DRUG SYNTHESIS METHODS AND MANUFACTURING TECHNOLOGY

NEW APPROACH TO THE SYNTHESIS OF FUNCTIONALLY-SUBSTITUTED PYRIDO[2,3-*b*]INDOLES (α-CARBOLINES)

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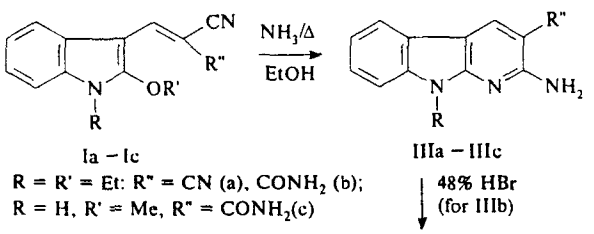
Pyrido[2,3-*b*]indoles (α-carbolines) constitute a rather insufficiently studied class of carboline derivatives, and only a few works were reported on the synthesis of α-carbolines having functional groups in positions 2 and 3 of the tricycle [1 – 7]. At the same time, compounds of this series exhibited antiviral, antitumor, and psychotropic activity [2, 3, 7].

The purpose of this work was to develop a general approach to the synthesis of functionally-substituted α-carbolines. Recently we have reported on the method for obtaining 2-alkoxy-3-[β-cyano-β-alkoxycarbonyl-(β-carbamoyl-, or β,β-dicyano)vinyl]indole derivatives, based on the condensation of hydroxyindole derivatives with amide acetals, with the subsequent O-alkylation of 3-(dimethylaminomethyl)hydroxyindoles with dimethyl sulfate or triethyloxonium fluoroborate, followed by the interaction with cyanoacetic acid derivatives [8].

Attempts to perform cyclization of the 2-alkoxy-3-vinylindole derivatives (e.g., for compound Ib) were unsuccessful: the process in acetic acid yielded the initial compound, while boiling in acetic anhydride led to the N-acylation product II.

The best results for compounds Ia – Ic were obtained by heating in ammonia-saturated ethanol at elevated pressures:



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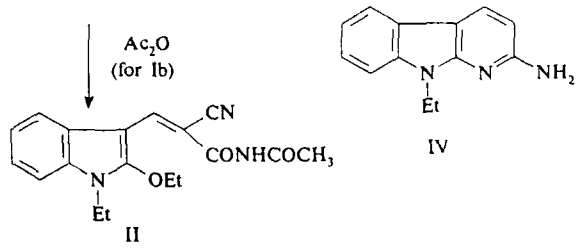
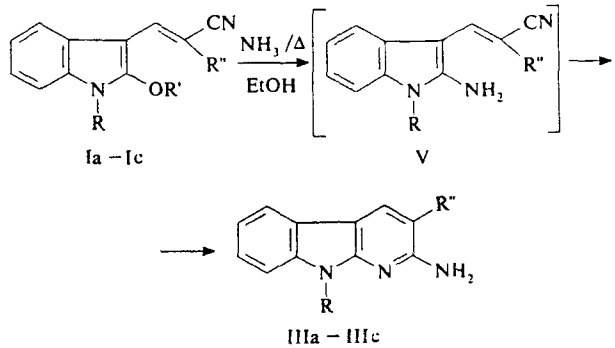


a: R = R' = Et, R" = CN;
b: R = R' = Et, R" = $CONH_2$;
c: R = H, R' = Me, R" = $CONH_2$

This treatment led to the formation of 2-amino-α-carbolines IIIa – IIIc whose structures were confirmed by the results of elemental analyses and the data of IR, NMR, and mass-spectroscopic measurements.

The formation of α-carboline derivatives apparently proceeds via the stage of amino group substitution for the 2-alkoxy group, followed by the cyclization of compound V with participation of the nitrile group. The fact that the 2-alkoxy groups are readily replaced by the amino groups was also confirmed by the formation of compound IX from 1-ethyl-2-ethoxy-3-(β-cyano-β-ethoxycarbonylvinyl)indole (VI).



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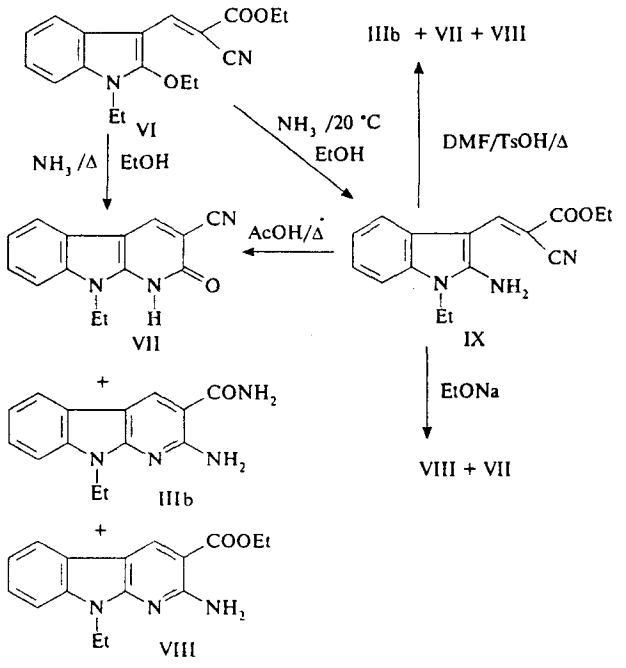
Hydrolysis of the carbamoyl group in compound IIIb, followed by decarboxylation on boiling in 48% aqueous HBr, leads smoothly to hydrobromide IV.

However, the results of cyclization are not as unambiguous in the case of compound VI. Indeed, conducting the process under the same conditions as above (heating of an alcohol ammonium solution in an autoclave) yields α-carbolin-2-one (VII) as the main product, while 2-amino-α-carbolines IIIb and VIII are only the minor products.

Chromatographic analysis of the mother liquor using Silufol UV-254 plates eluted in the heptane – ethyl acetate system showed the presence of 2-aminocarboline IIIb in addition to compound VII ($R_{f\,VII}$, 0.62; $R_{f\,IIIb}$, 0.396). The ethoxycarbonyl derivative VIII can be detected by mass spectrometric analysis of the mixture of products isolated from the mother liquor. The mass spectrum displays, besides the peaks of molecular ions with m/z = 237 (M_1^+) and 254 (M_2^+), an additional peak of the molecular ion with m/z = 283 (M_3^+). The latter peak was attributed to compound VIII, which was conformed by direct synthesis of the individual compound and the comparative analysis of the mass spectra.



Thus, cyclization of the ethoxy derivative VI to α-carboline can proceed via two pathways involving both the ethoxycarbonyl and the nitrile group.

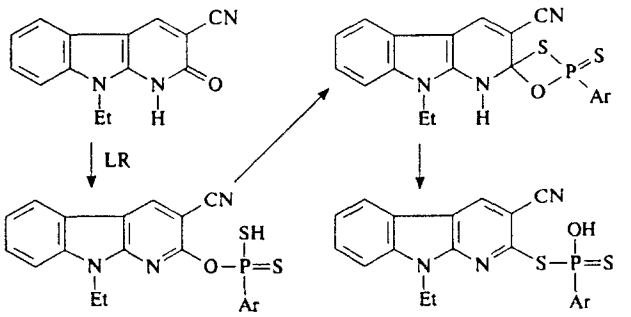
Because 2-aminocarbolines can be smoothly obtained in good yield proceeding from compounds Ia – Ic, it is important to develop a sufficiently simple method for the synthesis of carbolin-2-ones.

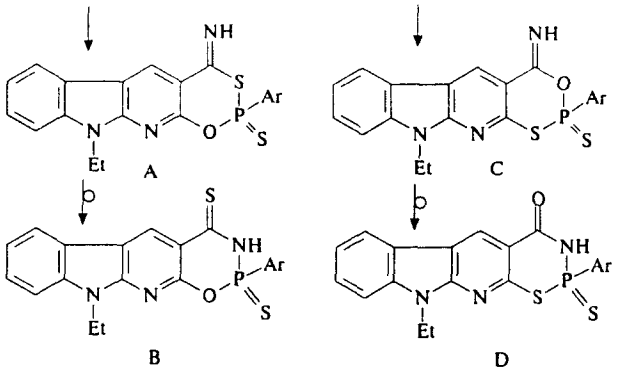
In this connection, we have studied the cyclization of 2-amino-3-vinylindole IX, obtained by treating compound VI with ammonia-saturated ethanol at room temperature. It was found that prolonged boiling of compound IX in glacial acetic acid leads smoothly to a high yield (above 70%) of carbolin-2-one VII. Boiling of compound IX in DMF in the presence of a catalytic amount of TsOH led to the formation of 2-amino-3-ethoxycarbonyl-9-ethyl-α-carboline VIII, whose structure was confirmed by the data of elemental analysis and IR spectroscopy. The IR spectrum contained no absorption band of the CN groups and had a band at 1680 cm^{-1} characteristic of an ester carbonyl group in an aromatic ring. It should be noted that the reaction under these conditions also yields an insignificant amounts of carbolines IIIb and VII, as indicated by the TLC chromatograms of the mother liquor on Silufol UV-254 plates eluted by the heptane – ethyl acetate system ($R_{f\,VIII}$, 0.808).

Cyclization of compound IX under the action of sodium ethylate also leads to a mixture of products VII and VIII (TLC data). The thermal cyclization of compound Ib by heating in diphenyl yields a mixture containing α-carbolines IIIb, VII and a dinitrile derivative Ia (mass-spectroscopic data).

In the course of study of the properties of 3-cyano-9-ethyl-α-carbolin-2(1H)-one VII, we have attempted to obtain a thiocarbonyl analog of this compound. On boiling compound VII in toluene in the presence of phosphorus pentasulfide, we obtained a mixture of products whose mass spectrum contained a peak of the molecular ion M^+ with m/z = 253, which can be assigned to α-carboline-2(1H)-thione X, but we failed to isolate this compound in the individual form.

Taking into account that the Lawesson reagent (LR) 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide is one of the best agents ensuring the conversion of carbonyl into thiocarbonyl group (the reaction is also known to take place in the series of heterocyclic compounds, e.g., when obtaining pyridine-2(1H)-thione from 2(1H)-pyridone [9, 10], we attempted to use LR for the synthesis of α-carboline-2(1H)-thione X. However, the interaction of VII with LR did not lead to thione X: instead, we observed the closure of the 1,3,2-oxaazaphosphorin ring and the formation of a tetracyclic compound XI (see also [11]). To our knowledge, no examples of the interaction of LR with 3-cyano-2(1H)-pyridones have been reported so far. Proceeding from the commonly accepted notions about the mechanism of thionation with the participation of LR [9] and about the interaction of LR with α-cyanoketones [9, 12], we suggest the following pathways of the process:



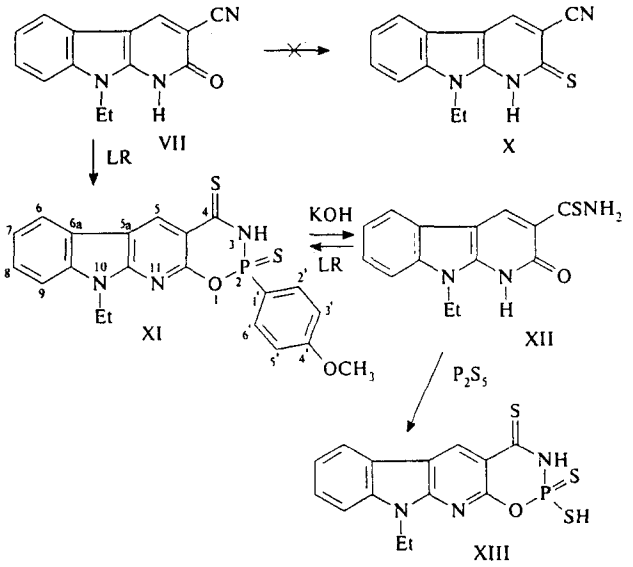


Thus, the reaction of LR with VII may lead to isomeric compounds of four types (A – D).

The structure of compound XI was confirmed by the predicted chemical transformations and spectroscopic data. Treatment of compound XI with an aqueous KOH solution leads to a 93% yield of thioamide XII.

Unambiguous evidence for the validity of the proposed structure of compound XI was obtained from the ^1H and ^{13}C NMR spectra. The ^1H NMR spectrum in DMSO-d_6 contained the following signals (δ, ppm): 1.35 (t, 3H, $NCH_2\underline{CH_3}$), 4.43 (q, 2H, $N\underline{CH_2}CH_3$), 3.86 (s, 3H, OCH_3), 7.37 (t, 1H), 7.58 (t, 1H), 7.73 (d, 1H), and 8.32 (d, 1H) (arom. 6,7,8,9-CH), 7.97 (q, 2H, 2′, 6′-CH, $^3J_{H^{2'6'},P}$ 15.1 Hz), 7.19 (q, 2H, 3′5′-CH, $^4J_{H^{3'5'},P}$ 3.5 Hz), 9.54 (s, 1H, 5-CH), 12.35 (bd, 3-NH, $^2J_{NH,P}$ 15 Hz). On the basis of these data, we may exclude compounds A and C from consideration, because these structures do not feature the interaction between NH protons and phosphorus atoms with spin – spin coupling constant $^2J_{NH,P}$ = 15 Hz. The choice between structures B and D can be based on analysis of the ^{13}C NMR data. It is expected that the ^{13}C NMR spectrum of compound D must contain a signal due to CO carbons in the region of 150 – 170 ppm, while the spectrum of structure B must contain a signal due to CS in the region of 180 – 200 ppm (both signals must be split as a result of interaction with phosphorus atoms). The ^{13}C NMR spectrum of compound XI in DMSO-d_6 showed the following signals (δ, ppm): 14.0 ($NCH_2\underline{CH_3}$), 36.8 ($N\underline{CH_2}CH_3$), 56.0 (OCH_3), 110.8 (9-C), 110.9 (5a-C), 114.6, 114.9 (7-C, 8-C), 114.8 (4a-C), 120.4 (6a-C), 122.0 (3′-C, 5′-C, $^3J_{C,P}$ 5.1 Hz), 122.1 (1′-C, $^1J_{C,P}$ 154.6 Hz), 127.8 (6-C), 134.4 (2′-C, 6′-C, $^2J_{C,P}$ 15.6 Hz), 135.2 (5-C), 139.8 (9a-C), 151.9 (10a-C), 152.0 (4′-C), 164.0 (11a-C, $^2J_{C,P}$ 4.3 Hz), 193.7 (C=S, $^2J_{C,P}$ 5.2 Hz). Therefore, the product of interaction of α-carbolin-2(1H)-one with LR has a structure of the B type, which also helps explain the splitting of this compound to thioamide XII observed in an alkaline medium.

It must be noted that heating of compound XII in the presence of phosphorus pentasulfide resulted in a quantitative yield of 2-mercapto-10-ethyl-2,3,4,10-tetrahydro-1,3,2-oxaazaphosphorino [5′,6′ : 5,6]pyrido-[2,3-*b*]indole-2,4-dithione XIII.

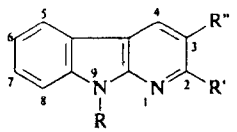


Thus, we have developed a general method for the synthesis of 2- and 2,3-functionally-substituted α-carbolines from hydroxyindole derivatives. Using this approach, we have successfully synthesized representatives (XI and XIII) of a new heterotetracyclic system, 1,3,2-oxaazaphosphorino[5′,6′ : 5,6]pyrido[2,3-*b*]indoles (1,3,2-oxaazaphosphorino[6,5-*b*]-α-carbolines).

TABLE 1. Yields and Characteristics of Synthesized Compounds

Compound	M.p., °C	Solvent for crystallization	Empirical formula	Yield, %
II	138 – 140	2-Propanol	$C_{18}H_{19}N_3O_3$	44
IIIa	201 – 202	Acetonitrile	$C_{14}H_{12}N_4$	100
IIIb	273 – 276	Acetonitrile 2-Propanol	$C_{14}H_{14}N_4O$	78
IIIc · HCl · 0.5H_2O	275 – 279	Methanol	$C_{12}H_{11}N_4OCl \cdot 0.5H_2O$	58
IV	145 – 148.5	Ethanol – water (1 : 1)	$C_{13}H_{13}N_3$	100 (from IV · HBr)
IV · HBr	302 – 306	Methanol	$C_{13}H_{14}N_3Br$	97
VII	307 – 309	Acetonitrile	$C_{14}H_{11}N_3O$	42 (method A) 71 (Method B)
VIII	176 – 178	Acetonitrile	$C_{16}H_{17}N_3O_2$	55 (method A)
IX	167 – 170	Ethanol	$C_{16}H_{17}N_3O_2$	85
XI	233 – 236	Acetonitrile	$C_{21}H_{18}N_3O_2PS_2$	75 (method A) 50 (Method B)
XII · 0.25 DMF	285	DMF	$C_{14}H_{13}N_3OS$	93
XIII	234 – 238	—	$C_{14}H_{12}N_3OPS_3$	100

TABLE 2. ^{1}H NMR Spectra of Compounds IIIa – IIIc, VII, and VIII:



Compound (solvent)	Chemical shift, δ, ppm									
	R		R′			5,6,7,8-CH	4-CH	R″		
	$\underline{CH_2}$–CH_3	CH_2–$\underline{CH_3}$	H	R′ = NH_2	R′ = OH			$CONH_2$	COOEt	H
IIIa (DMF-d_7)	4.39 (q, 2H)	1.37 (t, 3H)	—	6.94 (bs, 2H)	—	7.27 (t, 1H) 7.41 (t, 1H) 7.57 (d, 1H) 8.04 (d, 1H)	8.62 (s, 1H)	—	—	—
IIIb (DMF-d_7)	4.38 (q, 2H)	1.36 (t, 3H)	—	*	—	7.20 (t, 1H) 7.35 (t, 1H) 7.53 (d, 1H) 7.84 (d, 1H)	8.89 (s, 1H)	7.69 (bs, 2H)	—	—
IIIc (DMF-d_7)	—	—	13.04 (bs, 1H)	**	—	7.31 (t, 1H) 7.43 (t, 1H) 7.62 (d, 1H) 7.95 (d, 1H)	9.37 (s, 1H)	**	—	—
IV (DMSO-d_6)	4.32 (q, 2H)	1.28 (t, 3H)	—	6.19 (bs, 2H)	—	7.10 (t, 1H) 7.24 (t, 1H) 7.44 (d, 1H) 7.83 (d, 1H)	8.04 (d, 1H) ^3J 8.3 Hz	—	—	6.33 (d, 1H)
VII (DMF-d_7)	4.46(q, 2H)	1.41 (t, 3H)	—	—	***	7.31 (t, 1H) 7.49 (t, 1H) 7.68 (d, 1H) 8.14 (d, 1H)	8.85 (s, 1H)	—	—	—
VIII (DMSO-d_6)	4.33 (q, 2H)	1.31 (t, 3H)	—	7.25 (bs, 2H)	—	7.18 (t, 1H) 7.35 (t, 1H) 7.50 (d, 1H) 8.00 (d, 1H)	8.77 (s, 1H)	—	1.36 (t, 3H, $\underline{CH_3}CH_2O$), 4.32 (q, 2H, $CH_3\underline{CH_2}O$)	—

* The signal of NH_2 protons, centered at 7.50 ppm, is strongly broadened as a result of exchange interactions.
** Protons of the $CONH_2$ and NH_2 groups give a common broadened signal at 8.40 ppm.
*** Protons of the NH groups of the pyridine cycle, involved in strong exchange interactions, form a strongly broadened signal superimposed on the signal of water protons in the solvent at 3.50 ppm.

EXPERIMENTAL CHEMICAL PART

The ^{1}H and ^{13}H NMR spectra were recorded on the Varian XL-200 and Unity + 400 spectrometers using TMS as the internal standard. The mass spectra were obtained on a Varian MAT-112 spectrometer operating at an ionizing electron energy of 50 eV and ionization chamber temperature of 140°C. The melting temperatures were determined using a Boethius heating stage. The IR absorption spectra were measured on a Perkin-Elmer Model 457 spectrophotometer using samples prepared as nujol mulls. The data of elemental analyses agreed with the results of analytical calculations.

N-Acetyl-β-(1-ethyl-2-ethoxyindol-3-yl)-α-cyanoacrylamide (II). A mixture of 0.5 g of compound Ib and 10 ml of AcO_2 was boiled for 1.5 h. Then the reaction mixture was evaporated in vacuum and the residue sequentially triturated with petroleum and diethyl ethers to give 0.25 g of compound II; mass spectrum (*m*/*z*): M^+ 325; IR spectrum (ν_{max}, cm^{-1}): 3290 (NH), 2200 (CN), 1715, 1690 (CO).

2-Amino-3-cyano-9-ethyl-9H-pyrido[2,3-*b*]indole (IIIa). A mixture of 0.5 g (0.00189 mole) of compound Ia and 80 ml of an NH_3-saturated ethanol was treated in an autoclave at 115°C for 6 h. Then the reaction mixture was evaporated and the residue triturated with petroleum ether to give 0.45 g of compound IIIa; mass spectrum (*m*/*z*): M^+ 236; IR spectrum (ν_{max}, cm^{-1}): 3460, 3405, 3320, 3220 (NH_2), 2200 (CN).

2-Amino-3-aminocarbonyl-9-ethyl-9H-pyrido[2,3-*b*]-indole (IIIb). A mixture of 0.5 g (0.00177 mole) of compound Ib and 80 ml of an NH_3-saturated ethanol was treated in an autoclave at 120°C for 6 h. Then the reaction mixture was evaporated and the residue triturated with diethyl ether to give 0.35 g of compound IIIb; mass spectrum (*m*/*z*): M^+ 254;

IR spectrum (ν_{max}, cm^{-1}): 3420, 3300, 3200 (NH_2), 1620 (CO).

2-Amino-3-aminocarbonyl-9H-pyrido[2,3-*b*]indole (IIIc). A mixture of 0.54 g (0.00225 mole) of compound Ic and 80 ml of an NH_3-saturated ethanol was treated in an autoclave at 120°C for 6 h. Then the reaction mixture was evaporated and the residue sequentially triturated with diethyl ether and ethyl acetate and filtered. The ethyl acetate filtrate was acidified with an ethanol HCl solution to give 0.35 g of compound IIIc · HCl · $0.5H_2O$; mass spectrum (*m/z*): M^+ 226; IR spectrum (ν_{max}, cm^{-1}): 3330, 3160 (NH, NH_2), 1670 (CO).

2-Amino-9-ethyl-9H-pyrido[2,3-*b*]indole (IV). A mixture of 1.8 g (0.0071 mole) of compound IIIb and 50 ml of an aqueous HBr was stirred at 120°C for 6.5 h. Then the reaction mixture was cooled and the precipitate was filtered to give 2 g of compound IV · HBr.

Compound IV · HBr (0.4 g) was dissolved in 25 ml of hot water and alkalized with 2 N NaOH. The reaction mass was cooled and the precipitate was filtered to give 0.29 g of compound IV; mass spectrum (*m/z*): M^+ 211.

Ethyl ester of β-(1-ethyl-aminoindol-3-yl)-α-cyanoacrylic acid (IX). A mixture of 1.5 g of compound VI and 30 ml of an NH_3-saturated ethanol was stirred at room temperature for 3.5 h. Then the reaction mixture was evaporated and the residue triturated with heptane to give 1.15 g of compound IX; IR spectrum (ν_{max}, cm^{-1}): 3360, 3250 (NH_2), 2220 (CN), 1670 (CO).

3-Cyano-9-ethyl-2,9-dihydro-1H-pyrido[2,3-*b*]indol-2-one (VII). Method A. A mixture of 5 g (0.016 mole) of compound VI and 100 ml of an ammonia-saturated ethanol was treated in an autoclave at 100°C for 4.5 h. Then the reaction mixture was cooled and the precipitate was filtered to give 1.6 g of compound VII. The mother liquor was evaporated and the residue triturated with hexane to give 1.45 g of a mixture of compounds VII, IIIb, and VIII; mass spectrum (*m/z*): M_1^+ 237, M_2^+ 254, M_3^+ 283.

Method B. A mixture of 1 g (0.00353 mole) of compound IX and 30 ml of glacial acetic acid was boiled for 10.5 h. Then the reaction mixture was cooled and the precipitate was filtered to give 0.4 g of compound VII. The mother liquor was evaporated and the residue triturated with 2-propanol to give additionally 0.2 g of compound VII; mass spectrum (*m/z*): M^+ 237.

2-Amino-3-ethoxycarbonyl-9-ethyl-9H-pyrido[2,3-*b*]-indole (VIII). Method A. A mixture of 1 g (0.00353 mole) of compound IX, 20 ml of DMF, and a catalytic amount of TsOH was boiled for 6 h. Then the reaction mass was evaporated and the residue triturated with 2-propanol to give 0.55 g of compound VIII; mass spectrum (*m/z*): M^+ 283; IR spectrum (ν_{max}, cm^{-1}): 3460, 3350 (NH_2), 1680 (CO).

The propanol extract contains a mixture of compounds IIIb, VII, and VIII (as indicated by TLC on silufol UV-254 in the ethyl acetate – herptane system).

Method B. A mixture of 0.35 g (0.012 mole) of compound IX and 15 ml of an ethanol solution of sodium ethylate (giveed from 0.012 g Na) was stirred for 5 min at room temperature and then for 30 min at 0 – 5°C. The precipitate was filtered to give 0.55 g of a mixture of compounds VIII and VII (TLC in the ethyl acetate – heptane system). The filtrate was evaporated and the filtrate triturated with water to give 0.03 g of compound VIII.

Thermal cyclization of compound Ib. A mixture of 0.5 g of compound Ib and 5 ml of diphenyl was heated for 30 min at 250°C. Then the reaction mixture was washed with petroleum ether. The residue was separated by filtration to give 0.3 g of a mixture of compounds IIIb, VII, and Ia; mass spectrum (*m/z*): M_1^+ 254, M_2^+ 237, M_3^+ 265.

2-(4-Methoxyphenyl)-10-ethyl-2,3,4,10-tetrahydro-1,3,2-oxaazaphosphorino[5',6' : 5,6]pyrido-[2,3-*b*]indole-2,4-dithione (XI). Method A. A mixture of 1.18 g (5 mmole) of compound VII, 2.52 g (5 mmole) of 80% RL, and 40 ml of dry xylene was stirred for 2 h at 130°C. The reaction mass was filtered hot and the mother solution was cooled and precipitate filtered to give 1.65 g of compound XI; mass spectrum (*m/z*): M^+ 439.

Method B. A mixture of 0.68 g (2.5 mmole) of compound XII, 1.26 g (2.5 mmole) of 80% RL, and 20 ml of dry xylene was stirred for 3 h at 130°C. The reaction mass was filtered hot to give 0.15 g of unreacted compound XII. The filtrate was cooled and the precipitate filtered to give 0.55 g of compound XI.

3-Aminothiocarbonyl-9-ethyl-2,9-dihydro-1H-pyrido-[2,3-*b*]indol-2-one (XII). A mixture of 2.12 g (2.27 mmole) of compound XI and 127 ml of a 5% aqueous KOH was stirred until complete dissolution of the deposit. The solution was filtered and acidified by concentrated HCl to pH~3.5. The precipitate was filtered to give 1.22 g of compound XII; mass spectrum (*m/z*): M^+ 271; ^1H NMR spectrum, DMSO-d_6 (δ, ppm): 1.30 (t, 3H, $NCH_2\underline{CH_3}$), 4.43 (q, 2H, $N\underline{CH_2}CH_3$), 7.20 – 7.40 (m, 2H), 7.60 (d, 1H), 7.99 (d, 1H), (arom. protons), 9.59 (s, 1H, 4-CH), 9.68 (w.spl, s. 1H, NH), 11.10 (b, 1H, NH), 13.27 (b, 1H, 1-NH).

2-Mercapto-10-ethyl-2,3,4,10-tetrahydro-1,3,2-oxaazaphosphorino [5',6' : 5,6]pyrido[2,3-*b*]indole-2,4-dithione (XIII). A mixture of 0.42 g (1.5 mmole) of compound XII, 0.336 g (1.5 mmole), P_2S_5, and 15 ml of toluene was boiled for 5 h. Then the reaction mixture was cooled and the precipitate was filtered to give 0.56 g of compound XIII; mass spectrum (*m/z*): M^+ 365; ^1H NMR spectrum, DMSO-d_6 (δ, ppm): 1.36 (t, 3H, $NCH_2\underline{CH_3}$), 4.46 (q, 2H, $N\underline{CH_2}CH_3$), 7.32 (t, 1H), 7.53 (t, 1H), 7.69(d, 1H), 8.24 (d, 1H) (arom. protons), 9.40 (s, 1H, 5-CH), 11.39 (bd, 3-NH, $^2J_{NH,P}$ 16 Hz); the signal of SH proton is masked by the signal of water contained in the solvent (δ, 6.30 ppm).

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REFERENCES

1. R. A. Abramovich and D. Spenser, *Advances in Heterocyclic Chemistry*, Vol. 3, Acad. Press, New York (1964).
2. A. A. Semenov and V. V. Tolstikhina, *Khim. Geterotsikl. Soedin.*, No. 4, 435 – 447 (1984).
3. Fr. Patent No. 2003999 (1969); *Chem. Abstr.*, **72**, P111444d (1970).
4. L. Stephenson and W. K. Warburton, *J. Chem. Soc. C*, No. 10, 1355 – 1364 (1970).
5. P. Molina and P. Fresnefda, *Synthesis*, No. 11, 878 – 880 (1989).
6. S. Hibino, E. Sugino, T. Kuwada, et al., *Chem. Pharm. Bull.*, **39**(1), 79 – 80 (1991).
7. M. Thompson and I. T. Forbes, US Patent No. 4952584 (1990); *Chem. Abstr.*, **114**, P122347m (1991).
8. T. V. Golovko, N. P. Solov'eva, and V. G. Granik, *Khim.-Farm. Zh.*, **28**(5), 48 – 50 (1994).
9. M. P. Cavo and M. I. Levinson, *Tetrahedron*, **41**(22), 5061 – 5087 (1985).
10. R. A. Cherkasov, G. V. Kutyrev, and A. N. Pudovik, *Tetrahedron*, **41**(13), 2567 – 2624 (1985).
11. D. B. Nilov. A. V. Kadushkin, N. P. Solov'eva, et al., *Mendeleev Commun.*, No. 2, 67 (1995).
12. B. S. Petersen and S.-O. Lawesson, *Tetrahedron*, **35**(20), 2433 – 2437 (1979).