Methyl 3-Amino-1*H*-indole-2-carboxylates in the Synthesis of 5*H*-Pyrimido[5,4-*b*]indole Derivatives

A. S. Shestakov[a], Kh. S. Shikhaliev[a], O. E. Sidorenko[a] V. G. Kartsev[b], and S. V. Simakov[c]

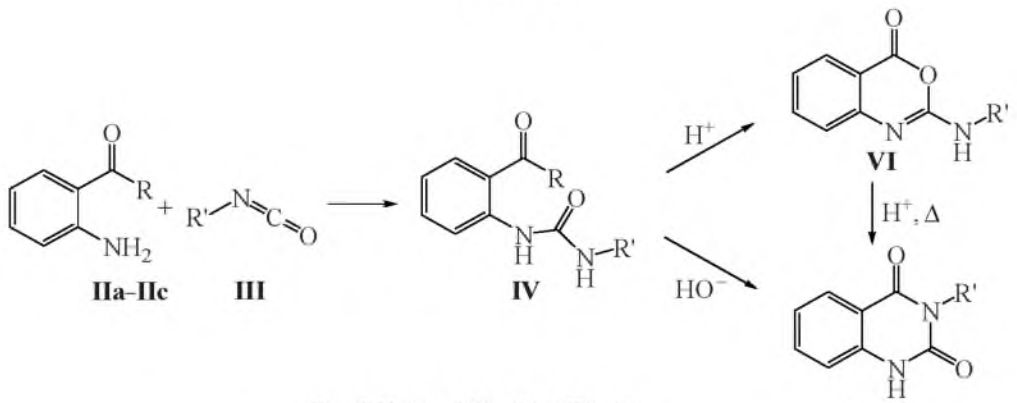
[a]*Voronezh State University, Voronezh, 394006 Russia*
e-mail: chocd261@chem.vsu.ru
[b]*InterBioScreen, Chernogolovka, Russia*
[c]*Belgorod State University, Belgorod, Russia*

Abstract—Reactions of methyl 3-amino-1*H*-indole-2-carboxylates with aryl isocyanates, aryl isothiocyanates, and cyanamides led to the formation of 5*H*-pyrimido[5,4-*b*]indole derivatives. In the reaction with isocyanates formed 3-aryl-1*H*-pyrimido[5,4-*b*]indole-2,4(3*H*,5*H*)-diones that were involved into the alkylation at two nitrogen atoms. The reaction with isothiocyanates afforded 3-aryl-2-thioxo-2,3-dihydro-1*H*-pyrimido[5,4-*b*]indol-4(5*H*)-ones undergoing alkylation at the sulfur atom. The reactions with benzoylcyanamide and *N*-(4,6-dimethylpyrimidin-2-yl)cyanamide resulted in *N*-(4-oxo-4,5-dihydro-3*H*-pyrimido-[5,4-*b*]indol-2-yl)benzamides and 2-(4,6-dimethylpyrimidin-2-ylamino)-3*H*-pyrimido[5,4-*b*]indol-4(5*H*)-ones respectively.

Indole is one of the widely spread in the nature heterocyclic compounds. About 1000 indole alkaloids are known, and many among these natural substances exhibit physiological action. No less widely spread are also pyrimidine-2,4-dione derivatives (uracyl, thymine, uric acid, purine alkaloids). At the presence in the indole structure of an ester group in the position *2* and of amino group in the position *3* these compounds may be used in the synthesis of tricyclic indole derivatives containing a fused fragment of pyrimidine-2,4-dione. This approach is similar to the biosynthetic way of obtaining purine nucleotides. In our case methyl 3-amino-1*H*-indole-2-carboxylates **Ia** and **Ib** were used obtained by a reductive amination of the corresponding ester derivatives of 4- and 6-methoxyindole.

The preparation of 3-R'-quinazoline-2,4(1*H*,3*H*)-diones **V** using isocyanates **III** and anthranilic acid and its derivatives **II** is a known procedure (Scheme 1) [1]. The reaction is catalyzed both by acids and bases and proceeds through the formation of intermediate carb-

Scheme 1.



amides **IV**. Under mild conditions of the acid catalysis the kinetic control leads to the formation of isomeric 2-(R'-amino)-4*H*-benzo[*d*][1,3]-oxazin-4-ones **VI**. Under the conditions of base catalysis and at severe acid treatment target compounds **V** are obtained.

Compounds **I** as structural analogs of methyl anthranilate (**IIb**) also react with isocyanates giving derivatives analogous to quinazolinediones **V**, 5*H*-pyrimido[5,4-*b*]-indole derivatives **VIII** (Scheme 2). A short treatment of compounds **I** with 4-chlorophenyl isocyanate in dioxane led to the formation of carbamides **VII** which at heating with sodium methylate underwent cyclization into 5*H*-pyrimido[5,4-*b*]indoles **VIII**. Therewith the formation cannot be excluded of isomeric derivatives of 2-amino[1,3]oxazin-4-one analogous to compounds **VI**, but it has been shown in [1] that under the base catalysis form exclusively quinazoline-2,4(1*H*,3*H*)-dione derivatives **V**. The formation of just these compounds is also confirmed by their high melting points characteristic of compounds **V**.

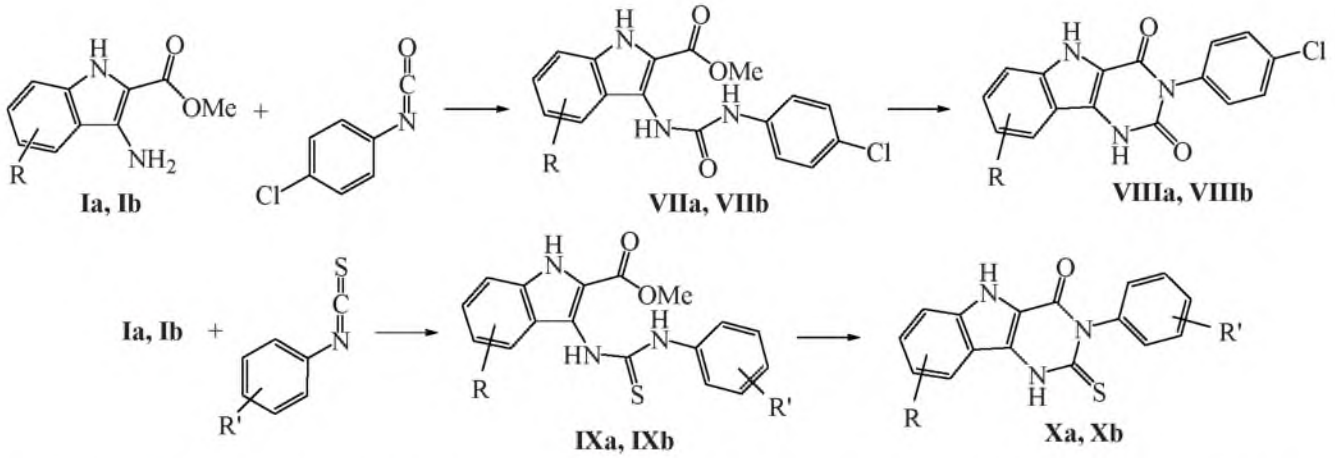
The reaction with isothiocyanates proceeded similarly. The lower reactivity of isothiocyanates compared with the isocyanates required a longer time of the first reaction stage. The formation of the isomer analogous to compounds **V** and not **VI** is proved, as we show further, by the S-alkylation of compounds **X**.

Compounds **VIII** and **X** are characterized by the lactim-lactam tautomerism. We chose for the prevailing tautomer by quantum-chemical calculations performed using GAUSSIAN 03 software [2]. The calculations were carried out by the density functional method applying functional B3LYP in the basic 6-31G*. For both compounds the lactam form proved to be preferable, and it differed from the lactim form by 38.3 kcal mol^{-1} for compound **VIII** and by 67.1 kcal mol^{-1} for compound **X**.

In the structure of 5*H*-pyrimido[5,4-*b*]-indole derivatives **VIII** and **X** two mobile protons are present providing a possibility to bring these compounds into alkylation. The protons in compound **VIII** are of similar mobility excluding the selective alkylation of each nitrogen atom. The attempt to alkylate compounds **VIII** with an equimolar amount of alkyl halide yielded a mixture of mono- and dialkyl derivatives with the initial compound. At the use of a four-fold excess of methyl iodide or ethyl bromide we obtained dimethyl **XIa** and diethyl **XIb** derivatives respectively (Scheme 3). Compounds **X** undergo alkylation exclusively at the sulfur atom, a characteristic reaction of these compounds. It was previously shown on 2-thioxo-2,3-dihydroquinazolin-4(1*H*)-ones, their structural analogs [3].

The organic reactions are known to occur under the charge or orbital control [4]. The alkylation of compounds **VIII** and **X** was carried out using their sodium salts and thus the charge control was possible. However the quantum-chemical calculations give another result. Actually, the difference between the HOMO of the nucleophile (compounds **VIII** and **X** in all tautomer forms) and the LUMO of the electrophile (methyl iodide and ethyl bromide) was no more than 0.17–0.20 eV. When compounds **VIII** and **X** give ionic forms this difference

Scheme 2.

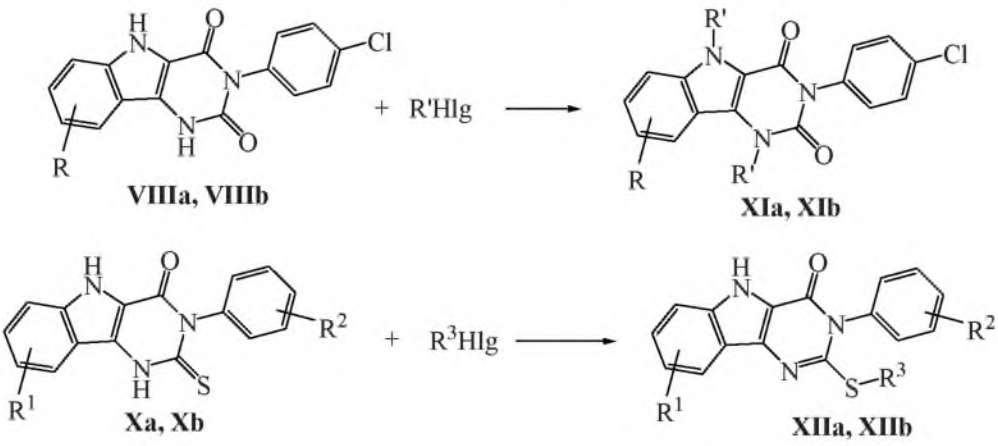


I,VII, R = 6-MeO (**a**), 4-MeO (**b**); **VIII**, R = 7-MeO (**a**), 9-MeO (**b**); **IX**, R = 6-MeO, R' = 2-Cl (**a**); R = 4-MeO, R' = H (**b**); **X**, R = 7-MeO, R' = 2-Cl (**a**); R = 9-MeO, R' = H (**b**).

even decreased to 0.02–0.05 eV. This small difference in the HOMO and the LUMO suggests the orbital control of the alkylation.

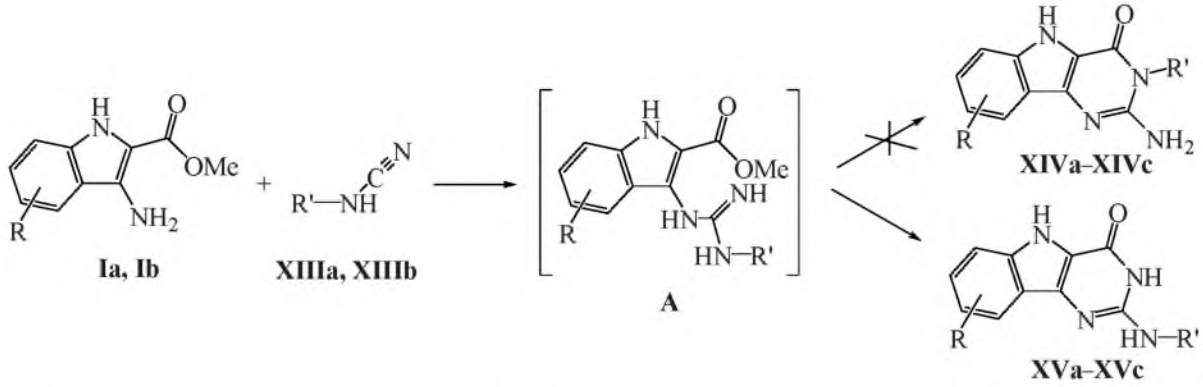
Mono-substituted cyanamides can be regarded as structural analogs of isocyanates and isothiocyanates where the oxygen or sulfur atom is replaced by NH. The reactivity of these compounds is lower and essentially depends on the substituent at the amine nitrogen [5]. Cyanamides like isocyanates and isothiocyanates react with 3-amino-1*H*-indole-2-carboxylates **Ia** and **Ib**, however without the formation of a stable intermediate. The intermediate guanidine **A** converted into 2-R-amino-3*H*-pyrimido[5,4-*b*]indol-4(5*H*)-one (**XV**) (Scheme 4). The reaction with benzoylcyanamide occurred without catalysis, with the less reactive N-(4,6-dimethylpyrimidin-2-yl)cyanamide (**XIIIb**) the reaction proceeded in the presence of HCl. Formerly the same feature was observed in reaction of these cyanamides with methyl anthranilate [6]. Like in event of isocyanates two isomeric compounds **XIV** and **XV** may form. In most reactions with compounds containing an ester and an amino groups formed compounds similar to **XV** [7]. In some cases a side product was isolated analogous to compound **XIV** [8]. Compound **XIV** forms as a result of the attack on the ester group of the nitrogen that has been an amine nitrogen in the initial cyanamide and that has acted as a nucleophile. In cyanamides **XIII** the NH group is of acid character. For instance, pK_α of cyanamide **XIIIb** amounts to 6.95 [9], and for benzoylcyanamides the pK_α values are 2.7–2.8 [10]. Therefore the involvement of this atom into the reaction as a nucleophile is dubious. The formation just of compound **XV** is also confirmed by appearance in ^{1}H NMR spectrum of three singlets in a weak field corresponding to three individual protons.

Scheme 3.



XII, R^1 = 2-Cl, R^2 = 7-MeO, R^3 = Me (**a**), R^1 = H, R^2 = 9-MeO, R^3 = Et(**b**). **XI**, R = 7-MeO, R' = Me (**a**); R = 9-MeO, R' =Et (**b**).

Scheme 4.



XIII, R' = Bz (**a**), 4,6-dimethylpyrimidin-2-yl (**b**); **XIV, XV**, R = 7-MeO, R' = Bz (**a**); R = 9-MeO, R' = Bz (**b**); R = 9-MeO, R' = 4,6-dimethylpyrimidin-2-yl (**c**).

In the spectrum of compound **XIV** a singlet should appear in the region 6–7 ppm corresponding to two protons of an amino group.

EXPERIMENTAL

The monitoring of reaction progress and checking of the homogeneity of compounds obtained was performed by TLC on Merck UV-254 plates, eluent chloroform–methanol, 20:1. ^{1}H NMR spectra were registered on a spectrometer Bruker AC-300 (300 MHz), internal reference TMS.

Methyl 3-amino-6-methoxy-1*H*-indole-2-carboxylate (Ia). To a solution of 40.4 g (0.2 mol) of methyl 6-methoxy-1*H*-indole-2-carboxylate in 1.2 l of DMF while stirring was added simultaneously a solution of phenyldiazonium chloride and a saturated solution of sodium carbonate. On the completion of addition the reaction mixture was stirred for 30 min maintaining the temperature at 0–5°C, pH at 8.0–9.0, then it was diluted with 2.0 l of water. The separated precipitate was filtered off, washed on the filter with hot water, and dried in air till constant weight. The obtained orange-red powder was dissolved at heating in 500 ml of 2-propanol, and 74.8 g (0.63 mol) of tin powder and 250 ml of concn. hydrochloric acid were added. The reaction mixture was boiled for 2 h, then 300 ml of 2-propanol was distilled off. The precipitate separated on cooling was filtered off, washed with cold water and dissolved in boiling water. The solution was treated with activated carbon, and to the filtrate was added aqueous ammonia till alkaline reaction. The settled precipitate was filtered off and recrystallized from 2-propanol. Yield 20.5 g (47%), mp 156–157°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.77 s (3H, $COOCH_3$), 3.90 s (3H, OCH_3), 6.24 br.s (2H, NH_2), 6.72 d (1H$_{arom}$, *J* 7 Hz), 6.89 s (1H$_{arom}$), 7.86 d (1H$_{arom}$, *J* 7 Hz), 11.82 C (1H, NH). Found, %: C 60.08; H 5.39; N 12.69. $C_{11}H_{12}N_2O_3$. Calculated, %: C 59.99; H 5.49; N 12.72.

Methyl 3-amino-4-methoxy-1*H*-indole-2-carboxylate (Ib) was similarly obtained. Yield 18.3 g (42%), mp 164–165°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.78 s (3H, $COOCH_3$), 3.88 s (3H, OCH_3), 6.18 br.s (2H, NH_2), 6.59 d (1H$_{arom}$, *J* 8 Hz), 7.09 d (1H$_{arom}$, *J* 7 Hz), 7.29 t (1H$_{arom}$, *J* 7 Hz), 11.85 C (1H, NH). Found, %: C 59.92; H 5.50; N 12.79. $C_{11}H_{12}N_2O_3$. Calculated, %: C 59.99; H 5.49; N 12.72.

Methyl 6-methoxy-3-[3-(4-chlorophenyl)ureido]-1*H*-indole-2-carboxylate (VIIa). A mixture of 1.54 g (7 mmol) of compound **Ib** and 1.08 g (7 mmol) of 4-chlorophenyl isocyanate was heated in anhydrous dioxane at 70°C for 0.5 h, the separated precipitate was filtered off and washed with 2-propanol. Yield 2.23 g (85%), mp 270–271°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.76 s (3H, $COOCH_3$), 3.92 s (3H, OCH_3), 6.70 d (1H$_{arom}$, *J* 7 Hz), 6.84 s (1H$_{arom}$), 7.25 d (2H$_{arom}$, *J* 8 Hz), 7.48 d (2H$_{arom}$, *J* 8 Hz), 7.85 d (1H$_{arom}$, *J* 7 Hz), 8.31 s (1H, NH), 9.71 s (1H, NH), 11.62 s (1H, NH$_{indole}$). Found, %: C 57.78; H 4.25; N 11.36. $C_{18}H_{16}ClN_3O_4$. Calculated, %: C 57.84; H 4.31; N 11.24.

Methyl 4-methoxy-3-[3-(4-chlorophenyl)ureido]-1*H*-indole-2-carboxylate (VIIb). Yield 2.49 g (95%), mp 261–262°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.83 s (3H, $COOCH_3$), 3.98 s (3H, OCH_3), 6.60 d (1H$_{arom}$, *J* 7 Hz), 7.05 d (1H$_{arom}$, *J* 7 Hz), 7.26 t (1H$_{arom}$, *J* 7 Hz), 7.58 d (2H$_{arom}$, *J* 8 Hz), 7.74 d (2H$_{arom}$, *J* 8 Hz), 8.43 s (1H, NH), 9.56 s (1H, NH), 11.60 s (1H, NH$_{indole}$). Found, %: C 57.86; H 4.33; N 11.20. $C_{18}H_{16}ClN_3O_4$. Calculated, %: C 57.84; H 4.31; N 11.24.

Methyl 6-methoxy-3-[3-(2-chlorophenyl)thioureido]-1*H*-indole-2-carboxylate (IXa). A mixture of 1.54 g (7 mmol) of compound **Ia** and 1.19 g (7 mmol) of 2-chlorophenyl isothiocyanate was heated in anhydrous dioxane at 70°C for 4 h. The reaction mixture was poured into 100 ml of distilled water, the separated precipitate was filtered off and washed with 2-propanol. Yield 2.27 g (83%), mp 197–199°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.78 s (3H, $COOCH_3$), 3.87 s (3H, OCH_3), 6.76 d (1H$_{arom}$, *J* 7 Hz), 6.84 s (1H$_{arom}$), 7.25 t (1H$_{arom}$, *J* 7 Hz), 7.36 t (1H$_{arom}$, *J* 7 Hz), 7.44–7.53 m (2H$_{arom}$), 7.70 d (1H$_{arom}$, *J* 7 Hz), 9.33 s (1H, NH), 9.59 s (1H, NH), 11.62 s (1H, NH$_{indole}$). Found, %: C 55.41; H 4.18; N 10.84. $C_{18}H_{16}ClN_3O_3S$. Calculated, %: C 55.46; H 4.14; N 10.78.

Methyl 4-methoxy-3-(3-phenylthioureido)-1*H*-indole-2-carboxylate (IXb). Yield 1.94 g (78%), mp 213–214°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.81 s (3H, $COOCH_3$), 3.96 s (3H, OCH_3), 6.72 d (1H$_{arom}$, *J* 7 Hz), 7.02–7.10 m (2H$_{arom}$), 7.12–7.21 m (2H$_{arom}$), 7.28 d (1H$_{arom}$, *J* 7 Hz), 7.37 t (1H$_{arom}$, *J* 7 Hz), 7.56 d (1H$_{arom}$, *J* 7 Hz), 9.03 s (1H, NH), 9.29 s (1H, NH), 11.66 s (1H, NH$_{indole}$). Found, %: C 60.78; H 4.75; N 11.76. $C_{18}H_{17}N_3O_3S$. Calculated, %: C 60.83; H 4.82; N 11.82.

7-Methoxy-3-(4-chlorophenyl)-1*H*-pyrimido[5,4-*b*]-indole-2,4(3*H*,5*H*)-dione (VIIIa). To a dispersion of 2.23 g (6 mmol) of carbamide **VIIa** in anhydrous dioxane was added 6 ml of 1 M solution of MeONa in

methanol. The reaction mixture was heated at stirring for 5 h, poured into 100 ml of distilled water, and acidified with hydrochloric acid to a weak acid reaction. The precipitate was filtered off, washed with distilled water, and recrystallized from DMF. Yield 1.94 g (95%), mp 345–346°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.82 s (3H, OCH_3), 6.77 d (1H$_{arom}$, *J* 7 Hz), 6.82 s (1H$_{arom}$), 7.37 d (2H$_{arom}$, *J* 8 Hz), 7.56 d (2H$_{arom}$, *J* 8 Hz), 7.83 d (1H$_{arom}$, *J* 7 Hz), 11.68 s (1H, NH), 12.01 s (1H, NH$_{indole}$). Found, %: C 59.68; H 3.54; N 12.37. $C_{17}H_{12}ClN_3O_3$. Calculated, %: C 59.75; H 3.54; N 12.30.

Likewise were obtained compounds **VIIIb, Xa**, and **Xb**.

9-Methoxy-3-(4-chlorophenyl)-1*H*-pyrimido[5,4-*b*]-indole-2,4(3*H*,5*H*)-dione (VIIIb). Yield 1.70 g (83%), mp 340–341°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.89 s (3H, OCH_3), 6.53 d (1H$_{arom}$, *J* 7 Hz), 6.96 d (1H$_{arom}$, *J* 7 Hz), 7.27 t (1H$_{arom}$, *J* 7 Hz), 7.37 d (2H$_{arom}$, *J* 8 Hz), 7.55 d (2H$_{arom}$, *J* 8 Hz), 11.09 s (1H, NH), 11.82 s (1H, NH$_{indole}$). Found, %: C 57.78; H 4.25; N 11.36. $C_{17}H_{12}ClN_3O_3$. Calculated, %: C 57.84; H 4.31; N 11.24.

7-Methoxy-2-thioxo-3-(2-chlorophenyl)-2,3-dihydro-1*H*-pyrimido[5,4-*b*]indol-4(5*H*)-one (Xa). Yield 1.70 g (79%), mp 332–333°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.81 s (3H, OCH_3), 6.84–6.90 m (2H$_{arom}$), 7.44–7.50 m (3H$_{arom}$), 7.61 d (1H$_{arom}$, *J* 7 Hz), 8.10 d (1H$_{arom}$, *J* 7 Hz), 12.08 s (1H, NH$_{indole}$), 13.74 s (1H, NH). Found, %: C 56.98; H 3.33; N 11.82. $C_{17}H_{12}ClN_3O_2S$. Calculated, %: C 57.06; H 3.38; N 11.74.

9-Methoxy-2-thioxo-3-phenyl-2,3-dihydro-1*H*-pyrimido[5,4-*b*]indol-4(5*H*)-one (Xb). Yield 1.66 g (78%), mp 337–338°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.98 s (3H, OCH_3), 6.65 d (1H$_{arom}$, *J* 7 Hz), 7.01–7.09 m (2H$_{arom}$), 7.12–7.21 m (3H$_{arom}$), 7.39 t (1H$_{arom}$, *J* 7 Hz), 7.48 d (1H$_{arom}$, *J* 7 Hz), 11.59 br.s (1H, NH), 12.08 s (1H, NH$_{indole}$). Found, %: C 63.18; H 4.11; N 13.06. $C_{17}H_{13}N_3O_2S$. Calculated, %: C 63.14; H 4.05; N 12.99.

1,5-Dimethyl-7-methoxy-3-(4-chlorophenyl)-1*H*-pyrimido[5,4-*b*]indole-2,4(3*H*,5*H*)-dione (XIa). In a mixture of 3 ml of 1 M solution of MeONa in methanol and 3 ml of DMF was dissolved 0.52 g (1.5 mmol) of compound **VIIIa**. The solution was evaporated on a rotary evaporator, the residue was dissolved in anhydrous DMF, 0.38 ml (6 mmol) of methyl iodide was added, the mixture was heated at 100°C for 10 min and on cooling it was poured into 50 ml of distilled water. The precipitate was filtered off and recrystallized from DMF. Yield 0.39 g (69%), mp 289–290°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.79 s (3H, OCH_3), 3.90 s (3H, NCH_3), 3.99 s (3H, NCH_3), 6.83 d (1H$_{arom}$, *J* 7 Hz), 7.02 s (1H$_{arom}$), 7.32 d (2H$_{arom}$, *J* 8 Hz), 7.51 d (2H$_{arom}$, *J* 8 Hz), 7.98 d (1H$_{arom}$, *J* 7 Hz). Found, %: C 61.67; H 4.42; N 11.32. $C_{19}H_{16}ClN_3O_3$. Calculated, %: C 61.71; H 4.36; N 11.36.

9-Methoxy-3-(4-chlorophenyl)-1,5-diethyl-1*H*-pyrimido[5,4-*b*]indole-2,4(3*H*,5*H*)-dione (XIb) was obtained with the use of ethyl bromide. Yield 0.42 g (71%), mp 236–237°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.20 t (3H, CH_2CH_3, *J* 8 Hz), 1.29 t (3H, CH_2CH_3, *J* 8 Hz), 3.90 s (3H, OCH_3), 4.50 q (2H, CH_2CH_3, *J* 7 Hz), 4.61 q (2H, CH_2CH_3, *J* 7 Hz), 6.75 d (1H$_{arom}$, *J* 7 Hz), 7.23 d (1H$_{arom}$, *J* 7 Hz), 7.38 d (2H$_{arom}$, *J* 8 Hz), 7.42 t (1H$_{arom}$, *J* 7 Hz), 7.53 d (2H$_{arom}$, *J* 8 Hz). Found, %: C 63.37; H 4.99; N 10.56. $C_{21}H_{20}ClN_3O_3$. Calculated, % C 63.40; H 5.07; N 10.56.

2-(Methylthio)-7-methoxy-3-(2-chlorophenyl)-3*H*-pyrimido[5,4-*b*]indol-4(5*H*)-one (XIIa). In a mixture of 1.5 ml of 1 M solution of MeONa in methanol and 1 ml of DMF was dissolved 0.54 g (1.5 mmol) of compound **Xa**. The solution was evaporated on a rotary evaporator, the residue was dissolved in anhydrous DMF, 0.19 ml (3 mmol) of methyl iodide was added, the mixture was heated at 100°C for 10 min and on cooling it was poured into 30 ml of distilled water. The precipitate was filtered off and recrystallized from DMF. Yield 0.34 g (61%), mp 267–269°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.58 s (3H, SCH_3), 3.80 s (3H, OCH_3), 6.90 d (1H$_{arom}$, *J* 7 Hz), 6.94 s (1H$_{arom}$), 7.53–7.64 m (3H$_{arom}$), 7.72 d (1H$_{arom}$, *J* 7 Hz), 7.90 d (1H$_{arom}$, *J* 7 Hz), 11.91 s (1H, NH$_{indole}$). Found, %: C 58.12; H 3.86; N 11.25. $C_{18}H_{14}ClN_3O_2S$. Calculated, %: C 58.14; H 3.79; N 11.30.

9-Methoxy-3-phenyl-2-(ethylthio)-3*H*-pyrimido-[5,4-*b*]indol-4(5*H*)-one (XIIb) was obtained with the use of ethyl bromide. Yield 0.28 g (52%), mp 214–216°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.26 t (3H, CH_2CH_3, *J* 8 Hz), 3.92 s (3H, OCH_3), 4.54 q (2H, CH_2CH_3, *J* 8 Hz), 6.71 d (1H$_{arom}$, *J* 7 Hz), 7.08–7.13 m (2H$_{arom}$), 7.19–7.26 m (3H$_{arom}$), 7.38 t (1H$_{arom}$, *J* 7 Hz), 7.48 d (1H$_{arom}$, *J* 7 Hz), 12.12 C (1H, NH$_{indole}$). Found, %: C 64.87; H 4.87; N 12.01. $C_{19}H_{17}N_3O_2S$. Calculated, %: C 64.94; H 4.88; N 11.96.

***N*-(9-Methoxy-4-oxo-4,5-dihydro-3*H*-pyrimido-[5,4-*b*]indol-2-yl)benzamide (XVb).** A mixture of 0.36 g (1.64 mmol) of ester **Ib** and 0.24 g (1.64 mmol) of benzoylcyanamide (**XIIIa**) was heated in anhydrous dioxane at 70°C for 2 h, the separated precipitate was

filtered off and recrystallized from DMF. Yield 0.35 g (64%), mp 308–309°C. ^{1}H NMR spectrum (DMSO-d_6–CCl_4), δ, ppm: 3.95 s (3H, OCH_3), 6.58 d ($1H_{arom}$, *J* 7 Hz), 7.09 d ($1H_{arom}$, *J* 7 Hz), 7.29 t ($1H_{arom}$, *J* 7 Hz), 7.53 m ($2H_{arom}$), 7.59 t ($1H_{arom}$, *J* 8 Hz), 8.12 d ($2H_{arom}$, *J* 8 Hz), 11.76 br.s (1H, NH), 11.98 s (1H, NH_{indole}), 12.60 br.s (1H, NH). Found, %: C 64.78; H 4.25; N 16.76. $C_{18}H_{14}N_4O_3$. Calculated, %: C 64.67; H 4.22; N 16.76.

***N*-(7-Methoxy-4-oxo-4,5-dihydro-3*H*-pyrimido-[5,4-*b*]indol-2-yl)benzamide (XVa).** Yield 0.29 g (52%), mp 311–312°C. ^{1}H NMR spectrum (DMSO-d_6–CCl_4), δ, ppm: 3.88 s (3H, OCH_3), 6.77 d ($1H_{arom}$, *J* 7 Hz), 6.90 s ($1H_{arom}$), 7.51 t ($2H_{arom}$, *J* 7 Hz), 7.62 t ($1H_{arom}$, *J* 7 Hz), 7.88 d ($1H_{arom}$, *J* 8 Hz), 8.13 d ($2H_{arom}$, *J* 8 Hz), 11.81 s (1H, NH), 11.86 s (1H, $NH_{indole.}$), 12.52 br.s (1H, NH). Found, %: C 64.65; H 4.30; N 16.64. $C_{18}H_{14}N_4O_3$. Calculated, %: C 64.67; H 4.22; N 16.76.

2-[(4,6-Dimethylpyrimidin-2-yl)amino]-9-methoxy-3*H*-pyrimido[5,4-*b*]indol-4(5*H*)-one (XVc). To a mixture of 0.41 g (1.86 mmol) of carboxylate **Ia** and 0.28 g (1.86 mmol) of *N*-(4,6-dimethylpyrimidin-2-yl)cyanamide (**XIIIb**) in dioxane was added 0.17 ml (1.90 mmol) of concn. HCl, and the mixture was boiled for 1 h. On cooling the reaction mixture was poured into 100 ml of dilute ammonia solution. The precipitate was filtered off, washed with distilled water, and recrystallized from DMF. Yield 0.36 g (58%), mp 335–337°C. ^{1}H NMR spectrum (DMSO-d_6–CCl_4), δ, ppm: 3.98 s (3H, OCH_3), 6.56 d ($1H_{arom}$, *J* 7 Hz), 6.81 s ($1H_{arom}$), 7.08 d ($1H_{arom}$, *J* 7 Hz), 7.37 t ($1H_{arom}$, *J* 8 Hz), 10.41 br.s (1H, NH), 11.72 s (1H, $NH_{indole.}$), 13.60 br.s (1H, NH). Found, %: C 60.65; H 4.84; N 25.08. $C_{17}H_{16}N_6O_2$. Calculated, %: C 60.71; H 4.79; N 24.99.

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