis of compounds with the isoquino-pyridazinoquinolinedione structure **II** was based on the analogously obtained from benzylhydrazine and 2,3-quinolinedicarboxylic acid anhydride (**VI**) benzyl-substituted 2,3-dihydropyridazino[4,5-*b*]-quinoline-1,4-diones (**Va, Vb**) (Scheme 2).

The structure of compounds **IIIa, IIIb** and **Va, Vb** was confirmed by spectral methods. In the ^{1}H NMR spectra the informative signals are the singlets of the methylene group of the benzyl fragment in the region δ 5.23 (**IIIa**), 5.21 (**IIIb**), 5.29 (**Va**), 5.21 ppm (**Vb**), and also the signals of the NH group protons in the region δ 9.02 (**IIIa**), 8.68 (**IIIb**), 9.28 (**Va**), 8.83 ppm (**Vb**). It was established from the integral intensity of the signals belonging to the isomers in the ^{1}H NMR spectra that their ratio was 1 : 2. The structure of the prevailing isomer was revealec from the characteristic signals of the carbon atoms of the oxo groups in the ^{13}C NMR spectra. For instance, the intense signals of the carbamide carbon atoms were observed at δ 167.83 (**IIIa**) and 168.97 ppm (**Va**), whereas the less intense signals of more electron-deficient carbamide carbon atoms in the β-position to the nitrogen atom of the pyridine ring (**IIIb**) and quinoline fragment (**Vb**) appeared upfield at δ 164.38 (**IIIb**) and 164.35 ppm (**Vb**) [10]. According to the ^{13}C NMR data the major isomers were compounds **IIIa** and **Va**; the precise isomers ratio was determined from the comparison of the integral intensities of the signals in the ^{1}H NMR spectra.

The acylation of the mixtures of benzyl-substituted 2,3-dihydropyrido[2,3-*d*]pyridazine-5,8-diones (**IIIa**, **IIIb**) and 2,3-dihydropyridazino[4,5-*b*]quinoline-1,4-diones (**Va, Vb**) with *o*-bromomethylbenzoyl chloride resulted in benzyl bromides **VIIa, VIIb** and **VIIIa, VIIIb** in an overall yield 86 and 83% respectively. These products react with PPh_3 in dry benzene to give phosphonium salts **IXa, IXb** and **Xa, Xb**. The deprotonation of the latter with NaH in THF under an argon atmosphere afforded phosphorus ylides **XIa, XIb** and **XIIa, XIIb** in an overall

Scheme 2.



X = N, Y = CH (**a**); Y = N, X = CH (**b**); **a** : **b** = 2 : 1.

yield 81 and 93% respectively.

The structures of all compounds obtained were confirmed by their spectra. In the ^{1}H NMR spectra the most informative signal is the two-proton singlet of the CH_2Br group in the region δ 4.79 (**VIIa, VIIb**) and 5.28 ppm (**VIIIa, VIIIb**); in the ^{13}C NMR spectrum the corresponding carbon atom gives rise to the signal at δ 31.33 (**VIIa, VIIb**) and 30.78 ppm (**VIIIa, VIIIb**). At the same time in the ^{1}H NMR spectra of compounds **XIa, XIb** and **XIIa, XIIb** the characteristic doublet signals of ylide groups were observed in the region δ 4.33, 4.37 and 5.09, 5.21 ppm respectively.

The heating of phosphorus ylides **XIa, XIb** and **XIIa, XIIb** in boiling dioxane led to the formation of polycyclic compounds **I** and **II** in the yield not exceeding 9%. However the use of ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate [bmim][BF_4] increased the yield of the target products to 42% with respect to compounds **XIb** and **XIIb**. The boiling of compounds **XIIa, XIIb** in 1,4-dioxane in the presence of a catalytic amount of benzoic acid resulted in the formation of methylbenzoylpyridazinoquinolinediones **XIIIa, XIIIb** in an overall yield 37%.

The structures of compounds **I** and **II** were proved by NMR spectra. For instance, in the ^{13}C NMR spectra of compounds **I** and **II** appeared the signals of carbon atoms at multiple bond in the region δ 105.86, 132.74 (**I**) and 105.89, 132.75 ppm (**II**); in the ^{1}H NMR spectra informative signals were those of the protons of the formed double bonds in the region δ 6.62 ppm. The formation of regioisomers **I** and **II** in the course of the intramolecular cyclization at the more electron-deficient carbon atom was proved by the NOE experiment. For instance, in compound **I** the irrariation of the singlet signal of the hydrogen at the double bond (δ_H 6.62 ppm) did not produce a considerable Overhauser effect on the pyridine proton. Analogous behavior was also observed in compound **II**.

Hence we synthesized compounds of pyridopyridazinoisoquinolinedione (**I**) and isoquinopyridazinoquinolinedione (**II**) structures from phosphorus ylides prepared starting from 2,3-pyridine- and 2,3-quinolinedicarboxylic acid anhydrides. It was established that employing the ionic liquid [bmim][BF_4] at the intramolecular cyclization of phosphorus ylides by Wittig reaction significantly increased the yield of the target products.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Specord M-80 (from thin films or mulls in mineral oil). NMR spectra were registered on a spectrometer Bruker AM-300 at operating frequencies 300.13 MHz (^{1}H), 75.25 MHz (^{13}C), internal reference TMS. The reaction progress was monitored by TLC on Sorbfil PTLC-AF-A plates, spots were visualized with UV irradiation, iodine vapor, spraying the plates with ninhydrine or anisaldehyde followed by heating at 100–120°C. The reaction products were isolated by column chromatography on silica gel (eluent petroleum ether–ethyl acetate, 4:1). We did not isolate compounds **IIIa**, **IIIb, Va, Vb, VIIa, VIIb, VIIIa, VIIIb, IXa, IXb, Xa, Xb, XIa, XIb**, **XIIa, XIIb, XIIIa, XIIIb** in an individual state and used them in subsequent reactions as isomer mixtures.

Dihydropyridopyridazinediones IIIa, IIIb and dihydropyridazinoquinolinediones Va, Vb. A mixture of 4.6 mmol of anhydride and 4.6 mmol of benzylhydrazine was heated for 15 min at the temperature of the oil bath of 155–160°C. On cooling the solid reaction product was reprecipitated from methanol. The separated precipitate was filtered off and washed with ether.

7-Benzyl-6,7-dihydropyrido[2,3-*d*]pyridazine-5,8-dione (IIIa), 6-benzyl-6,7-dihydropyrido[2,3-*d*]pyridazine-5,8-dione (IIIb). Overall yield 79%, mp 95–101°C. ^{1}H NMR spectrum, δ, ppm, (**IIIa**): 5.23 s (2H, CH_2), 7.18–7.65 m (5H, C_6H_5), 7.51–9.08 m (3H, C_6H_3N), 9.02 s (1H, NH); (**IIIb**): 5.21 s (2H, CH_2), 7.18–7.65 m (5H, C_6H_5), 7.51–9.08 m (3H, C_6H_3N), 8.68 s (1H, NH). ^{13}C NMR spectra, δ, ppm, (**IIIa**): 55.06 (CH_2), 128.97, 130.01, 130.27 (CH_{arom}), 130.53 (C_{arom}), 130.62 (CH_{arom}), 134.03 (C_{arom}), 138.56 (CH_{arom}), 149.97 (N=C), 150.95 (N=C), 158.43(C=O), 167.83(C=O); (**IIIb**): 54.8 (CH_2), 128.48, 128.97, 130.27, 130.62 (CH_{arom}), 130.85 (C_{arom}), 134.46 (C_{arom}), 136.42 (CH_{arom}), 151.18 (N=C), 152.25 (N=C), 156.16 (C=O), 164.38 (C=O).

3-Benzyl-2,3-dihydropyridazino[4,5-*b*]quinoline-1,4-dione (Va), 2-benzyl-2,3-dihydropyridazino[4,5-*b*]quinoline-1,4-dione (Vb). Overall yield 87%, mp 173–178°C. ^{1}H NMR spectra, δ, ppm, (**Va**): 5.29 s (2H, CH_2), 7.23–7.36 m (5H, C_6H_5), 7.46–8.38 m (5H, C_9H_5N), 9.28 s (1H, NH); (**Vb**): 5.21 s (2H, CH_2), 7.23–7.36 m (5H, C_6H_5), 7.46–8.38 m (5H, C_9H_5N), 8.83 s (1H, NH). ^{13}C NMR spectra, δ, ppm, (**Va**): 56.16 (CH_2), 126.23 (C_{arom}), 129.32, 129.76, 130.1, 130.33, 130.41, 130.56 (CH_{arom}), 133.51 (C_{arom}), 137.93 (CH_{arom}), 139.29 (C_{arom}), 140.21

(CH_{arom}), 154.57 (N=C), 157.08 (N=C), 160.09 (C=O), 168.97 (C=O); (**Vb**): 56.3 (CH_2), 127.73 (C_{arom}), 129.32, 129.76, 129.96, 130.33, 130.41, 130.68, 135.82 (CH_{arom}), 136.4 (C_{arom}), 137.03 (C_{arom}), 142.84 (CH_{arom}), 153.56 (N=C), 156.47 (N=C), 160.03 (C=O), 164.35 (C=O).

Benzyl bromides VIIa, VIIb, VIIIa, VIIIb. To a dispersion of 1.65 mmol of *o*-bromomethylbenzoic acid in 15 ml of dry benzene was added 4.95 mmol of thionyl chloride, and the mixture was heated at reflux to the end of gas liberation (~6 h). On evaporation of the solution the acid chloride was brought into further reaction without additional purification. The solution of the acid chloride in 5 ml of dichloromethane was at cooling and stirring slowly added dropwise over 39 min to a dispersion of 1.65 mmol of compound **IIIa, IIIb** or **Va, Vb** and 1.65 mmol of Et_3N in 20 ml of dichloromethane, the mixture was stirred for 1 h more at room temperature and left standing for 24 h. The formed solution was washed with 1N HCl, the organic layer was dried with $MgSO_4$. The solvent was distilled off, the oily residue was subjected to column chromatography on silica gel (eluent chloroform–acetone, 9:1).

7-Benzyl-6-[2-(bromomethyl)benzoyl]-6,7-dihydropyrido[2,3-*d*]pyridazine-5,8-dione (VIIa), 6-benzyl-7-[2-(bromomethyl)benzoyl]-6,7-dihydropyrido[2,3-*d*]pyridazine-5,8-dione (VIIb). Overall yield 86%. ^{1}H NMR spectra, δ, ppm, **(VIIa)**: 4.79 s (2H, CH_2), 4.90 s (2H, CH_2), 7.18–7.74 m (9H, C_6H_4, C_6H_5), 8.06–9.05 m (3H, C_6H_3N); (**VIIb**): 4.79 s (2H, CH_2), 5.09 s (2H, CH_2), 7.18–7.74 m (9H, C_6H_4, C_6H_5), 8.06–9.05 m (3H, C_6H_3N). ^{13}C NMR spectra, δ, ppm, (**VIIa**): 31.33 (CH_2Br), 54.49 (CH_2), 125.59 (CH_{arom}), 127.75 (C_{arom}), 128.70, 128.86, 128.93, 129.63, 130.68, 131.82, 132.03 (CH_{arom}), 134.36, 135.93, 140.35 (C_{arom}), 145.51 (CH_{arom}), 146.41 (CH_{arom}), 155.24 (C_{arom}), 159.17 (C=O), 160.10 (C=O), 171.05 (C=O); (**VIIb**): 31.33 (CH_2Br), 54.52 (CH_2), 125.59 (CH_{arom}), 125.64 (C_{arom}), 126.68, 128.70, 128.86, 128.93, 130.68, 131.82, 132.03 (CH_{arom}), 135.76, 135.93, 139.41 (C_{arom}), 139.92 (CH_{arom}), 146.41 (CH_{arom}), 150.16 (C_{arom}), 155.22 (C=O), 160.02 (C=O), 170.79 (C=O). Found, %: C 58.67; H 3.61; Br 17.71; N 9.35. $C_{22}H_{16}BrN_3O_3$. Calculated, %: C 58.68; H 3.58; Br 17.75; N 9.33

3-Benzyl-2-[2-(bromomethyl)benzoyl]-2,3-dihydropyridazino[4,5-*b*]quinoline-1,4-dione (VIIIa), 2-benzyl-3-[2-(bromomethyl)benzoyl]-2,3-dihydropyridazino[4,5-*b*]quinoline-1,4-dione (VIIIb). Overall yield 83%. ^{1}H NMR spectra, δ, ppm, (**VIIIa**): 5.28 s (2H, CH_2), 5.49 s (2H, CH_2), 7.21–7.75 m (4H, C_6H_4), 7.22–7.57 m (5H, C_6H_5), 7.56–8.58 m (4H, C_6H_4), 8.67 s (1H, C_6HN); (**VIIIb**): 5.28 s (2H, CH_2), 5.42 s (2H, CH_2), 7.21–7.75 m (4H, C_6H_4), 7.22–7.57 m (5H, C_6H_5), 7.56–8.58 m (4H, C_6H_4), 9.31 s (1H, C_6HN). ^{13}C NMR spectra, δ, ppm, (**VIIIa**): 31.08 (CH_2Br), 54.87 (CH_2), 126.34 (C_{arom}), 127.89, 128.27, 128.53, 128.61, 128.84, 128.91, 129.03, 129.19, 129.37, 129.57 (all CH_{arom}), 130.32 (C_{arom}), 132.15 (CH_{arom}), 132.26 (CH_{arom}), 133.10, 133.61, 134.25, 136.24, 140.86 (C_{arom}), 143.84 (C=O Ht), 150.62 (C=O, Ht), 163.83 (C=O, Bz); (**VIIIb**): 30.78 (CH_2Br), 54.55 (CH_2), 125.70 (C_{arom}), 127.55 (C_{arom}), 127.89 (CH_{arom}), 128.27, 128.53, 128.61, 128.84, 128.91, 129.03, 129.19, 129.37, 131.04 (CH_{arom}), 132.04 (C_{arom}), 132.15 (CH_{arom}), 132.26 (CH_{arom}), 133.61, 133.93, 138.15, 140.25 (C_{arom}), 143.04 (C=O, Ht), 150.45 (C=O, Ht), 158.08 (C=O, Bz). Found, %: C 62.43; H 3.66; Br 15.94; N 8.38. $C_{26}H_{18}BrN_3O_3$. Calculated, %: C 62.41; H 3.63; Br 15.97; N 8.40.

Phosphonium salts IXa, IXb, Xa, Xb. To a solution of 1.2 mmol of an appropriate benzyl bromide in 10 ml of dry benzene was added in one portion at stirring 1.32 mmol of triphenylphosphine dissolved in 5 ml of benzene. The reaction mixture was stirred for 2 h nad then it was heated at refluxfor 6 h. The precipitate formed in the course of the reaction was filtered off, washed with benzene and left to dry in air.

2-[(7-Benzyl-5,8-dioxo-7,8-dihydropyrido-[2,3-*d*]pyridazin-6(5*H*)-yl)carbonyl]benzyltriphenylphosphonium bromide (IXa) and **2-[(6-benzyl-5,8-dioxo-5,8-dihydropyrido[2,3-*d*]pyridazin6(5*H*)-yl)carbonyl]benzyltriphenylphosphonium bromide (IXb).** Overall yield 75%, mp 140–142°C. Found, %: C 67.37; H 4.46; Br 11.28; N 5.98. $C_{40}H_{31}BrN_3O_3P$. Calculated, %: C 67.42; H 4.38; Br 11.21; N 5.90.

2-[(3-Benzyl-1,4-dioxo-3,4-dihydropyridazino[4,5-*b*]quinoline-2(1*H*)-yl)carbonyl]benzyl-(triphenyl)phosphonium bromide (Xa) and **2-[(2-benzyl-1,4-dioxo-3,4-dihydropyridazino[4,5-*b*]quinolin-3(2*H*)-yl)carbonyl]benzyl(triphenyl)phosphonium bromide (Xb).** Overall yield 68%, mp 185–186°C. Found, %: C 69.28; H 4.38; Br 10.45; N 5.53. $C_{44}H_{33}BrN_3O_3P$. Calculated, %: C 69.30; H 4.36; Br 10.48; N 5.51.

Phosphorus ylides XIa,XIb, XIIa, XIIb. To a dispersion of 1 mmol of phosphonium salt **IXa, IXb, Xa, Xb** in 20 ml of THF was added at stirring 3 mmol of NaH. The reaction mixture was stirred over 1 h, the separated precipitate was filtered off, the solvent was distilled off to leave dark-red oily residue.

7-Benzyl-6-{2-[(triphenylphosphoranilidene)-methyl]benzoyl}-6,7-dihydropyrido[2,3-*d*]-pyridazine-5,8-dione (XIa), 6-benzyl-7-{2-[(triphenylphosphoranilidene)methyl]benzoyl}-6,7-dihydropyrido[2,3-*d*]pyridazine-5,8-dione (XIb). Overall yield 81%. ^{1}H NMR spectra, δ, ppm, (**XIa**): 4.33 s (1H, CH), 5.49 s (2H, CH_2), 6.90–7.94 m (24H, $4C_6H_5$, C_6H_4), 8.07–8.34 m (3H, C_6H_3N); (**XIb**): 4.37 s (1H, CH), 5.45 s (2H, CH_2), 6.90–7.94 m (24H, $4C_6H_5$, C_6H_4), 8.07–8.34 m (3H, C_6H_3N).

3-Benzyl-2-{2-[(triphenylphosphoranilidene)methyl]benzoyl}-2,3-dihydropyridazino[4,5-*b*]-quinoline-1,4-dione (XIIa), 2-benzyl-3-{2-[(triphenylphosphoranilidene)methyl]benzoyl}-2,3-dihydropyridazino[4,5-*b*]quinoline-1,4-dione (XIIb). Overall yield 93%. ^{1}H NMR spectra, δ, ppm, (**XIIa**): 5.09 s (1H, CH), 5.38 s (2H, CH_2), 6.93–7.75 m (4H, C_6H_4), 7.14–7.33 m (5H, C_6H_5), 7.29–7.64 m (15H, $3C_6H_5$), 7.74–8.49 m (4H, C_6H_4), 8.97 s (1H, C_6HN); (**XIIb**): 5.21 s (1H, CH), 5.33 s (2H, CH_2), 6.93–7.75 m (4H, C_6H_4), 7.14–7.33 m (5H, C_6H_5), 7.29–7.64 m (15H, $3C_6H_5$), 7.74–8.49 m (4H, C_6H_4), 9.23 s (1H, C_6HN).

Thermolysis of phosphorus ylides XIa,XIb, XIIa, XIIb. *a*. To a dispersion of 0.5 mmol of phosphorus ylide in 10 ml of anhydrous dioxane was added a catalytic quantity of benzoic acid, and the mixture was refluxed for 24 h. The solvent was distilled off, the thermolysis products **I** and **XIIIa, XIIIb** were subjected to chromatography on silica gel (eluent ethyl acetate–petroleum ether, 1:4).

b. To a dispersion of 0.3 mmol of phosphorus ylide in 10 ml of dry dioxane was added 1 ml of 1-butyl-3-methylimidazolium tetrafluoroborate [bmim][BF_4], and the reaction mixture was boiled for 24 h. The solvent was distilled off, the thermolysis products **I** and **II** were isolated by column chromatography on silica gel (eluent ethyl acetate–petroleum ether, 1:4).

6-Benzyl-6*H*-pyrido[3',2':4,5]pyridazino[1,6-*b*]isoquinoline-5,8-dione (I). Orange oily substance. Yield 9 (*a*), 36% (*b*) with respect to compound **XIb**. ^{1}H NMR spectrum, δ, ppm: 4.22–4.37 m (2H, CH_2), 6.62 s (H, CH), 7.16–7.55 m (9H, C_6H_5, C_6H_4), 7.68–8.35 m (3H, C_6H_3N). ^{13}C NMR spectrum, δ, ppm: 60.76 (CH_2), 105.86 (CH=), 120.31(C_{arom}), 125.79, 125.94, 127.11, 128.19, 129.15, 129.56, 129.75, 130.94, 131.75 (CH_{arom}), 132.74(C_{arom}), 134.78 (CH_{arom}), 136.73, 137.46, 139.83, 146.06 (C_{arom}), 155.56 (C=O), 162.53 (C=O). Found, %: C 74.82; H 4.24; N 11.93. $C_{22}H_{15}N_3O_2$. Calculated, %: C 74.78; H 4.28; N 11.89.

3-Benzyl-2-(2-methylbenzoyl)-2,3-dihydropyridazino[4,5-*b*]quinoline-1,4-dione (XIIIa), 2-benzyl-3-(2-methylbenzoyl)-2,3-dihydropyridazino[4,5-*b*]-quinoline-1,4-dione (XIIIb). Overall yield 37 (*a*), mp 153–160°C. ^{1}H NMR spectra, δ, ppm, (**XIIIa**): 2.72 s (3H, CH_3), 5.48 s (2H, CH_2), 7.24–7.74 m (4H, C_6H_4), 7.31–7.49 m (5H, C_6H_5), 7.86–8.54 m (4H, C_6H_4), 8.52 s (1H, C_6HN); (**XIIIb**): 2.73 s (3H, CH_3), 5.43 s (2H, CH_2), 7.24–7.74 m (4H, C_6H_4), 7.31–7.49 m (5H, C_6H_5), 7.86–8.54 m (4H, C_6H_4), 9.31 s (1H, C_6HN). ^{13}C NMR spectra, δ, ppm, (**XIIIa**): 21.98 (CH_3), 54.82 (CH_2), 126.22 (C_{arom}), 127.78, 128.33, 128.45, 128.49, 128.74 (CH_{arom}), 129.11 (C_{arom}), 129.41 (C_{arom}), 131.16, 131.67, 131.83, 131.94, 132.08, 132.28 (CH_{arom}), 132.80, 133.84, 142.57, 144.09 (C_{arom}), 150.54 (C=O, Ht), 158.11(C=O, Ht), 164.40 (C=O, Bz); (**XIIIb**): 21.54 (CH_3), 54.50 (CH_2), 125.90 (C_{arom}), 126.36 (C_{arom}), 127.78 (CH_{arom}), 128.33 (CH_{arom}), 128.45 (CH_{arom}), 128.49 (CH_{arom}), 128.74 (CH_{arom}), 128.88 (C_{arom}), 131.16 (CH_{arom}), 131.67 (CH_{arom}), 131.83 (CH_{arom}), 131.94 (CH_{arom}), 132.08 (CH_{arom}), 132.28 (CH_{arom}), 133.01 (C_{arom}), 133.18 (C_{arom}), 136.33 (C_{arom}), 143.27 (C_{arom}), 150.23 ($C{=}O_{quinoline.}$), 158.03 ($C{=}O_{quinoline.}$), 164.26 (C=O). Found, %: C 74.13; H 4.57; N 9.95. $C_{26}H_{19}N_3O_3$. Calculated, %: C 74.10; H 4.54; N 9.97.

7-Benzyl-5*H*-isoquino[2',3':2,3]pyridazino-[4,5-*b*]quinoline-5,8(7*H*)-dione (II). Orange oily substance. Yield 42% (*b*) with respect to compound **XIIb**. ^{1}H NMR spectrum, δ, ppm: 4.32–4.43 m (2H, CH_2), 6.62 s (1H, CH), 7.32–7.63 m (4H, C_6H_4), 7.16–7.42 m (5H, C_6H_5), 7.31–7.62 m (4H, C_6H_4), 8.38 s (1H, C_6HN). ^{13}C NMR spectrum, δ, ppm: 61.50 (CH_2), 105.89 (CH=), 120.33 (C_{arom}), 120.93 (C_{arom}), 125.09, 125.73, 125.79, 125.96, 127.52, 128.17, 129.59, 129.69, 129.77, 130.52, 131.74 (CH_{arom}), 132.74 (C_{arom}), 134.80 (CH_{arom}), 134.95, 136.76, 137.48, 138.20, 141.42 (C_{arom}), 155.57 (C=O, Ht), 162.58 (C=O, Bz). Found, %: C 77.38; H 4.27; N 10.43. $C_{26}H_{17}N_3O_2$. Calculated, %: C 77.41; H 4.25; N 10.42.

The study was carried out under a financial support of the Council for grants of the President of the Russian Federation (Program for support of the leading scientific schools, NSh-1725.2008.3) and of the Presidium of the Russian Academy of Sciences (Program of basic research no. 18).

REFERENCES

1. Tisler, M. and Stanovnik, B., *Comprehensive Heterocycl. Chem.,* 1984, vol. 3, p. 57.

2. Chevallier, F. and Mongin, F., *Chem. Soc. Rev.*, 2008, vol. 37, p. 595.
3. *Galavit. Klinicheskoe ispol'zovanie i mekhanizmy deistviya. Sb. nauch. trudov* (Galavit: Chemical Application and Action Mechanism, Collection of Transactions), MoscowMGMSU. M., 2002, 55.
4. Jiang, Y., Scofield, V.L., Yan, M., Qiang, W., Liu, N., Reid, A.J., Lynn, W.S., and Wong, P.K.Y., *J. Virology*, 2006, p. 4557.
5. Abidov, M.T. and Khokhlov, A.P., RF Inventor's Certificate 2113222, 1997; *RF Byull. Izobr.,* 1998, vol. 17, p. 189.
6. Bestmann, H.J., Moenius, T., and Soliman, F. *Chem. Lett.,* 1986, p. 1527.
7. Aitken, A.R. and Harris, R. *J. Chem. Soc., Perkin Trans. 1*, 1995, p. 475.
8. Aitken, A.R., Martin, J.D., Ferguson, G., and Lough, A.J., *J. Chem. Soc., Perkin Trans. 1*, 1998, p. 875.
9. Galin, F.Z., Sakhautdinov, I.M., Khalikov, I.G., Lakeev, S.N., Maidanova, I.O., and Fatykhov, A.A., *Izv. Akad. Nauk, Ser. Khim.*, 2007, p. 2394.
10. Levy, G.C. and Nelson, G.L., *Carbon-13 Nuclear Magnetic Resonance for Organic Chemists*, New York: Wiley, 1972.